

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-K**

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2021

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Transition Period from to

Commission File Number: 001-38501

**SCHOLAR ROCK HOLDING CORPORATION**

(Exact name of Registrant as specified in its charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

82-3750435  
(I.R.S. Employer  
Identification Number)

301 Binney Street, 3<sup>rd</sup> Floor  
Cambridge, MA 02142  
(857) 259-3860

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	SRRK	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer   
Non-accelerated Filer

Accelerated Filer   
Smaller Reporting Company   
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act.) Yes  No

As of June 30, 2021, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately \$531.8 million based on the closing price of the registrant's common stock on June 30, 2021. The calculation excludes shares of the registrant's common stock held by current executive officers, directors and stockholders that the registrant has concluded are affiliates of the registrant. This determination of affiliate status is not a determination for other purposes.

As of March 2, 2022, there were 35,297,455 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement for its 2022 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (“Annual Report”), including the documents incorporated by reference, contains forward-looking statements within the meaning of the federal securities laws, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and are including this statement for purposes of complying with those safe harbor provisions. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. Some of the risks and uncertainties that may cause our actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements include, among others, the following:

- the success, cost and timing of clinical trials for apitegromab (SRK-015), including the progress and completion of clinical trials, and the results, and the timing of results, from these trials;
- the success, cost and timing of preclinical studies and clinical trials for SRK-181, including, but not limited to, the progress and completion of our DRAGON Phase 1 clinical trial for SRK-181, any preclinical studies and any future clinical trials for SRK-181, and the results, and the timing of results, from these trials;
- the success, cost and timing of our other product development activities, preclinical studies and clinical trials, and the results, and timing of results, from these studies and trials;
- our success in identifying and executing a development program for additional indications for apitegromab, SRK-181 and in identifying product candidates from our other programs;
- the clinical utility of our product candidates and their potential advantages over other therapeutic options;
- our ability to obtain, generally or on terms acceptable to us, funding for our operations, including funding necessary to complete further development and, upon successful development, if approved, commercialization of apitegromab, SRK-181 or any of our future product candidates;
- risks associated with the COVID-19 pandemic, which may adversely impact our workforce, global supply chain, business, preclinical studies, clinical trials and financial results;
- the potential for our identified research priorities to advance our proprietary platform, development programs or product candidates;
- the timing, scope, or likelihood of our ability to obtain and maintain regulatory approval from the U.S. Food and Drug Administration (“FDA”), the European Commission (“EC”) and other regulatory authorities for apitegromab, SRK-181 and any future product candidates, and any related restrictions, limitations or warnings in the label of any approved product candidate;
- our ability to continue to grow our organization, including our personnel, systems and relationships with third parties;
- our ability to retain our executives and highly skilled technical and managerial personnel, which could be affected due to any transition in management, or if we fail to recruit additional highly skilled personnel;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates and the duration of such protection;
- our ability and the potential to successfully manufacture our product candidates for clinical trials and for commercial use, if approved;

- our ability to establish or maintain collaborations or strategic relationships;
- our expectations relating to the potential of our proprietary platform technology;
- our ability to obtain additional funding when necessary;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets, either alone or in combination with others;
- our expectations related to the use of our cash reserves;
- the impact of new laws and regulations or amendments to existing laws and regulations;
- developments and projections relating to our competitors and our industry;
- our estimates and expectations regarding cash and expense levels, future revenue, capital requirements and needs for additional financing, including our expected use of proceeds from our public offerings, and liquidity sources;
- our expectations regarding the period during which we qualify as an emerging growth company (“EGC”) under the Jumpstart Our Business Startups Act; and
- other risks and uncertainties, including those listed under the caption Part I, Item 1A “Risk Factors”.

The risks set forth above are not exhaustive. Other sections of this report may include additional factors that could adversely affect our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for management to predict all risk factors, nor can we assess the impact of all risk factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Given these risks and uncertainties, investors should not place undue reliance on forward-looking statements as a prediction of actual results. Investors should also refer to our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for future periods and Current Reports on Form 8-K as we file them with the SEC, and to other materials we may furnish to the public from time to time through Current Reports on Form 8-K or otherwise, for a discussion of risks and uncertainties that may cause actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements. We expressly disclaim any responsibility to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events, or otherwise, and you should not rely upon these forward-looking statements after the date of this report.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Annual Report. Unless otherwise expressly stated, we obtained this industry data, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

## PART I

### Item 1. Business

#### Overview

We are a biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of serious diseases in which signaling by protein growth factors plays a fundamental role. Our novel understanding of the molecular mechanisms of growth factor activation enabled us to develop a proprietary platform for the discovery and development of monoclonal antibodies that locally and selectively target the precursor, or latent, forms of growth factors. By targeting the signaling proteins at the cellular level and acting in the disease microenvironment, we believe we may avoid the historical dose-limiting safety challenges associated with inhibiting growth factors for therapeutic effect. We believe our focus on biologically validated growth factors may facilitate a more efficient development path.

We have a productive scientific platform and are building our portfolio of novel product candidates with the aim of transforming the lives of patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer, and fibrosis. We have discovered and progressed the development of:

- Apitegromab, an inhibitor of the activation of latent myostatin, for the treatment of spinal muscular atrophy (“SMA”). We also believe apitegromab could have potential in the treatment of other myostatin-related disorders.
- SRK-181, an inhibitor of the activation of latent transforming growth factor beta-1 (“TGFβ1”), for the treatment of cancers that are resistant to anti-PD-(L)1 antibody therapies.
- Potent and selective inhibitors of the activation of transforming growth factor beta (“TGFβ”) for the treatment of fibrotic diseases. We are advancing multiple antibody profiles toward product candidate selection including antibodies that selectively inhibit the activation of latent TGFβ1 in the context of fibrotic extracellular matrix and that avoid perturbing TGFβ1 presented by cells of the immune system.
- Additional discovery and early preclinical programs related to the selective modulation of growth factor signaling including BMP6 and other growth factors.

Our first product candidate, apitegromab (formerly SRK-015), is a highly selective, fully human, monoclonal antibody, with a unique mechanism of action that results in inhibition of the activation of the growth factor, myostatin, in skeletal muscle. Apitegromab is being developed as a potential first muscle-directed therapy for the treatment of SMA. We are conducting SAPPHIRE, a pivotal Phase 3 trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA (which is estimated to represent the majority of the current prevalent SMA patient population in the U.S. and Europe). Apitegromab was evaluated in our TOPAZ Phase 2 proof-of-concept clinical trial for the treatment of patients with Type 2 and Type 3 SMA. Positive 12-month top-line results were announced in April 2021 showing apitegromab’s transformative potential (see “TOPAZ Phase 2 Trial Analysis” below). The FDA granted fast track designation, rare pediatric disease designation and orphan drug designation to apitegromab for the treatment of SMA in May 2021, August 2020 and March 2018, respectively. The European Medicines Agency (“EMA”) granted PRiority MEdicines (“PRIME”) designation in March 2021 and the EC granted orphan medicinal product designation in December 2018 to apitegromab for the treatment of SMA.

Our second product candidate, SRK-181, is being developed for the treatment of cancers that are resistant to checkpoint inhibitor therapies (“CPI therapies”), such as anti-PD-1 or anti-PD-L1 antibody therapies. SRK-181 is a highly selective inhibitor of the activation of latent TGFβ1 that is being investigated in our DRAGON Phase 1 proof-of-concept clinical trial in patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibodies. This two-part clinical trial consists of a dose escalation portion (Part A) and a dose expansion portion evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody therapy (Part B). Part B encompasses five cohorts, including urothelial carcinoma, cutaneous melanoma, non-small cell lung cancer, clear cell renal cell carcinoma

and other solid tumors and commenced in 2021. Initial clinical data from Part A were presented in November 2021 at the Society for Immunotherapy of Cancer (“SITC”) 36<sup>th</sup> Annual Meeting.

Beyond these programs, we continue to discover and develop highly specific monoclonal antibodies to selectively modulate growth factor signaling. Growth factors are naturally occurring proteins that typically act as signaling molecules between cells and play a fundamental role in regulating a variety of normal cellular processes, including cell growth and differentiation. Current therapeutic approaches to treating diseases in which growth factors play a fundamental role involve directly targeting the active form of the growth factor or its receptor systemically throughout the body. These approaches have suffered from a variety of shortcomings, including lack of pathway selectivity, lack of target selectivity, and non-localized target inhibition.

Our innovative approach is rooted in our structural biology insights into the mechanism by which certain growth factors are activated in close proximity to the cell surface. We integrate these insights with sophisticated protein expression, assay development and monoclonal antibody discovery capabilities. We believe our proprietary platform can address the challenges of treating diseases in which growth factors play a fundamental role by:

- targeting the natural activation mechanism to prevent activation of the growth factor rather than attempting to inhibit the growth factor after activation;
- achieving heightened specificity for the targeted growth factor while minimizing interactions with structurally similar and related growth factors, thereby potentially reducing the risk of unintended systemic adverse events; and
- targeting the disease microenvironment, where we believe we can interfere with the disease process while minimizing the effects on the normal physiological processes mediated by the same growth factors.

Our structural insights and unique antibody discovery capabilities can be applied to other protein classes beyond growth factors, with an aim of generating differentiated candidates targeting cell surface receptors such as immune cell receptors or G-protein coupled receptors, where selectivity remains challenging.

### **Our Approach and Proprietary Platform**

Our innovative approach is rooted in our novel understanding of the molecular mechanisms of growth factor activation and signaling and is designed to discover and develop monoclonal antibody product candidates that can inhibit the activation of a growth factor with an unprecedented degree of selectivity. Our proprietary platform is designed to generate product candidates that target the growth factor’s latent precursor form prior to its activation within the disease microenvironment, or tissue where it is localized, and would normally signal upon activation.

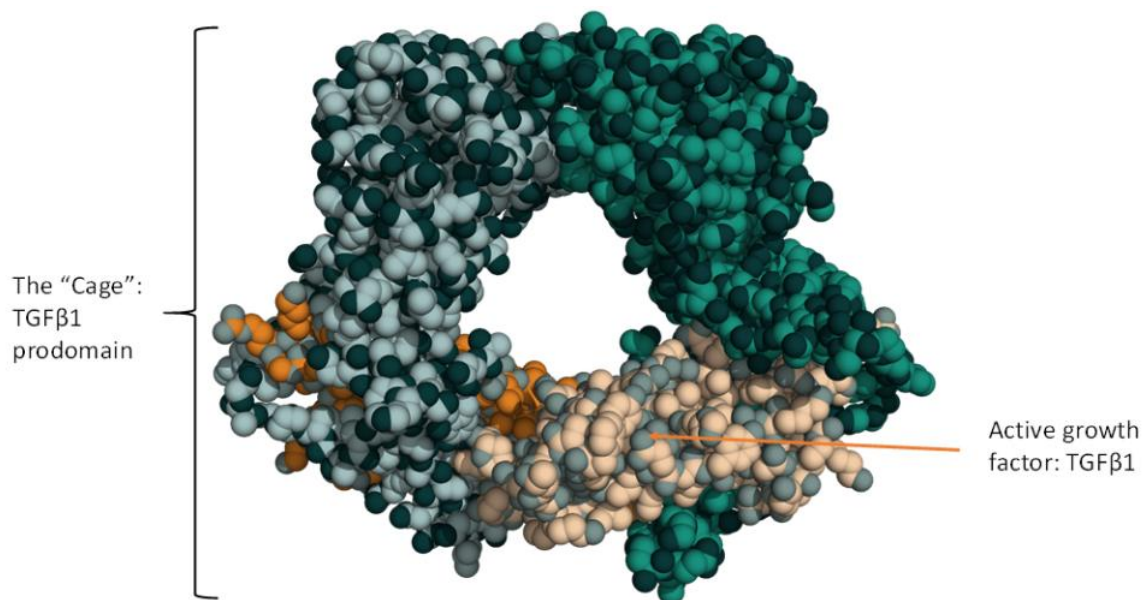
Growth factors are naturally occurring proteins that typically act as signaling molecules between cells and play a fundamental role in regulating a variety of normal cellular processes. Members of the TGF $\beta$  superfamily of growth factors, for example, can mediate diverse biological functions, including cell growth and differentiation, tissue homeostasis, immune modulation and extracellular matrix remodeling. Growth factors have also been shown to play a fundamental role in a variety of disease processes. Because of the importance of growth factors in multiple diseases, the pharmaceutical industry has made many attempts to inhibit growth factors in a variety of therapeutic settings. However, products utilizing conventional approaches have seen only limited success. Current therapeutic approaches to treating diseases in which growth factors play a fundamental role involve directly targeting an activated growth factor or its receptor systemically throughout the body and have suffered from a variety of shortcomings:

- Lack of pathway selectivity—multiple growth factors often signal through the same or overlapping sets of related receptors, making it difficult to specifically modulate one pathway over another;
- Lack of target selectivity—members of the same growth factor superfamily share considerable structural similarities, making it difficult to achieve specific inhibition of the targeted growth factor; this can result in broad systemic inhibition that can cause undesirable, and in many cases toxic, side effects; and

- Non-localized-target inhibition—systemic and non-selective inhibition of a growth factor can block the growth factor’s role in the disease process, but can also simultaneously interfere with its other normal physiological roles.

Our approach to the discovery and development of growth factor targeted drugs is fundamentally new and different from traditional approaches. Our approach of targeting the precursor, or latent forms of growth factors is based on the breakthrough discovery by the laboratory of our cofounder, Timothy A. Springer, Ph.D. of Harvard Medical School and Boston Children’s Hospital.

Unlike many other proteins that are produced and secreted by cells in a mature, or active, form, many growth factors are expressed by cells in a latent form. For example, TGF $\beta$ 1 is produced by cells as a single protein which is then enzymatically processed by the cells into two distinct and physically separated domains — the mature growth factor and the remaining portion of the original protein, referred to as the prodomain — which remain associated as part of a complex. This secreted complex is latent, or inactive, and must first be activated to carry out its normal function in a highly localized tissue or disease microenvironment. In a seminal peer-reviewed publication in 2011, Dr. Springer elucidated a new understanding of the mechanism of activation of the latent growth factor complex among members of the TGF $\beta$  superfamily by solving a high resolution x-ray crystal structure of this latent form of TGF $\beta$ 1 (as illustrated in the graphic below).



***Structural representation of the latent form of TGF $\beta$ 1  
wherein the prodomain wraps around the active growth factor***

This research explained at a molecular level why the secreted form of TGF $\beta$ 1 is inactive. The prodomain, though physically separated from the mature growth factor domain, forms a “cage” around the active form of TGF $\beta$ 1, blocking the growth factor from signaling through its receptor. Only when the cage is “unlocked” by a precursor activation event can the growth factor be released and mediate its effects in the local microenvironment. Dr. Springer further hypothesized that this phenomenon likely holds true for most members of the TGF $\beta$  superfamily, though the exact nature of the activation event, such as integrin binding or enzymatic cleavage, may differ among members of the superfamily. Importantly, while many growth factors are structurally very similar, their cages are structurally diverse, and this provides the basis for our approach to improved selectivity.

We believe that there are several important advantages to our approach of targeting the precursor, or latent, forms of growth factors over conventional therapeutic approaches, which inhibit mature growth factors or their receptors systemically throughout the body:

- targeting the latent precursor allows intervention at the site of action, within the microenvironment of the diseased tissue. Because our antibodies specifically bind the latent forms of the growth factors, we can prevent the activation of the growth factors. Given that many growth factors act primarily within the microenvironment where they are activated, as opposed to exerting their effects systemically, we believe that prevention of activation is a preferred mode of action for achieving improved outcomes. In contrast, traditional approaches to targeting growth factor signaling are focused on inhibiting the growth factor after it has been activated and released systemically;
- targeting the latent precursor allows heightened selectivity among structurally related growth factors, which we believe could limit off-target effects. For example, two members of the TGF $\beta$  superfamily, myostatin and GDF11, are 90% identical in their growth factor domains. Therefore, many of the traditional inhibitors that target myostatin also inadvertently inhibit GDF11. Similarly, most of the known inhibitors of TGF $\beta$  are pan-inhibitors, meaning that they do not distinguish among the three isoforms of TGF $\beta$ , namely, TGF $\beta$ 1, TGF $\beta$  2 and TGF $\beta$ 3. Despite the sequence similarities of the active forms of these growth factors, their cages are structurally diverse. We have been able to harness this diversity to generate antibodies that specifically bind the inactive growth factor precursors and inhibit activation of a particular growth factor of interest, but not others that are closely related; and
- targeting these precursor forms in the disease microenvironment, we believe we can interfere with the disease process while minimizing the effects on the normal physiological processes mediated by growth factors.

To enable our novel approach, we have built a proprietary platform that is rooted in our structural biology insights into activation of latent growth factor precursors. We integrate these insights with sophisticated protein expression, assay development and monoclonal antibody discovery capabilities. In addition to such know-how, our proprietary platform is covered by two patent families, with issued patents projected to expire well into the 2030s, excluding any patent term adjustments or extensions. The key elements of our proprietary platform include the following:

- focusing on growth factor targets with a high degree of evidence implicating them in a disease process or processes;
- utilizing structural biology insights to generate recombinant versions of the latent forms of targeted growth factors, as well as versions of closely related growth factors utilizing proprietary technology and in-house expertise;
- developing proprietary assays in which we are able to recapitulate the natural activation mechanism that these growth factors undergo in the human body;
- designing sophisticated selection strategies utilizing recombinant antibody libraries such as phage and yeast display that allow us to identify monoclonal antibodies, a well-established therapeutic modality, that can modulate the activation of these growth factors without having an effect on the activation of other closely related growth factors; and
- optimizing the output of such selections to ensure that our product candidates have the appropriate characteristics for manufacturability and further development.



Using our innovative approach and proprietary platform, we are creating a pipeline of novel product candidates that selectively modulate the activation of growth factors implicated in a variety of serious diseases. Our structural insights and unique antibody discovery capabilities can also be applied to other protein classes beyond growth factors, with an aim of generating differentiated candidates targeting cell surface receptors such as immune cell receptors or G-protein coupled receptors, where selectivity remains challenging.

### **Our Expertise**

We have assembled an experienced management team, board of directors, scientific founders and advisory board who bring extensive industry experience to our company. The members of our team have deep experience in discovering, developing and commercializing therapeutics, having worked at companies such as: Alnylam Pharmaceuticals, Inc.; Avila Therapeutics, Inc.; Dyax Corp.; AMAG Pharmaceuticals, Inc; Ocata Therapeutics, Inc; Foundation Medicine, Inc.; Merck; and Pfizer Inc. We were founded by internationally respected scientists, Drs. Timothy A. Springer and Leonard I. Zon of Harvard Medical School and Boston Children's Hospital.

### **Our Strategy**

Using our proprietary platform to unlock the therapeutic potential of targeting growth factor signaling in the disease microenvironment, our goal is to deliver novel therapies to underserved patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer and fibrosis. To achieve this goal, we plan to:

- **Continue advancing apitegromab in its registrational program in SMA and offer meaningful benefit to patients.** We are developing our first product candidate, apitegromab, for the treatment of patients with SMA. By targeting the latent form of myostatin and specifically inhibiting its activation in muscle, we believe apitegromab holds considerable promise in improving motor function in patients with SMA. We are currently conducting SAPPHIRE, a pivotal Phase 3 trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA being treated with background survival motor neuron ("SMN") upregulator therapy (e.g., therapies that upregulate the expression of SMN, such as SMN splicing modulators).
- **Identify the next indication(s) for apitegromab.** Our goal is to maximize the value of apitegromab by exploring its potential across SMA types and in other myostatin-related indications. We believe that the role of apitegromab as a muscle-directed therapy could have broad potential beyond SMA, spanning a number of muscle disorders in which fast-twitch fibers may play an important role in motor function. There is also increasing recognition of the important role of skeletal muscle in modulating metabolic physiology, highlighting a potential therapeutic opportunity for myostatin blockade. We have efforts underway to evaluate these opportunities, including preclinical and translational research, development path assessments, and commercial evaluations.
- **Advance our TGFβ1 product candidate, SRK-181, through clinical proof-of-concept.** Our second antibody program is focused on the discovery and development of potent and selective inhibitors of the activation of latent TGFβ1. We believe that the selectivity of SRK-181 is a significant differentiator in our efforts to address the historical dose-limiting safety challenges resulting from non-selectively inhibiting multiple isoforms that activate the TGFβ signaling pathway. We are conducting a Phase 1 proof-of-concept clinical trial of SRK-181 in patients with locally advanced or metastatic solid tumors that are experiencing primary resistance to anti-PD-(L)1 antibody therapy. Additionally, we believe that SRK-181 has the potential to address unmet medical needs in other oncology indications, and we will endeavor to maximize the value of this product candidate by exploring its potential in additional oncology indications.
- **Advance additional TGFβ program candidates in non-oncology indications.** We believe that additional product candidates in the TGFβ portfolio have the potential to address other disorders associated with increased TGFβ signaling, including tissue and organ fibrosis. To advance the discovery and development of selected inhibitors originating from our TGFβ program that we believe have the potential to address unmet medical needs in non-oncology indications, we entered into a three-year fibrosis-focused collaboration with Gilead Sciences, Inc. ("Gilead") which concluded in December 2021. We have identified a suite of anti-fibrotic

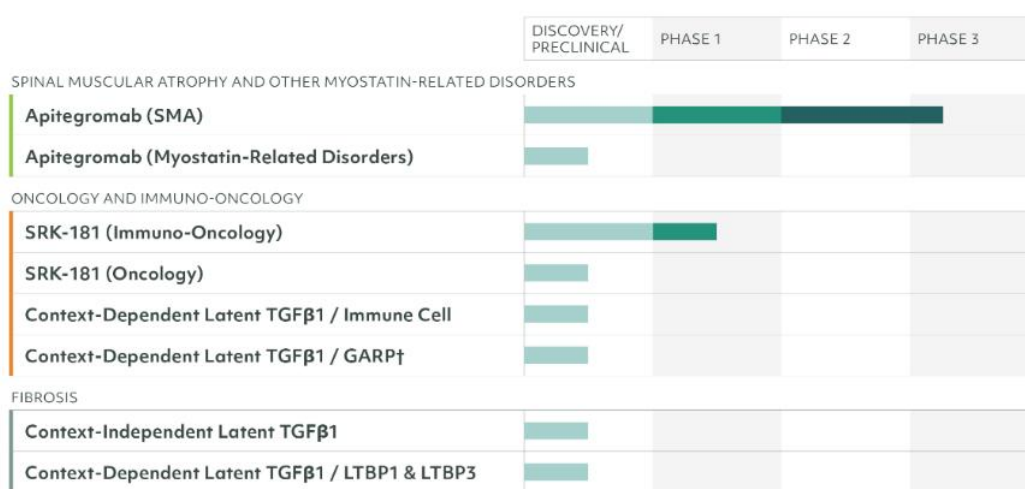
antibodies with novel selectivity profiles that were discovered over the course of the collaboration including those which may have therapeutic potential for the treatment of organ fibrosis by inhibiting TGF $\beta$ 1 function in connective tissue while having no impact on the activation or signaling of TGF $\beta$ 1 in the immune system. We plan to continue the advancement of these assets as part of our growing preclinical pipeline.

- ***Continue to leverage our proprietary platform to expand our pipeline beyond current lead programs.*** We will continue to leverage and expand our proprietary platform to selectively target the activation of additional growth factors, both within and beyond the TGF $\beta$  superfamily. Given the established role of signaling by protein growth factors in numerous diseases, we believe that these efforts could result in new opportunities to treat diseases with unmet medical need. In order to support our pipeline expansion and intention to be the leader in the field of growth factor-targeted drug development, we are investing in the technologies supporting our proprietary platform. We have designed a proprietary, state of the art antibody display library, to more efficiently identify differentiated candidate antibodies. Furthermore, we believe that our structural insights have applicability beyond growth factor activation to include other cell signaling mechanisms. Using our structural insight, we have identified modulators of bone morphogenic protein 6 (a TGF $\beta$  superfamily growth factor) by selectively inhibiting its co-receptor RGMc or hemojuvelin which is required for activation. BMP6 functions as a critical control point in iron modulation via regulation of hepcidin. Traditional approaches to inhibiting the signaling of BMP6 systemically would likely perturb the numerous different physiological processes in which BMP6 is involved. Our approach could provide the potential for tissue specific modulation of BMP signaling and iron regulation.
- ***Selectively seek strategic collaborations to maximize the value of our proprietary platform and pipeline.*** Given the potential of our proprietary platform to generate novel product candidates that could treat a wide variety of diseases, we believe that we can maintain in-house discipline with respect to our key development and commercialization efforts, while at the same time maximizing the full potential of our proprietary platform for other disease areas and indications. As a result, and as exemplified by our ongoing and past collaborations, we may seek to form additional strategic collaborations around certain targets, product candidates or disease areas that we believe could benefit from the resources of either larger biopharmaceutical companies or those specialized in a particular area of relevance.

## Our Pipeline

Using our innovative approach and proprietary platform, we are creating a differentiated pipeline of novel product candidates that selectively inhibit the activation of latent growth factors believed to be important drivers in a variety of diseases, including neuromuscular disorders, cancer and fibrosis. Our proprietary platform includes (i) our know-how enabling expression and purification of latent protein growth factor complexes in quantity and quality sufficient to enable antibody discovery; (ii) strategies to identify rare antibodies that selectively bind targeted latent protein growth factor complexes using our own proprietary antibody libraries; and (iii) assays developed by us in which to test the highly selective antibodies' ability to modulate the activation of specific latent growth factors. We have worldwide rights to our proprietary platform and all of our product candidates, with the exception of certain early-stage antibodies that specifically inhibit the activation of TGFβ1 in the context of regulatory T cells, which we licensed to Janssen.

The following summarizes our pipeline programs:



† We retain worldwide development and commercial rights for Context-Dependent Latent TGFβ1/GARP, except for certain early stage antibodies that specifically inhibit the activation of TGFβ1 in the context of regulatory T cells, which we licensed to Janssen.

## Our Product Candidates and Additional Programs

### ***Apitegromab — Our Inhibitor of Latent Myostatin Activation for SMA***

We are developing apitegromab, a novel, highly selective inhibitor of the activation of the growth factor myostatin, as a potential first muscle-directed therapy for the treatment of SMA. Myostatin, a member of the TGFβ superfamily of growth factors, is expressed primarily in skeletal muscle cells and the absence of its gene is associated with an increase in muscle mass and strength in multiple animal species. We believe that inhibition of the activation of myostatin may promote a clinically meaningful increase in motor function.

In preclinical studies, we have shown that apitegromab selectively avoids interaction with other closely related growth factors that play distinct physiological roles. We observed multi-fold increases in serum latent myostatin levels in mouse models of both early and late SMN restoration and that apitegromab promoted increased strength (as measured by torque generation) in SMN-deficient mice. In a Phase 1 clinical trial designed to evaluate the safety, tolerability, and pharmacokinetic (“PK”) /pharmacodynamic (“PD”) profile of apitegromab in adult healthy volunteers, there were no dose-limiting toxicities and robust and sustained target engagement following administration of apitegromab was observed. Apitegromab was evaluated in our TOPAZ Phase 2 proof-of-concept clinical trial for the treatment of patients

with Type 2 and Type 3 SMA and positive 12-month top-line results were announced in April 2021 showing apitegromab's transformative potential. See "TOPAZ Phase 2 Trial Analysis" below. We are currently conducting SAPPHERE, a pivotal Phase 3 clinical trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA receiving background SMN upregulator treatment.

We believe that apitegromab has the potential to be the first muscle-directed therapy, which is aimed at improving motor function in patients with SMA and could be used in conjunction with SMN upregulator therapies or as a monotherapy. We have identified multiple other diseases for which the selective inhibition of the activation of myostatin may offer therapeutic benefit, including additional patient populations in SMA (such as Type 1 SMA and ambulatory SMA) and indications outside of SMA.

### **Background on SMA**

SMA is a rare, and often fatal, genetic disorder that typically manifests in young children. It is characterized by the loss of motor neurons, atrophy of the voluntary muscles of the limbs and trunk and progressive muscle weakness. Disease severity in SMA can range from patients who die soon after birth to patients who live into adulthood with varying degrees of morbidity. The underlying pathology of SMA is caused by insufficient production of a protein known as "survival of motor neuron," or SMN. The SMN protein, essential for the survival of motor neurons, is encoded by two genes, SMN1 and SMN2.

- SMN1 genes produce the majority of functional SMN protein; healthy individuals have one or two functional copies of SMN1, while patients with SMA have mutations in or deletions of both copies of the gene.
- SMN2 genes produce only 10% to 20% of functional SMN protein and an individual's copy number of the SMN2 gene can range from zero to eight. In SMA patients, the number of SMN2 genes present in their genome is correlated with disease onset and severity; patients who have a lower number of SMN2 gene copies generally develop earlier and more severe SMA, because they produce less SMN protein.

### **SMA Natural History and Epidemiology**

SMA, the most common monogenic cause of death in infants, is a rare neuromuscular disorder. An estimated 30,000 to 35,000 patients suffer from SMA in the U.S. and Europe alone. Patients with SMA can be categorized as one of four types, Type 1 through Type 4. Approximately 85% of SMA patients currently living in the U.S. and Europe are estimated as having Type 2 or Type 3 disease, although it should be noted that this percentage may evolve over time. Type 2 and Type 3 SMA will be the initial focus of investigation in the development program.

- Type 1 disease is the most severe form, with clinical signs emerging at or shortly following birth. Patients with Type 1 SMA suffer from respiratory compromise and often require mechanical ventilation shortly after birth. Without intervention, Type 1 infants are never able to sit without support. Type 1 patients begin to lose motor neurons and muscle mass before birth.
- Type 2 disease manifests in early childhood and is less severe than Type 1 disease, although patients exhibit profound deficits in motor function. Patients with Type 2 disease may be able to sit independently but they are typically unable to walk without assistance.
- Type 3 disease manifests usually in childhood. While Type 3 SMA patients develop the ability to walk unaided, many individuals lose that ability over time. Ambulatory Type 3 SMA patients commonly suffer from substantial motor functional impairment, as evidenced by Expanded Hammersmith Functional Motor Scale ("HFMSE") scores and Six-Minute Walk Test distances, two commonly used measures of motor function.
- Type 4 disease is the mildest form of SMA, and its population is not well characterized. After symptom onset, which is most commonly reported between 20 and 30 years of age, patients experience mild to moderate muscle weakness and increasing disabilities. Patients are ambulatory and their life expectancy is normal.

### **Unmet Medical Need in SMA**

We view the emerging landscape for the development of novel medicines for SMA as being classified into two distinct but complementary therapeutic strategies: 1) SMN upregulator therapy (or also known as SMN corrector therapy, SMN-directed therapy or SMN therapy) and 2) muscle-directed therapy. Despite progress in the development of SMN upregulator therapies, a high unmet medical need to improve motor function remains. We believe that the advancement of muscle-directed therapy will be necessary to address this important gap.

SMN upregulator therapies are aimed at addressing the SMN deficiency to prevent further motor neuron deterioration. This category includes antisense oligonucleotide and small molecule approaches to increase SMN2 expression as well as gene therapy to deliver the SMN1 gene. The primary benefit of such an approach appears to be to address the SMN deficiency and to modify the course of disease. Early intervention at a very young age is therefore thought to be essential to prevent significant motor functional deterioration. However, for the vast majority of SMA patients living today, this early intervention window has been missed, and such individuals suffer from severe functional impairment. Thus, regardless of the precise nature or mechanism of action for any given SMN upregulator therapy, we believe that most SMA patients will continue to experience clinically significant functional deficits.

To address this need, apitegromab is being developed as a potential first muscle-directed therapy for SMA. We envision the potential for apitegromab to be a critical complement to any SMN upregulator therapy in patients with Type 2 and 3 SMA in order to drive absolute increases in functional performance over baseline. We also view apitegromab as having potential in the treatment of Type 1 SMA as well as presymptomatic SMA in conjunction with SMN upregulator therapy. Our vision is that apitegromab has the potential to become the backbone treatment for the broadest group of patients with SMA.

### **Myostatin in SMA and Challenges with Traditional Approaches**

Apitegromab is a highly selective inhibitor of the activation of latent myostatin that acts locally within skeletal muscle. Myostatin, also known as growth differentiation factor 8 (“GDF8”), is a member of the TGF $\beta$  superfamily and is produced by skeletal muscle cells. As with other tissues and organs in the human body, healthy muscle homeostasis is maintained by a proper balance of growth signals, or anabolic stimuli, and breakdown signals, or catabolic stimuli. In humans, the anabolic stimuli that drive muscle growth are proteins, such as the human growth hormone and the insulin-like growth factor 1. In contrast, myostatin is a catabolic agent that functions as a negative regulator of muscle mass.

Skeletal muscle fibers are generally classified as fast-twitch or slow-twitch. Fast-twitch fibers play a key role in motor activities, such as those involving quick bursts of strength. In contrast, slow-twitch fibers are important for endurance activities. Animals lacking functional myostatin genes, or its receptor, have larger muscles and increased strength compared to normal animals. While the absence of myostatin does lead to overall increases in muscle mass, a preferential effect on muscles enriched for fast-twitch muscle fibers has been observed in animals. Such animals are otherwise healthy and live a normal life-span.

Because of its role in regulating muscle mass, myostatin has been a popular target for a variety of drug development programs. There have been two general approaches to trying to inhibit the signaling of myostatin in humans. The first is to develop an antibody, or an antibody-like molecule, that binds to mature myostatin in circulation and prevents its ability to signal through its receptor, the ActRIIb receptor. The second is to develop an antibody to the ActRIIb receptor itself, or a soluble decoy of the ActRIIb receptor, with a goal of preventing myostatin signaling through its receptor. Both of these approaches, however, have significant limitations.

As a member of the TGF $\beta$  superfamily, mature myostatin shares considerable structural similarity with other family members. For example, the active form of myostatin and its most closely related family member, GDF11, are 90% identical in the growth factor domains, making it extremely challenging to identify antibodies that are truly specific for myostatin and do not interfere with other targets. Moreover, attempts to interrupt myostatin signaling through its receptor are complicated by the fact that the ActRIIb receptor, in addition to being the receptor for myostatin, is also the receptor for a number of related family members, including GDF11, activins and other growth factors. Attempts to block

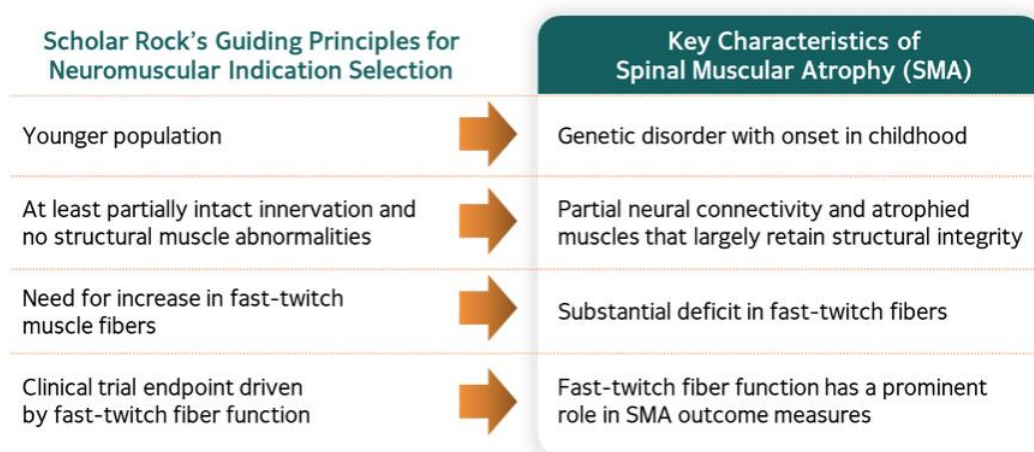
the signaling of myostatin by targeting its receptor therefore inevitably interfere with the signaling of these other growth factors, many of which are involved in normal biological processes unrelated to muscle.

There are multiple examples of clinical trials demonstrating the risk of non-selective inhibition of myostatin. For example, in a Phase 2 clinical trial in Duchenne Muscular Dystrophy reported in 2017, a soluble decoy of the ActRIIb receptor resulted in bleeding side effects believed by the sponsor to be unrelated to inhibition of myostatin signaling, but instead related to the inhibition of signaling by certain other members of the TGF $\beta$  superfamily known to be important in the maintenance of vascular integrity. These side effects resulted in termination of the clinical program. More recently, results from a clinical trial were reported showing that treatment of patients with an antibody to the ActRIIb receptor resulted in suppression of the levels of follicle stimulating hormone, an important reproductive hormone. In this clinical trial, the sponsor believed that these effects were likely related to inhibition of signaling through the ActRIIb receptor.

### **Our Solution**

Utilizing our proprietary platform, we targeted the precursor form of myostatin and generated apitegromab, a novel, highly selective inhibitor of the activation of myostatin from its inactive precursor in skeletal muscles, where myostatin resides and signals upon activation. While mature myostatin is 90% identical in the growth factor domain to its most closely related TGF $\beta$  superfamily member, GDF11, the prodomain that cages mature myostatin and keeps it in its latent precursor form is only 52% identical to the GDF11 prodomain. In preclinical studies, we observed that apitegromab bound to latent myostatin with a high level of selectivity, while having no binding to, and no effect on, the activation of related TGF $\beta$  family members.

We believe that the therapeutic potential for apitegromab in improving motor function is more optimal when a given disease bears certain features. Based on our translational and preclinical efforts, we have formulated a set of guiding principles to inform indication selection within the category of neuromuscular disease. As summarized in the table below, we believe that the pathobiological and clinical characteristics of SMA are well-aligned with these guiding principles. Since myostatin regulates muscle catabolism rather than anabolism, we believe that having a background of anabolic capacity is important to drive muscle growth in the setting of myostatin inhibition. Anabolic capacity is most robust in younger individuals and diminishes as one ages. SMA is a genetic disorder with onset commonly in childhood, and the initial focus of the development program will be in children and young adults. Furthermore, in SMA, there is a significant but incomplete loss of motor neurons, ensuring at least some intact signaling between skeletal muscle and nerve. In addition, generally, there are also no apparent structural abnormalities in the skeletal muscle. The partial loss of motor neurons causes substantial atrophy of fast-twitch muscle fibers that in turn leads to many of the motor function impairments. Validated outcome measures are available for SMA clinical trials that are relevant to fast-twitch fiber activity. These outcome measures, such as the HFMSE, assess a large number of motor activities that involve short-term bursts of strength, which are driven by fast-twitch muscle fibers. These endpoints therefore measure an outcome that may be more likely to be directly affected by apitegromab.



***Key disease features of SMA are aligned with Scholar Rock's guiding principles for neuromuscular indication selection for apitegromab***

### **Clinical Development Overview**

We are currently conducting SAPPHIRE, a pivotal Phase 3 clinical trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA being treated with background SMN upregulator therapy.

Beyond Type 2 and Type 3 SMA, we believe that apitegromab has the potential to contribute an important therapeutic benefit to patients with either more or less severe forms of SMA as well as pre-symptomatic patients receiving early intervention with a SMN upregulator therapy.

Our aim is to develop apitegromab for the broadest group of patients suffering from SMA. The FDA granted fast track designation, rare pediatric disease designation and orphan drug designation to apitegromab for the treatment of SMA in May 2021, August 2020 and March 2018, respectively. The EMA granted PRIME designation in March 2021 and the EC granted orphan medicinal product designation in December 2018 to apitegromab for the treatment of SMA.

### **SAPPHIRE Phase 3 Pivotal Trial Design**

SAPPHIRE is a randomized, double-blind, placebo-controlled, Phase 3 clinical trial. Approximately 156 patients aged 2-12 years old with non-ambulatory Type 2 or Type 3 SMA are anticipated to be enrolled in the main efficacy population. Patients will be randomized 1:1:1 to receive for 12 months either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by intravenous (IV) infusion every 4 weeks in addition to background SMN treatment. Patients receiving the background SMN treatment of nusinersen as well as patients receiving background SMN treatment of risdiplam will both be eligible for enrollment.

Additional key elements of the study design include the following:

- At baseline, all patients will be required to be in the chronic maintenance phase of SMN treatment, corresponding to either at least 6 months of prior treatment in the case of risdiplam or at least 10 months of prior treatment in the case of nusinersen.



- Randomization of patients will be stratified by both the background SMN treatment (nusinersen vs. risdiplam) as well as the age at which SMN treatment had been initiated ( $\leq 5$  years vs.  $> 5$  years).
- The primary efficacy endpoint will evaluate the mean change from baseline in the HFMSE total score after 12 months of treatment.
- Additional endpoints will evaluate safety, proportion of patients with  $\geq 3$ -point HFMSE increase, Revised Upper Limb Module (“RULM”), World Health Organization (“WHO”) motor developmental milestones, pharmacokinetics, pharmacodynamics, anti-drug antibody, and other outcome measures.

In addition, this clinical trial provides the opportunity for an interim analysis when at least 50% of patients in the main efficacy population (age 2-12 years) have completed 12 months of treatment.

Separately from the main efficacy population, an exploratory population of 48 patients aged 13-21 years old with non-ambulatory Type 2 or Type 3 SMA will be evaluated. These patients will be randomized 2:1 to receive either apitegromab 20 mg/kg or placebo added to background SMN treatment with nusinersen or risdiplam. In this subpopulation of older individuals with SMA, the safety and tolerability of apitegromab will be characterized, and efficacy will also be evaluated in an exploratory, nonpowered manner.

### **TOPAZ Phase 2 Proof-of-Concept Trial**

We completed enrollment of 58 patients in our TOPAZ Phase 2 proof-of-concept trial of apitegromab in SMA in January 2020. One patient discontinued from the 12-month treatment period for reasons that were determined to be unrelated to apitegromab treatment. All remaining 57 patients completed the 12-month treatment period and opted into the extension period. As of February 2022, 55 of the patients remain enrolled.

The clinical trial consisted of three distinct cohorts of patients with Type 2 or Type 3 SMA and evaluated the safety and efficacy of apitegromab over a 12-month treatment period. All patients in the clinical trial received apitegromab dosed every four weeks (Q4W) either as a monotherapy or in conjunction with an approved SMN upregulator therapy.

In our view, this approach of having evaluated multiple distinct cohorts offers a greater number of opportunities to discern the effects of apitegromab on clinically meaningful motor function measures across multiple patient subpopulations. It is estimated that patients with Type 2 or Type 3 SMA represent over 85% of the overall patient population. We view each of the cohorts evaluated in the TOPAZ trial as representing a significant proportion of patients suffering from SMA.

The primary efficacy objectives evaluated in the TOPAZ trial, HFMSE and Revised Hammersmith Scale (“RHS”), are clinically meaningful outcome measures validated for SMA. These endpoints assess motor tasks involving short-term bursts of strength and thus involve fast-twitch fiber function. As the hypothesized effect of myostatin blockade under investigation is to drive increases in fast-twitch fiber function, we believe these endpoints are of direct relevance in assessing the clinical effect of apitegromab.

Our overall approach to the efficacy analysis is informed by SMA disease biology, the anticipated mechanism of action of apitegromab, the effects of SMN upregulators, and available clinical data on SMA. The primary effect of SMN upregulator therapy appears to be to address the SMN deficiency and to modify the disease course; thus, the key in preventing significant motor functional deterioration is intervening at a very young age. For most patients with SMA, however, this window for early intervention is no longer available. As a result, these individuals have already suffered considerable atrophy and motor function impairment. Natural history data indicate that most patients with Type 2 or 3 SMA, other than very young individuals, generally have a stable functional baseline over a 12-month period as evidenced by their HFMSE scores. A one-point improvement on the Hammersmith scale may be considered meaningful on an individual level and a spontaneous improvement of 3 or more points from one’s baseline would be a notable divergence from the otherwise expected course of disease for most patients.

### **TOPAZ Twelve-Month Analysis**

On April 6, 2021, we announced positive top-line data for the 12-month treatment period of our TOPAZ Phase 2 proof-of-concept trial, which enrolled 58 patients with Type 2 and Type 3 SMA across 16 study sites in the United States and



Europe. The clinical trial evaluated the safety and efficacy of intravenous apitegromab dosed every four weeks (Q4W) over a 12-month treatment period. Four patients (one in Cohort 2 and three in Cohort 3) each missed three consecutive doses of apitegromab over the course of the 12-month treatment period due to COVID-19-related site access restrictions and were excluded from the prespecified intent-to-treat primary analysis.

Cohort 1: This open-label, single-arm cohort enrolled 23 patients with ambulatory Type 3 SMA. Patients were treated with 20 mg/kg of apitegromab either as a monotherapy or in conjunction with an approved SMN upregulator therapy (nusinersen). The primary objectives of Cohort 1 were to assess safety and the mean change from baseline in RHS following 12 months of treatment.

Cohort 1 (Intent-to-treat population)	Apitegromab 20 mg/kg monotherapy (n=11)	Apitegromab 20 mg/kg + nusinersen (n=12)	Apitegromab pooled (n=23)
Mean change from baseline in RHS score (95% CI)	-0.4 (-3.9, +3.1)	-0.3 (-2.0, +1.4)	-0.3 (-2.1, +1.4)
% of patients attaining ≥0-point increase in RHS score	6/11 (55%)	7/12 (58%)	13/23 (57%)
% of patients attaining ≥1-point increase in RHS score	4/11 (36%)	5/12 (42%)	9/23 (39%)
% of patients attaining ≥3-point increase in RHS score	3/11 (27%)	2/12 (17%)	5/23 (22%)
% of patients attaining ≥5-point increase in RHS score	1/11 (9%)	0/12 (0%)	1/23 (4%)

Cohort 2: This open-label, single-arm cohort enrolled 15 patients with Type 2 or non-ambulatory Type 3 SMA and who were already receiving treatment with an approved SMN upregulator (nusinersen) initiated at age five years or older. One patient missed three consecutive doses of apitegromab due to COVID-19-related site access restrictions and was excluded from the prespecified intent-to-treat primary analysis. The primary objectives of the cohort were to assess safety and the mean change from baseline in HFMSE following 12 months of treatment.

One patient in Cohort 2 was identified as having received concomitant treatment with an acetylcholinesterase inhibitor before and during the study, which was not permitted by the trial protocol. This patient experienced a 7-point decline in HFMSE score at the 12-month timepoint. In the per protocol analysis conducted in accordance with the prespecified approach, which excludes this patient as well as the patient who missed three consecutive doses due to COVID-19-related site access restrictions, the mean change from baseline in HFMSE score for Cohort 2 was a 1.2-point improvement.

Cohort 2	Apitegromab 20 mg/kg + nusinersen	
	Intent-to-treat (n=14)	Per Protocol (n=13)
Mean change from baseline in HFMSE score (95% CI)	+0.6 (-1.4, +2.7)	+1.2 (-0.5, 2.9)
% of patients attaining ≥1 point increase in HFMSE score	9/14 (64%)	9/13 (69%)
% of patients attaining ≥3 point increase in HFMSE score	4/14 (29%)	4/13 (31%)
% of patients attaining ≥5 point increase in HFMSE score	2/14 (14%)	2/13 (15%)

Cohort 3: This randomized, double-blind, parallel arm portion of the clinical trial enrolled patients with Type 2 SMA who had initiated treatment with an approved SMN upregulator (nusinersen) before five years of age. Twenty patients were randomized in a 1:1 ratio to receive the low dose (apitegromab 2 mg /kg Q4W) or high dose (apitegromab 20 mg/kg Q4W); both treatment arms were in conjunction with an approved SMN upregulator therapy (nusinersen). Three

patients (two in high-dose arm and one in low-dose arm) each missed three consecutive doses of apitegromab due to COVID-19-related site access restrictions and were excluded from the prespecified intent-to-treat primary analysis. The primary objectives of the cohort were to assess safety and the mean change from baseline in HFMSE following 12 months of treatment.

Cohort 3 (Intent-to-treat population)	Apitegromab 20 mg/kg + nusinersen (n=8)	Apitegromab 2 mg/kg + nusinersen (n=9)	Apitegromab pooled (n=17)
Mean change from baseline in HFMSE score (95% CI)	+7.1 (+1.8, +12.5)	+5.3 (-1.5, +12.2)	+6.2 (+2.2, +10.1)
% of patients attaining ≥1-point increase in HFMSE score	7/8 (88%)	7/9 (78%)	14/17 (82%)
% of patients attaining ≥3-point increase in HFMSE score	5/8 (63%)	5/9 (56%)	10/17 (59%)
% of patients attaining ≥5-point increase in HFMSE score	5/8 (63%)	5/9 (56%)	10/17 (59%)
% of patients attaining >10-point increase in HFMSE score	3/8 (38%)	3/9 (33%)	6/17 (35%)

Dose response was observed; the 20 mg/kg dose achieved numerically greater mean improvements from baseline in HFMSE scores than the 2 mg/kg dose across all assessed timepoints in the 12-month treatment period. The clinically observed dose response was consistent with the pharmacodynamic (target engagement) results. Both the 20 mg/kg and 2 mg/kg doses yielded high levels of target engagement (>100-fold increase from baseline), but the 20 mg/kg dose led to a relatively higher absolute level of target engagement.

Overall safety and tolerability profile:

- Incidence and severity of adverse events were consistent with the underlying patient population and background therapy.
- Five most frequently reported treatment-emergent adverse events: Headache (24%), pyrexia (22%), upper respiratory tract infection (22%), cough (22%), and nasopharyngitis (21%).
- Five patients experienced a serious treatment-emergent adverse event, all assessed by the respective trial investigator as unrelated to apitegromab:
  - One patient treated with 2 mg/kg dose (Cohort 3) hospitalized due to adenoidal hypertrophy and tonsillar hypertrophy to perform scheduled adenotonsillectomy (Grade 2). Event resolved without sequelae.
  - Two patients treated with 20 mg/kg dose (both Cohort 1) with gait inability considered a significant disability (both Grade 3). Events remain ongoing.
  - One patient treated with 20 mg/kg dose (Cohort 1) hospitalized with post lumbar puncture syndrome (Grade 2). Event resolved without sequelae.
  - One patient treated with 20 mg/kg dose (Cohort 1) hospitalized due to viral upper respiratory tract infection (Grade 2). Event resolved without sequelae.
- One patient (Cohort 1) presented with a non-serious Grade 3 post lumbar puncture syndrome; assessed by trial investigator as unrelated to apitegromab. Event resolved without sequelae.
- One patient (Cohort 1) discontinued from the clinical trial due to Grade 2 muscle fatigue that started prior to initiation of dosing with study drug; assessed by the clinical trial investigator as unrelated to apitegromab.

From June to October 2021, we announced supportive data from additional exploratory analyses from the TOPAZ Phase 2 clinical trial at various medical congresses, including the Cure SMA virtual conference, the World Muscle Society virtual congress, the Child Neurology Society annual meeting, and the World Congress of Neurology. We believe these exploratory analyses further demonstrate the potential of apitegromab in patients with SMA:

- Time to achieving various thresholds of improvement in HFMSE scores further supported the dose response in clinical efficacy.
- Increases in RULM were also observed in both non-ambulatory cohorts.
- Greater increases in HFMSE (non-ambulatory) and RHS (ambulatory) scores were seen in patients who were not limited by scoliosis or joint contractures.

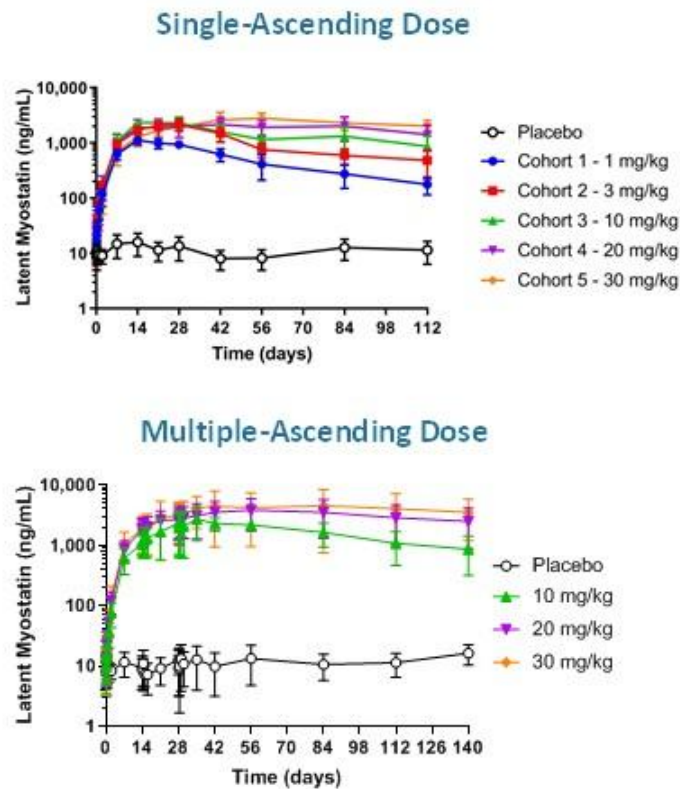
#### **Phase 1 Healthy Volunteer Clinical Trial Results**

The randomized, double-blind, placebo-controlled, first-in-human, Phase 1 clinical trial was designed to evaluate the safety and tolerability, immunogenicity, PK, and PD of IV administered apitegromab in adult healthy volunteers. A total of 66 subjects were enrolled, including 40 subjects in the single ascending dose (“SAD”) and 26 subjects in the multiple ascending dose (“MAD”) portions of the study. Full results from the Phase 1 clinical trial were presented at the Cure SMA Annual Conference in June 2019.

*Safety and immunogenicity results.* Apitegromab was shown to be well-tolerated with no apparent safety signals. There were no dose-limiting toxicities identified up to the highest tested dose of 30 mg/kg, treatment-related serious adverse events (“SAEs”) or hypersensitivity reactions. Immunogenicity was assessed by anti-drug antibody testing, and all subjects tested negative.

*Pharmacokinetics and pharmacodynamics results.* Apitegromab displayed a PK profile generally consistent with that commonly observed with monoclonal antibodies. Drug exposure was dose proportional, and the serum half-life was approximately 23 to 33 days across the apitegromab dose groups. The findings supported the investigation of a once every 4-week dosing regimen in the TOPAZ Phase 2 clinical trial.

Mean serum concentrations of latent myostatin in the SAD were < 20 ng/ml in the pre-treatment baselines for apitegromab treated subjects as well as in placebo subjects throughout the study. Following placebo treatment, there was no meaningful change in the latent myostatin biomarker concentrations. Following single doses of apitegromab at dose levels of 3 mg/kg or greater, marked increases in latent myostatin biomarker concentrations in the serum, by at least an order of magnitude, were observed following apitegromab treatment. This finding demonstrates successful target engagement and provides initial proof-of-mechanism in humans of our therapeutic approach of targeting the latent form of growth factors. The observation also corroborates our biological understanding that the vast majority of drug target (pro and latent forms of myostatin) resides within skeletal muscle rather than within the systemic circulation.



***Apitegromab engages latent myostatin in Phase 1 clinical trial subjects***

**Apitegromab in Other Myostatin-Related Disorders**

We see potential for apitegromab broadly across SMA (i.e., Type 1 SMA and ambulatory SMA) and our intention is to further investigate this potential. We also believe that the role of apitegromab as a muscle-directed therapy has broad potential beyond SMA, spanning a number of muscle disorders in which fast-twitch fibers may play an important role in motor function. In some settings, we believe that disease-stabilizing therapy may be necessary to address the underlying defect, which can then be complemented by the potential motor function-building benefit of apitegromab. In settings in which the defect may be less severe and/or the disease may have a slower rate of progression, apitegromab may have the potential to serve as a monotherapy.

There is also increasing recognition of the important role of skeletal muscle in modulating metabolic physiology, highlighting a potential therapeutic opportunity for myostatin blockade. For example, data emerging from our preclinical experiments support the hypothesis that blockade of the myostatin pathway has the potential to reduce the mass of visceral fat, a significant driver of cardiometabolic pathophysiology. Excessive fat mass and metabolic abnormalities have been observed in many muscle atrophy states, such as SMA and spinal cord injury. More broadly, reducing visceral fat mass, or improving body compositions (e.g., enhanced muscle-to-fat ratios), may be a potential therapeutic strategy to address a wide range of disorders, such as non-alcoholic steatohepatitis (“NASH”), diabetes, and obesity.

Based on this evidence, we believe a wide range of potential therapeutic applications may be envisioned for apitegromab. We are considering the investigation of apitegromab in multiple indications beyond SMA and have efforts underway to evaluate these opportunities (including preclinical and translational research, clinical development and regulatory path assessments, and commercial assessments).

### **SRK-181 in Cancer Immunotherapy - Inhibitor of Latent TGF $\beta$ 1 Activation**

Our second antibody product candidate, SRK-181, a highly selective inhibitor of the activation of latent TGF $\beta$ 1, is in clinical development for the treatment of locally advanced or metastatic solid tumors that are resistant to anti-PD-(L)1 therapies. We estimate at least 750,000 cancer patients in the US are eligible for treatment with checkpoint inhibitor therapies every year, of which the majority do not respond to treatment.

Increased signaling by TGF $\beta$ 1 is a key driver of a number of disease-relevant processes, including immune system evasion by cancer cells, bone marrow fibrosis associated with hematological disorders, and tissue and organ fibrosis. Historically, selectively targeting TGF $\beta$ 1 signaling has been challenging due to the inability of either small molecule inhibitors or antibodies to avoid off-target inhibition of other, closely related growth factors, TGF $\beta$ 2 and TGF $\beta$ 3. Treatment of animals with these non-selective TGF $\beta$  inhibitors has been associated with a range of toxicities, most notably cardiac toxicity. Furthermore, since each of these growth factors signals through the same TGF $\beta$  receptor, ALK5, inhibitors of the TGF $\beta$  receptor kinase suffer from similar dose-limiting toxicities. In preclinical studies of our antibodies, we have observed selective inhibition of TGF $\beta$ 1 activation *in vitro* and immunomodulatory and antifibrotic activity in multiple disease models *in vivo*. A 28-day pilot nonclinical toxicology study in rats of our leading antibody did not observe any drug-related toxicity up to the highest dose (100 mg/kg weekly) tested in the study. In the same study, we tested non-selective TGF $\beta$  inhibitors and observed the published toxicities, including cardiac toxicity as well as death. We have also completed four-week GLP toxicology studies in rats and non-human primates and no SRK-181 related adverse effects were observed up to the highest evaluated dose of 200 mg/kg per week and 300 mg/kg per week, respectively.

In many human cancers, TGF $\beta$  signaling is associated with lack of response to PD-(L)1 blockade, particularly in patients with tumors harboring an immune excluded phenotype (i.e., CD8 $^+$  T cells present in nearby stroma but excluded from the tumor parenchyma). We have observed multiple mouse models that recapitulate the immune-excluded phenotype and are resistant to PD-1 blockade become responsive to the combination of SRK-181-mIgG1, the murine analog of SRK-181, and an anti-PD-1 antibody. These models, including the MBT-2 bladder cancer model, the Cloudman S91 melanoma model and the EMT6 breast cancer model, were poorly responsive or unresponsive to single agent treatment with either anti-PD-1 or SRK-181-mIgG1, with little or no effect on tumor growth. However, in representative experiments, the combination of SRK-181-mIgG1 and anti-PD-1 resulted in tumor regressions of 72%, 57% and 70% in these three mouse models, respectively. Furthermore, the combination treatment led to statistically significant survival benefit in all three models (See “Preclinical Evidence in Overcoming Resistance to Checkpoint Inhibition”).

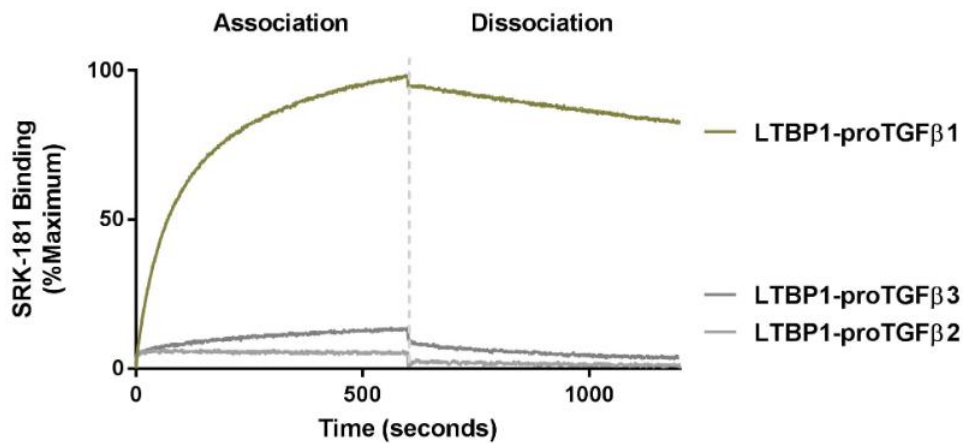
Our DRAGON Phase 1 clinical trial is intended to initially evaluate our therapeutic hypothesis that SRK-181 in combination with anti-PD-(L)1 therapy may overcome primary resistance to anti-PD-(L)1 therapy and lead to anti-tumor responses. This clinical trial in patients with locally advanced or metastatic solid tumors is ongoing and investigates the safety, PK and efficacy of SRK-181. The DRAGON trial consists of two parts: Part A (dose escalation of SRK-181 as a single-agent or in combination with an approved anti-PD-(L)1 therapy) and Part B (dose expansion evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody therapy). Part B encompasses five cohorts, including urothelial carcinoma, cutaneous melanoma, non-small cell lung cancer, clear cell renal cell carcinoma and other solid tumors and commenced in 2021. Initial clinical data from Part A, primarily focused on safety and PK, was presented in November 2021 at the SITC 36th Annual Meeting.

#### **Selection of a Potent and Highly Selective Inhibitor of TGF $\beta$ 1 Activation**

TGF $\beta$ 1 is produced by cells as a single protein chain and is then enzymatically processed by the cells into two distinct and physically separated domains — the mature, active growth factor and the remaining portion of the original protein, referred to as the prodomain, or latency associated peptide — which remains associated with and keeps the growth factor in an inactive state. This complex is further associated with one of a number of “presenting molecules” which when secreted serve to tether the latent precursor in specific locations in the body. TGF $\beta$ 1 is produced by a variety of cell types, including fibroblasts, which deposit latent TGF $\beta$ 1 in connective tissue, as well as regulatory T cells and macrophages, which display latent TGF $\beta$ 1 on their cell surfaces.

In a seminal peer-reviewed publication in 2011, by solving a high-resolution x-ray crystal structure of the latent form of TGF $\beta$ 1, our founder, Dr. Springer elucidated a new understanding of the mechanism that underlies the activation of latent precursor forms of members of the TGF $\beta$  superfamily of protein growth factors. This research explained at a molecular level why the secreted form of TGF $\beta$ 1 is inactive. The prodomain, though physically separated from the mature growth factor domain, forms a “cage” around the active form of TGF $\beta$ 1, blocking the ability of the growth factor to signal through its receptor. Integrin proteins are able to unlock the “cage” by binding to the prodomain of the latent TGF $\beta$ 1 complex and applying force to pull the complex open, allowing the mature growth factor to be released and signal in its microenvironment. While mature TGF $\beta$ 1 shares a high degree of structural similarity with its closely related family members, TGF $\beta$ 2 and TGF $\beta$ 3, their respective cages are structurally diverse. By taking advantage of the differences among the prodomains, together with our understanding of the activation mechanism and ability to recapitulate the activation mechanism *in vitro*, we were able to identify multiple highly selective inhibitors of the activation of latent TGF $\beta$ 1.

By specifically targeting the TGF $\beta$ 1 isoform, we believe we have the key to unlock the power of checkpoint inhibitors and meaningfully increase response rates across multiple solid tumor types. In March 2019, we selected SRK-181 as a product candidate in our TGF $\beta$ 1 cancer immunotherapy program based on the strength of preclinical data and human translational insights. *In vitro* and *in vivo* studies of SRK-181 showed that it binds to latent TGF $\beta$ 1 with high affinity and high selectivity, which is evidenced by minimal or no binding to latent TGF $\beta$ 2 or latent TGF $\beta$ 3 isoforms. Integrins, such as  $\alpha$ V $\beta$ 6 and  $\alpha$ V $\beta$ 8, can trigger the activation of TGF $\beta$ 1 and TGF $\beta$ 3. In addition, biochemical evidence suggests that certain proteases (e.g., Plasmin and Kallikreins) may also induce TGF $\beta$  activation. Notably, these integrins and proteases have been implicated in tumor biology in a number of human cancers. SRK-181 is capable of inhibiting both integrin-dependent- and protease-induced activation of TGF $\beta$ 1.



***SRK-181 selectively binds to proTGF $\beta$ 1 complexes with minimal or no binding to proTGF $\beta$ 2 or proTGF $\beta$ 3 complexes.***

### TGF $\beta$ 1 in Cancer Therapy

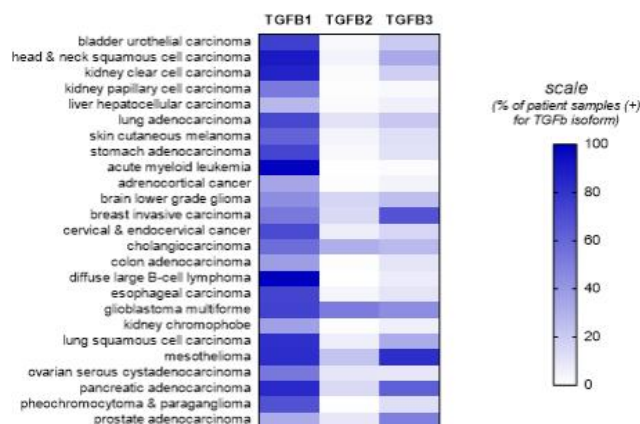
We believe that specific inhibition of TGF $\beta$ 1 may have a significant impact on the treatment of patients in certain oncology settings.

Immune checkpoints are cellular mechanisms that act as a brake on the immune system, and expression of these proteins in the tumor microenvironment creates an immunosuppressive environment that allows tumor cells to evade being killed by the immune system. Immune checkpoint proteins, such as PD-1/PD-L1, have therefore become key therapeutic targets in the tumor microenvironment. By inhibiting these proteins, the brakes on the immune system are released,

allowing the T cells to kill the cancer cells. There are currently multiple approved checkpoint inhibitor therapies that target the PD-1/PD-L1 pathway.

A significant proportion of patients, in many cases the majority, fail to respond to these checkpoint inhibitor therapies, because they have what appears to be a pre-existing, or primary, resistance to immunotherapy. Other patients' cancers appear to initially respond but subsequently progress. In many human cancers, TGF $\beta$  signaling is associated with lack of response to PD(L)-1 blockade, particularly in patients with tumors harboring an immune excluded phenotype (i.e., CD8+ T cells present in nearby stroma but excluded from the tumor parenchyma). Gene expression analysis of pre-treatment melanoma tumors identified multiple TGF $\beta$ -related signaling signatures associated with pre-existing or primary resistance to anti-PD-(L)1 antibody therapy. Similarly, it has also been reported that retrospective pathway analysis of tumor samples from an atezolizumab bladder cancer trial identified the TGF $\beta$  pathway as a major determinant of primary resistance to atezolizumab.

Our analysis of publicly available human tumor data has identified TGF $\beta$ 1 as the predominant TGF $\beta$  isoform expressed in many solid tumors.

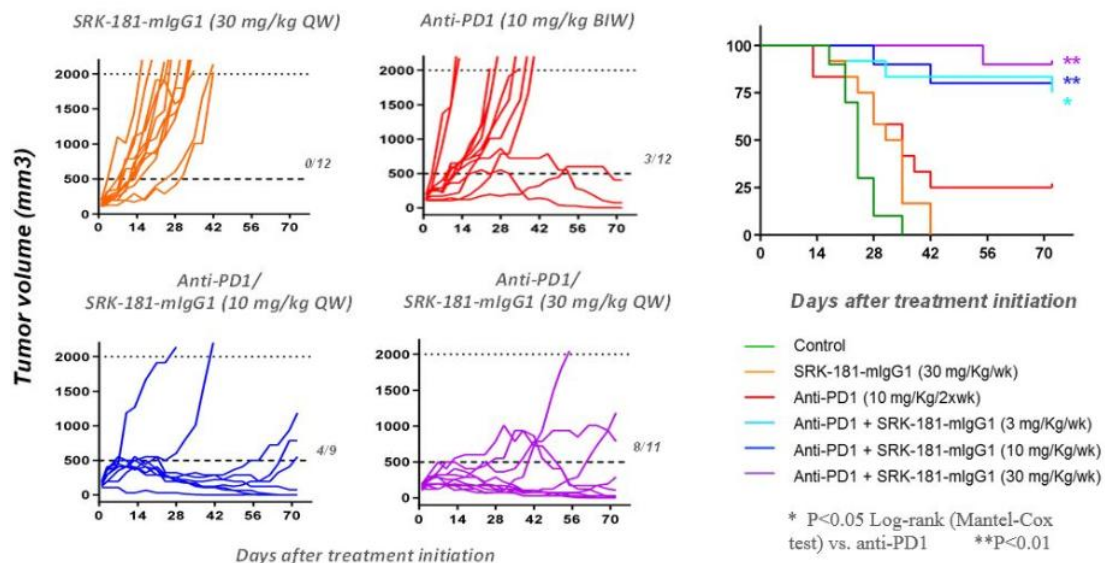


***National Cancer Institute - Cancer Genome Atlas Program RNAseq analysis of >10,000 samples spanning 33 tumor types show high expression of the TGF $\beta$ 1 isoform across many in many tumor types***

### **Preclinical Evidence in Overcoming Resistance to Checkpoint Inhibition**

Using multiple mouse models that recapitulate the immune-excluded phenotype, we have observed that co-administration of SRK-181-mIgG1, the murine version of SRK-181, with an anti-PD-1 antibody renders these tumor models sensitive to the combination treatment. These models, including the MBT-2 bladder cancer model, the Cloudman S91 melanoma model and the EMT6 breast cancer model, are poorly responsive or unresponsive to single agent treatment with either anti-PD-1 or SRK-181-mIgG1, with little or no effect on tumor growth. However, the combination of SRK-181-mIgG1 and anti-PD-1 resulted in tumor regressions. Furthermore, the combination treatment led to significant survival benefit in both models.

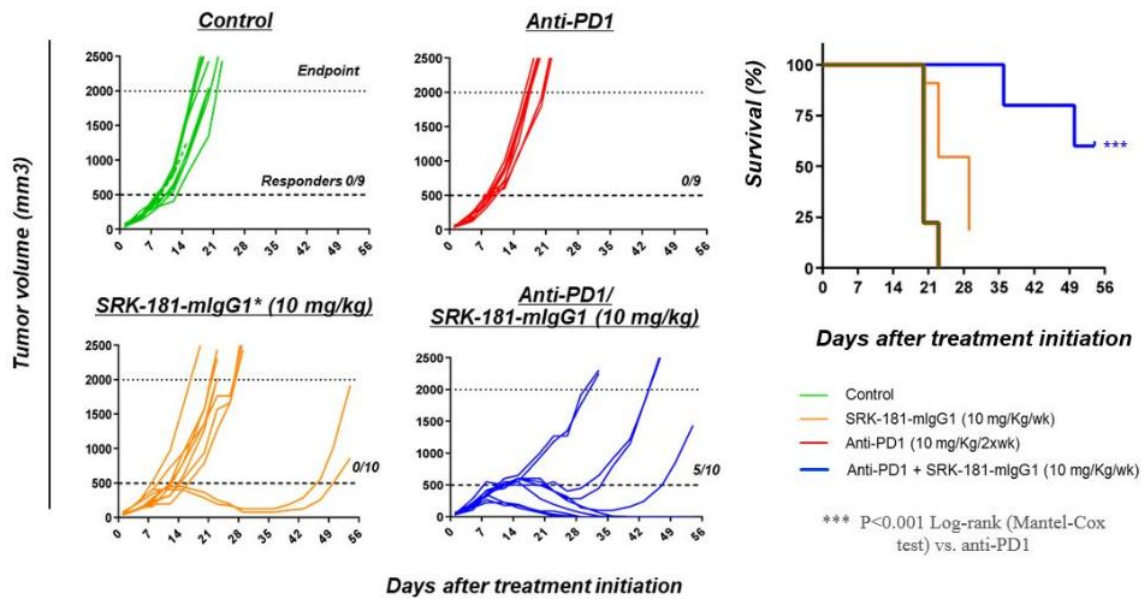




***SRK-181-mIgG1 renders the syngeneic Cloudman S91 melanoma model susceptible to anti-PD-1 CPI therapy, as measured by tumor regression and growth control, and survival benefit***

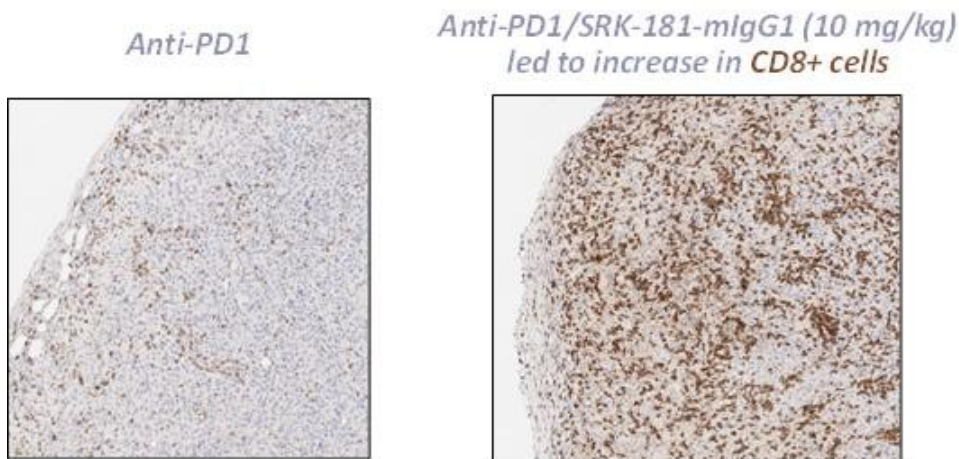
This effect on tumor regression and survival benefit was also observed in the EMT6 breast cancer model, which expresses both TGFβ1 and TGFβ3, suggesting that potently inhibiting TGFβ1 alone is sufficient for enabling a synergistic anti-tumor response in conjunction with anti-PD-1 antibody treatment.





**SRK-181-mIgG1 renders the syngeneic EMT6 breast cancer model susceptible to anti-PD-1 CPI therapy, as measured by tumor regression and growth control, and survival benefit**

Furthermore, in *in vivo* mechanistic studies of the same tumor models, we observed an increase in the number of effector T cells in tumors from mice treated with the SRK-181-mIgG1/anti-PD-1 combination versus control or single agent treatment, suggesting that overcoming innate CPI resistance involves enhanced presence and activity of killer T cells. CD8<sup>+</sup> population expanded to an average of 34% of the tumor's immune cells from a control average of 3.5%. We also observed a decrease in intratumoral immunosuppressive myeloid cells – a reduction in TAM/MDSC population to 14% of the tumor's immune cells from a control average of 47%.



***Combination treatment of MBT-2 tumor bearing mice with SRK-181-mIgG1 and an anti-PD-1 antibody causes an increase in intra-tumoral effector T cells and a decrease in intratumoral immunosuppressive myeloid cells***

We have demonstrated preclinically the potential of SRK-181 for reduced toxicity that has historically limited drug exposure with non-selective TGF $\beta$  inhibition. In a 28-day pilot nonclinical toxicology study in adult rats, we did not observe any drug-related toxicity up to the highest tested dose (100 mg/kg weekly) of SRK-181. In the same study, we tested non-selective TGF $\beta$  inhibitors and observed the published toxicities, including cardiac toxicity and death. We have also completed four-week GLP-toxicology studies in rats and non-human primates and no SRK-181 related adverse effects were observed up to the highest evaluated dose of 200 mg/kg per week and 300 mg/kg per week, respectively.

**DRAGON Phase 1 Clinical Trial**

Our DRAGON Phase 1, open-label, proof-of-concept trial is evaluating the safety, tolerability, PK/PD, and efficacy of SRK-181 administered intravenously every 3 weeks (Q3W) in patients with locally advanced or metastatic solid tumors. This clinical trial will investigate if SRK-181 in combination with anti-PD-(L)1 therapy may overcome primary resistance to anti-PD-(L)1 therapy and lead to anti-tumor responses.

This two-part clinical trial consists of a dose escalation portion (Part A) for SRK-181 as both a single agent and in combination with an approved anti-PD-(L)1 antibody therapy, followed by a dose expansion portion (Part B) evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody therapy in multiple tumor-specific cohorts. Patients must have locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibody therapy. Lack of response is characterized as either stable disease or progressive disease following treatment with an approved anti-PD(L)1 therapy, either alone or in combination with other therapy. Up to 3 lines of treatment are allowed between the last dose of anti-PD-1 and this study treatment in non-small cell lung cancer, cutaneous melanoma, clear cell renal cell carcinoma, and urothelial carcinoma cohorts.

- **Part A:** The dose escalation portion of this clinical trial is assessing SRK-181 as a single agent (Part A1) and in combination with an anti-PD-(L)1 therapy approved for the tumor (Part A2). Parts A1 and A2 are being conducted in a staggered fashion.
  - The primary objectives of Part A are to evaluate safety and tolerability, determine the maximum tolerated dose (MTD) or maximum administered dose (MAD), and the recommended Phase 2 dose (RP2D) and evaluate dose-limiting toxicities. The secondary and exploratory objectives include evaluating PK and anti-drug antibodies (ADA), anti-tumor activity and biomarkers.
- **Part B:** The dose expansion portion of the clinical trial evaluates SRK-181 in combination with an approved anti-PD-(L)1 therapy in multiple solid tumors for which anti-PD-(L)1 therapy is approved, including non-small cell lung cancer, urothelial carcinoma, clear cell renal cell carcinoma and cutaneous melanoma.
  - The primary and secondary objectives of Part B are to evaluate safety and tolerability, anti-tumor activity, PK, and ADA. Biomarkers will also be evaluated as exploratory measures.

Based on the safety and pharmacokinetic data from Part A of the DRAGON Phase 1 trial, we initiated the Part B dose expansion portion of the clinical trial, which is evaluating SRK-181 dosed 1500 mg every three weeks (Q3W) in patients receiving an approved anti-PD-(L)1 therapy dosed Q3W and 1000 mg every two weeks (Q2W) in patients receiving an approved anti-PD-(L)1 therapy dosed Q2W. Part B will enroll and dose patients in multiple proof of concept cohorts conducted in parallel. Each cohort is expected to enroll up to 40 patients with various locally advanced or metastatic solid tumors who have demonstrated primary resistance to anti-PD-(L)1 therapy. Initial efficacy and safety data are anticipated in 2022.

### **Potential Applications of SRK-181 in Additional Oncology Settings**

Furthermore, in addition to cancer immunotherapy, we believe SRK-181 has the potential for use in additional oncology settings, such as in immunotherapy-naïve patients, in combination with other therapies beyond checkpoint inhibitors and in myelofibrosis.

#### ***TGFβ1 in Fibrotic Diseases***

In December 2018, we entered into a three-year collaboration with Gilead to discover and develop therapeutics that target TGFβ-driven signaling, a central regulator of fibrosis. Under the collaboration, Gilead had exclusive options to license worldwide rights to antibodies from certain TGFβ programs being developed by us. We received \$80.0 million in proceeds upon signing the agreement and an additional \$25.0 million for a preclinical milestone achieved in December 2019 for the successful demonstration of efficacy in preclinical *in vivo* proof-of-concept studies. The collaboration period concluded on December 19, 2021 and on January 6, 2022, Gilead agreed that its option exercise period for all programs terminated which returned rights to us to a suite of antibodies with novel pharmacological profiles that were discovered over the course of the collaboration with Gilead.

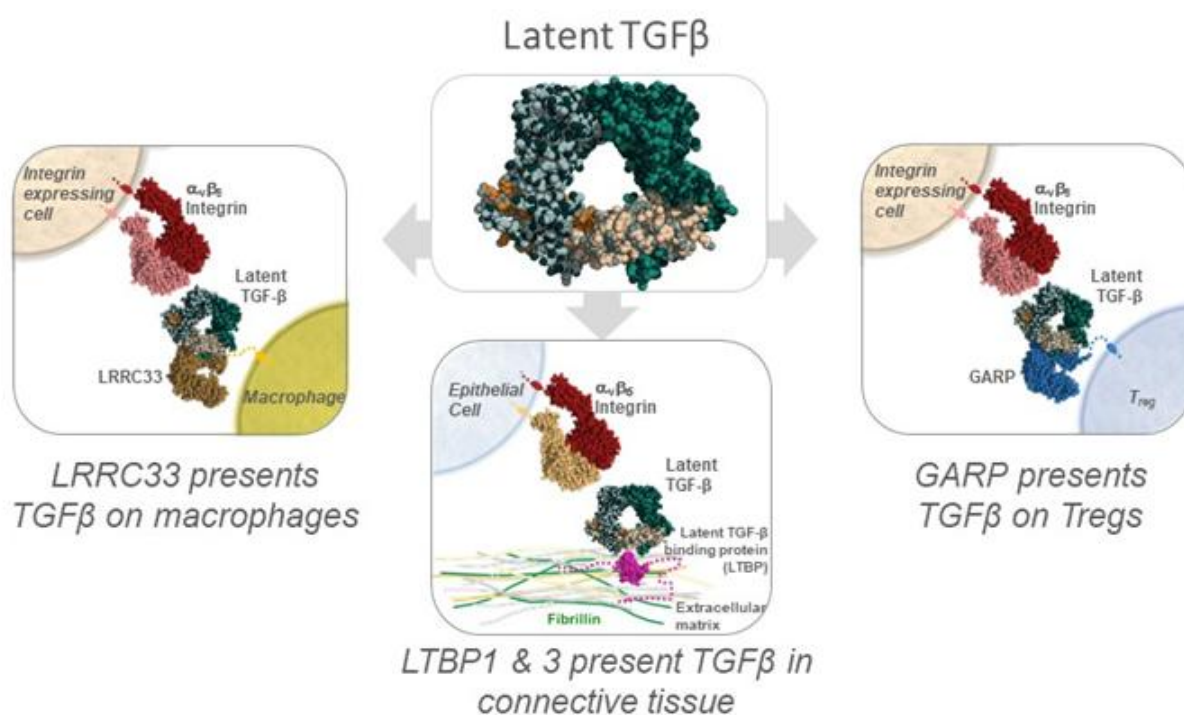
Of particular note, we have discovered antibodies that selectively inhibit the activation of latent TGFβ1 in the context of fibrotic extracellular matrix and that avoid perturbing TGFβ1 presented by cells of immune system. Such antibodies demonstrated significant antifibrotic activity in a variety of preclinical rodent models and safety at all doses tested in a non-GLP mouse safety study.

#### **TGFβ1 in Fibrosis**

Fibrosis is a pathological feature of disease which can occur in virtually all organs, characterized by excessive accumulation of extracellular matrix in the affected tissue and accounts for substantial morbidity and mortality. The TGFβ signaling pathway as a central regulator of fibrosis has been well-established. TGFβ is upregulated in many animal models of fibrosis, and overexpression of TGFβ *in vivo* induces fibrotic changes. Furthermore, TGFβ inhibition in animal models has been shown to reduce fibrosis in models of hepatic, renal and cardiac fibrosis. Additionally, fresolisumab, an inhibitor of all three TGFβ isoforms, was evaluated in an open-label clinical trial involving patients with systemic sclerosis, a fibrotic connective tissue disease. Improvement in clinical skin disease as measured by the modified Rodnan skin score, a commonly used measure of skin thickness, was observed, although bleeding episodes and other safety findings similar to those associated with non-selective TGFβ inhibition were also reported in this clinical trial. These data suggest that novel approaches to targeting TGFβ signaling may have broad applicability to the treatment of fibrotic disease, where more selective approaches may offer an improved safety profile. We have identified a suite of antibodies with anti-fibrotic activity acting through novel selectivity profiles that were discovered over the course of the collaboration including those which may have therapeutic potential for the treatment of organ fibrosis by inhibiting TGFβ1 function in connective tissue while having no impact on the activation or signaling of TGFβ1 in the immune system. We plan to continue the advancement of these assets as part of our growing preclinical pipeline

#### **Context-dependent TGFβ1 Inhibitors**

As mentioned, when latent TGFβ1 is secreted from cells, it is further associated with a third protein, referred to as a presenting molecule. The presenting molecules are covalently bound to the prodomain and serve to tether the latent TGFβ1 complex in a particular microenvironment. Unlike TGFβ1, a given presenting molecule's expression pattern is restricted to particular cellular and tissue environments. For example, the presenting molecule GARP is found primarily on regulatory T cells, the presenting molecules LTBP1 and LTBP3 are localized to the connective tissue in the extracellular matrix, and the presenting molecule LRRC33 is found primarily on certain myeloid lineage cells such as macrophages.



Using our proprietary platform, we are also able to identify antibodies that we believe selectively (i) inhibit the activation of latent TGF $\beta$ 1 both independently—our context-independent program— and (ii) selectively in the context of specific presenting molecules—our context-dependent programs—which we refer to as context-dependent inhibition. For example, we have identified antibodies that specifically bind to and inhibit the activation of GARP-presented latent TGF $\beta$ 1 on regulatory T cells with no detectable binding to latent TGF $\beta$ 1 associated with other presenting molecules. These antibodies are the subject of our license agreement with Janssen.

#### **Discovery and Preclinical Programs**

Utilizing our proprietary platform, we have multiple early stage and preclinical programs directed against targets that are known to be important in serious diseases. We are discovering and generating highly selective and differentiated monoclonal antibodies against difficult targets by 1) applying our structural insights and antibody discovery expertise, 2) prioritizing human biology, and 3) embedding translational thinking early in the research and development process.

Additional therapeutic areas and targets that we could potentially apply our scientific platform and expertise include:

- Advancing active discovery programs for context-dependent inhibitors of TGF $\beta$ 1.
- Advancing programs which selectively inhibit other TGF $\beta$  superfamily pathways such as BMPs via targeting of BMP co-receptors as controllers of iron regulation. This approach could provide the potential for tissue specific modulation of BMP signaling and iron regulation.
- Exploring opportunities in modulating metabolic physiology including understanding the important role of skeletal muscle in modulating metabolism. This is highlighted by potential therapeutic opportunity for myostatin blockade. For example, evidence is emerging that blockade of the myostatin pathway can reduce the mass of visceral fat, a significant driver of cardiometabolic pathophysiology. We have efforts underway to

evaluate these opportunities, including preclinical and translational research, development path assessments, and commercial evaluations.

- Exploring mechanisms to selectively modulate growth and survival mechanisms among multiple immune cell types which are important in human disease including plasma cells, macrophages, T cells and NK cells.
- Exploring the tumor microenvironment and its critical role in tumor initiation and progression. A major avenue of communication between tumor cells and their microenvironment is through secretion of stimulatory growth factors and via cell surface receptors for these growth factors. Through the tumor microenvironment, tumor cells can efficiently recruit stromal cells, immune cells and vascular cells which, in-turn, release further tumor growth-promoting signals to remodel tissue structures and promote pro-tumor environments.

We continue to enhance our internal biologics discovery capabilities including the use of humanized transgenic rodents as well as single-domain antibody libraries. These new capabilities allow us to more efficiently discover antibodies and furthers our commitment to building a differentiated portfolio of product candidates.

## **License Agreements**

### ***Gilead Collaboration***

On December 19, 2018 (the “Effective Date”), we entered into a three-year collaboration with Gilead to discover and develop therapeutics that target TGF $\beta$ -driven signaling, a central regulator of fibrosis (“the Collaboration Agreement”). In connection with the Collaboration Agreement, we received an upfront payment of \$50 million and an equity investment of \$30 million.

In December 2019, we achieved a \$25 million preclinical milestone under the Gilead Collaboration Agreement for the successful demonstration of efficacy in preclinical *in vivo* proof-of-concept studies.

On January 6, 2022, we entered into a letter agreement with Gilead which (i) confirmed that the collaboration period under the Collaboration Agreement had expired as of December 19, 2021, and (ii) agreed the option exercise period for all programs under the Collaboration Agreement had been terminated as January 6, 2022.

### ***License Agreement with Janssen***

On December 17, 2013, we entered into an option and license agreement with Janssen (the “Janssen Agreement”). Pursuant to the Janssen Agreement, Janssen funded our drug discovery research to identify molecules with either one or two pharmacological profiles, over a two-year period beginning on December 17, 2013 (the “collaboration period”).

Janssen exercised its option under this agreement in December 2015 to exclusively license certain collaboration molecules for one pharmacological profile, the selective inhibition of TGF $\beta$ 1 in the context of regulatory T cells, and our obligations under the program plan for the molecule and related pharmacological profile ceased and Janssen assumed full responsibility for further development of the molecules at its sole cost.

Janssen is obligated to pay us up to \$25 million upon the achievement of specified development milestones and up to \$97 million upon the achievement of specified regulatory milestones. In addition, for any licensed product, Janssen is required to pay to us up to \$130 million upon the achievement of specified annual net sales thresholds. For a period commencing on the first commercial sale of a product, on a product-by-product and country-by-country basis, until the latest to occur of (i) the expiration date of the last valid claim within the licensed patent rights covering the licensed product, (ii) the tenth anniversary date of the first commercial sale of a licensed product, or (iii) the termination or expiration of regulatory exclusivity for a licensed product, such period the royalty period, Janssen is required to pay to us, single digit percentage tiered royalties based on annual net sales thresholds.

The Janssen Agreement will expire on a country-by-country basis on the expiration of the last royalty period for a licensed product within such country. Janssen has the right to terminate the Janssen Agreement, in whole or in part, without cause upon 90 days written notice to us. In addition, either we, or Janssen may terminate the Janssen Agreement if the other party commits a material breach of the agreement and fails to cure such breach within 60 days (or 30 days in the case of a failure to make any payment) after written notice is provided, or, upon the other party's bankruptcy, insolvency, dissolution or winding up. Upon termination, any licensed product reverts to us and if Janssen has commenced clinical trials for such licensed product, upon commercialization of such licensed product, we will be required to pay Janssen single digit percentage tiered royalties on such licensed product based on annual net sales thresholds.

#### ***License Agreement with Children's Medical Corporation***

On December 17, 2013, we entered into an exclusive license agreement (the "CMCC Agreement") with Children's Medical Center Corporation ("CMCC"), to gain exclusive control over co-owned patent rights related to our platform technology. Under the CMCC Agreement, we received an exclusive worldwide license to CMCC's rights in certain patent rights jointly owned by us and CMCC, to develop and commercialize any product or process that but for the licenses granted to us under the CMCC Agreement would infringe such patent rights, a licensed product and licensed process, respectively, for any use. We are entitled to sublicense the rights granted to us under the CMCC Agreement. These licenses and rights are subject to certain limitations and retained rights, including retained rights to practice and use the patent rights for research, educational, clinical and charitable purposes. In addition, the CMCC Agreement obligates us to meeting certain diligence milestones, including obligations to raise funds, seek collaborations and initiate discovery efforts.

We must pay CMCC annual license maintenance fees of \$10,000. We will also be responsible for up to \$1.3 million of development and regulatory milestone payments through the first regulatory approval of a licensed product, tiered royalty payments of low single-digit percentages on net sales of licensed products in the event that we realize sales from products covered by the license agreement, and between 10% and 20% of non-royalty income attributable to a sublicense of the CMCC rights. Such products include products developed using our proprietary platform that are covered by a valid claim contained in any patent under the license agreement. Amounts paid to CMCC are recorded as research and development expense in the statement of operations. The royalty term will terminate on the expiration date of the last valid claim within the licensed patent rights.

CMCC may terminate the CMCC Agreement if we commit a breach of the agreement and fail to cure such breach within 60 days (or 30 days in the case of our failure to make any payment) after written notice is provided, or immediately upon our bankruptcy, insolvency, dissolution or winding up, or upon 30 days' notice if we bring patent challenges relating to any patent families licensed by us under the CMCC Agreement. In addition, we may terminate the CMCC Agreement for convenience upon three months prior written notice to CMCC. Upon expiration of the CMCC Agreement, we will have a worldwide, perpetual, irrevocable, sublicensable license to the intellectual property previously covered by the CMCC Agreement.

#### ***Adimab Agreement***

On March 12, 2019, we entered into an amended and restated collaboration agreement ("Adimab Agreement") with Adimab, LLC ("Adimab"). Under the Adimab Agreement, as amended, we selected a number of biological targets against which Adimab used its proprietary platform technology to discover and/or optimize antibodies based upon mutually agreed upon research plans, and we have the ability to select a specified number of additional biological targets against which Adimab will provide additional antibody discovery and optimization services. During the research term and evaluation term for a given research program with Adimab ("Research Program"), we have a non-exclusive worldwide license under Adimab's technology to perform certain research activities and to evaluate the program



antibodies to determine whether we want to exercise our option to obtain an exclusive license to exploit such antibodies (a “Development and Commercialization Option”).

Pursuant to the Adimab Agreement, we previously paid Adimab a one-time, non-creditable, non-refundable technology access fee. We are also obligated to make certain technical milestone payments to Adimab on a Research Program-by-Research Program basis. Upon exercise of a Development and Commercialization Option, we are obligated to pay to Adimab a non-creditable, nonrefundable option exercise fee of either (i) a low seven-digit dollar amount or (ii) a mid six-digit dollar amount, based on the antibodies in the given Research Program, plus, in either case, an amount equal to any technical milestone payment which was not previously paid with respect to such Research Program and less, in either case, any option extension fees paid with respect to such Research Program. On a Product (as defined in the Adimab Agreement)-by-Product basis, we will pay Adimab upon the achievement of various clinical and regulatory milestone events with total milestone payments not to exceed mid-teen millions in the aggregate for a given Product. For any Product that is commercialized, on a country-by-country and Product-by-Product basis, we are obligated to pay to Adimab a low-to-mid single-digit percentage of annual worldwide net sales of such Product during the applicable royalty period in each country.

SRK-181 is subject to the terms of the Adimab Agreement, and in March 2019, we exercised our Development and Commercialization Option for the Research Program from which SRK-181 was generated. In January 2020 and December 2020, we exercised our Development and Commercialization Option for additional Research Programs.

### **Intellectual Property**

Our commercial success depends in part on our ability to protect intellectual property for our product candidates, including apitegromab and SRK-181, and related methods, as well as our novel approach and proprietary platform for generating monoclonal antibodies; to secure freedom-to-operate to enable commercialization of our product candidates, if approved; and to prevent others from infringing upon our patent rights. Our policy is to seek to protect our intellectual property position by filing patent applications in key jurisdictions, including the U.S., Europe, Canada, Japan and Australia, covering our proprietary technology, inventions and improvements that are important to innovate, develop, sustain and implement our business.

We file patent applications directed to compositions comprising our antibodies, classes of antibodies covering our product candidates, use of such antibodies for treating diseases, as well as related manufacturing methods. As of January 1, 2022, we have 26 pending patent families across multiple programs. Among the pending families, 16 have been nationalized, from which 15 applications have matured into U.S. issued patents, six granted in Australia, one granted in China, one granted in Colombia, one granted in Eurasia, four granted in Europe, two granted in Israel, one granted in Hong Kong, three granted in Japan, one granted in South Korea, one granted in Mexico, one granted in Malaysia, two granted in Singapore, and one granted in South Africa. Collectively, there are 203 national or direct utility applications pending or issued. In addition, there are seven patent family filings which are in the priority year. We continue to review and harvest new inventions for new patent filings.

Two granted patents, EP2981822 and EP3368069, are currently the subject of ongoing opposition proceedings before the European Patent Office (“EPO”). We have no other contested proceedings relating to any patents at this time, but we cannot provide any assurances that we will not have such proceedings at a later date. For more information regarding the risks related to our intellectual property, please see “Risk factors—Risks Related to Our Intellectual Property.”

### **Ownership and IP Rights**

Our earliest patent family, PCT/US2013/068613 (published as WO 2014/074532), is jointly owned by us and CMCC. CMCC is the assignee of the intellectual property rights transferred from two of our co-founders, Drs. Timothy A.

Springer and Leonard I. Zon. The portion of rights owned by CMCC is exclusively licensed to us. We are the sole legal owner of all subsequent patent families we have to date.

As described, a portion of our TGF $\beta$  technology is out-licensed to Janssen. This is carved out as PCT/US2017/042162 (published as WO 2018/013939), which has been nationalized. The licensee takes lead in the prosecution of this patent family. The licensee also has a non-exclusive license to our platform technology to enable their development in the licensed field.

Brief descriptions of our patent families are provided below, with projected patent terms excluding any possible patent term adjustments or extensions.

### **Platform**

Our novel approach to generating selective modulators of supracellular activation of growth factors is broadly embodied in our two earliest “platform” patent families, PCT/US2013/068613 (published as WO 2014/074532) and PCT/US2014/036933 (published as WO 2014/182676). These patent families are directed to methods for modulating the activation of the TGF $\beta$  superfamily of growth factors and methods for screening for a monoclonal antibody that specifically targets an inactive form of the growth factor, thereby preventing activation (e.g., release) of mature growth factor. The TGF $\beta$  superfamily is a group of more than 30 related growth factors/cytokines that mediate diverse biological processes and includes TGF $\beta$ 1 and myostatin (also known as GDF-8). Issued U.S. patents in the platform families include: U.S. Patents Nos. 9,573,995 (issued 02/21/2017); 9,758,576 (issued 09/12/2017); 9,580,500 (issued 02/28/2017); 9,399,676 (issued 07/26/2016); 9,758,577 (issued 09/12/2017); 10,597,443 (issued 03/24/2020); and 10,981,981 (04/20/2021). There is also a granted European (“EP”) platform patent: EP2981822 (granted on 09/02/2020), which was validated in 37 states. These US and EP patents are projected to expire in 2034.

Specifically, EP2981822 has granted composition of matter claims directed to an antibody capable of binding a recombinant antigen comprising pro-TGF $\beta$ 1 or a growth factor-prodomain complex which comprises the TGF $\beta$ 1 LAP complex, in addition to claims directed to methods of making such antibodies. EP2981822 is currently the subject of ongoing opposition proceedings before the EPO.

U.S. Patent No. 9,573,995 has issued composition of matter claims directed to an antibody that specifically binds to GARP associated with a human TGF $\beta$ 1 LAP complex.

U.S. Patent No. 9,758,576 has issued composition of matter claims directed to an isolated monoclonal antibody, or a fragment thereof, that specifically binds the prodomain of a pro/latent GDF-8/myostatin complex, thereby preventing proteolytic cleavage between residues Arg 75 and Asp 76 of GDF-8/myostatin prodomain, so as to inhibit the release of mature GDF-8/myostatin growth factor from the complex.

U.S. Patent No. 9,580,500 has issued claims directed to phage display library-based antibody production methods for identifying an antibody that binds a GARP/proTGF $\beta$ 1 complex.

U.S. Patent No. 9,399,676 has issued claims directed to phage display library-based antibody production methods for identifying an antibody that binds a pro/latent GDF-8 complex that has been subjected to enzymatic cleavage. Related product-by-process claims are included in issued U.S. Patent No. 9,758,577.

U.S. Patent No. 10,597,443 has issued with claims that broadly cover manufacturing methods for a pharmaceutical composition containing an antibody that binds a large latent complex of TGF $\beta$ , thereby modulating TGF $\beta$  signaling.

In addition, U.S. Patent No. 10,981,981 has issued with claims that broadly cover manufacturing methods for a pharmaceutical composition containing an antibody that binds pro/latent GDF-8, but does not bind to mature GDF-8, and inhibits GDF-8 signaling.



### ***Myostatin Activation Inhibitors***

Seven patent families have been filed to date to cover proprietary myostatin inhibitors and their use in the treatment of various muscle and metabolic diseases. Patent prosecution of these pending patent families is ongoing but relatively early.

Two families are directed to composition of matter claims that cover our proprietary antibodies. PCT/US2015/059468 (published as WO 2016/073853) broadly covers a class of monoclonal antibodies that specifically bind inactive precursors thereby preventing activation of myostatin. This patent family is projected to expire in November 2035. U.S. Patents 10,307,480 and 11,135,291 have issued in June 2019 and October 2021, respectively, with issued claims directed to Scholar Rock proprietary antibodies that specifically bind pro/latent myostatin, including 29H4, the parental clone of apitegromab, and variants, as well as methods of making antibodies with pH sensitive binding to pro/latent myostatin. A second family, PCT/US2016/052014 (published as WO 2017/049011), discloses the specific amino acid sequence of apitegromab and is projected to expire in September 2036. U.S. Patent 10,751,413 issued in August 2020, with claims directed to antibodies and pharmaceutical compositions comprising the heavy and light chain sequences of apitegromab. The European counterpart also granted as EP 3350220 B1 in May 2021. The granted claims relate to antibodies comprising the heavy and light chain variable region sequences of apitegromab, and pharmaceutical compositions of the antibodies.

The following three patent families are directed to therapeutic uses/methods:

PCT/US2017/012606 (published as WO 2017/120523) broadly covers treatment methods for a number of muscle and neuromuscular disease and disorders using an antibody that specifically blocks the activation step of myostatin. The related U.S. application issued in May 2019 as U.S. Patent 10,287,345 and is projected to expire in September 2036. The issued claims are drawn to methods for inhibiting myostatin activation using our proprietary activation inhibitors (such as apitegromab) to cause specified pharmacological effects to treat a variety of conditions including, muscle and metabolic disorders. A second U.S. application issued as U.S. Patent 10,882,904 in January 2021. The issued claims recite methods for inhibiting myostatin activation using an antibody comprising the heavy and light chain sequences of apitegromab for various indications.

PCT/US2017/037332 (published as WO 2017/218592) is directed to methods for treating neuromuscular diseases and selecting patient populations that are likely to respond to myostatin inhibition. This filing includes the treatment of SMA in patients who are on an SMN corrector therapy (e.g., SMN upregulators). This patent family is projected to expire in June 2037. The PCT application was nationalized in 11 jurisdictions, and applications in the three key jurisdictions (i.e., U.S., Europe and Japan) have granted. Specifically, the U.S. application granted in May of 2021. The granted claims are directed to add-on or combination therapy for treating spinal muscular atrophy with a myostatin inhibitor and a neuronal corrector (such as smn upregulator therapy). Similar claims have also granted in Japan (JP Patent No. 6823167). Likewise, the European counterpart granted as EP 3368069B1, and has been validated in 37 states. The granted European claims are directed to add-on therapy and combination therapy for the treatment of SMA using a myostatin-selective inhibitor, in conjunction with an SMN corrector therapy. EP 3368069B1 is currently the subject of ongoing opposition proceedings before the EPO.

PCT/US2018/012686 (published as WO 2018/129395) relates to the treatment of metabolic diseases with a myostatin activation inhibitor and is projected to expire in January 2038. The PCT was nationalized in 2019 and is in the early stages of prosecution. A US patent issued in October of 2021 as US 11,155,611, with claims directed to methods of making a pharmaceutical composition comprising a myostatin-selective inhibitor, comprising screening for an antibody that is capable of decreasing expression of pyruvate dehydrogenase kinase 4 (PDK4) and increasing expression of pyruvate dehydrogenase phosphatase 1 (PDP1).

In addition to the five pending patent families listed above, there is also a recently-filed PCT application directed to inventions deriving from the phase 2 clinical trial of apitegromab. Moreover, issued claims of U.S. Patent 9,758,576 from the platform patents discussed in detail above cover monoclonal antibodies that selectively inhibit myostatin signaling by blocking the proteolytic activation of latent myostatin. These issued composition of matter claims provide

protection for our first antibody apitegromab, as well as any other monoclonal antibodies that work by this unique mechanism of action. This patent expires in May 2034, not including any potential patent term extension.

### ***TGFβ1 Activation Inhibitors***

In addition to the patent families discussed above in the “*Intellectual Property-Platform*” section that generically cover certain aspects of the TGFβ1 program, thirteen patent families have been filed to date, covering various specific aspects of our TGFβ1 program.

Isoform-specific inhibitors of TGFβ1 which confer improved safety profile and related methods are described in PCT/US2017/021972 (published as WO 2017/156500). This family is projected to expire in March 2037. Among TGFβ1 inhibitors, one of our context-independent antibodies is separately claimed and related preclinical data are described in PCT/US2018/012601 (published as WO 2018/129329). This patent application is projected to expire in January 2038.

In addition, high-affinity, isoform-selective TGFβ1 inhibitors are disclosed in PCT/2019/041373 (published as WO US2020/014460). Patents of this family are projected to expire in 2039. Separately, three direct national/regional applications covering related subject matter have been filed, in the U.S., Europe and Hong Kong, and are projected to expire in 2039. A US patent issued in September of 2021 as US 11,130,803, with claims which cover the SRK-181 clinical candidate and pharmaceutical compositions thereof; and a European patent issued in November of 2021 as EP3677278, with claims that cover the SRK-181 clinical candidate, pharmaceutical compositions, use for treating cancer and myelofibrosis, and methods for manufacturing. Additionally, PCT/US2021/012969 (published as WO 2021/142448) discloses data related to biomarkers for the high-affinity, isoform-selective TGFβ1 inhibitors and is projected to expire in 2041. Antibodies claimed in these patent families protect our SRK-181 clinical candidate.

Separately, other improved isoform-selective, context-independent inhibitors of TGFβ1 are disclosed in PCT/US2019/041390 (published as WO 2020/014473). This family is projected to expire in 2039. PCT/US2021/12930 (published as WO 2021/142427) is directed to optimized isoform-selective, context-independent inhibitors of TGFβ1. This family is projected to expire in 2041.

LTBP complex-specific inhibitors of TGFβ1 are described in two patent families: PCT/US2018/44216 (published as WO 2019/023661) which is expected to expire in July of 2038; and PCT/US2020/15915 (published as WO2020/160291), which is expected to expire in 2040. A US patent has been allowed in the second patent family with claims directed to antibodies and pharmaceutical compositions.

LRRC33-specific inhibitors are described in a further patent family: PCT/US2018/031759 (published as WO 2018/208888) which is expected to expire in May of 2038. A second patent family has been filed and is in the priority year, which will be converted to international patent application (PCT) in July of 2022.

PCT/US2017/042162 (published as WO 2018/013939) is a collaboration patent family exclusively licensed to Janssen. This patent family covers antibodies that specifically inhibit GARP-associated TGFβ, and is projected to expire in July 2037. Janssen takes prosecution lead in this case.

Finally, four other TGFβ patent families have been filed and are in the priority year.

### ***RGMc-Selective Inhibitors***

PCT/US2019/57687 (published as WO2020/86736) is directed to RGMc-selective inhibitors and will expire in 2039. A second family has been filed and is in the priority year, which will be converted to international patent application (PCT) in October of 2022.

### ***Intellectual Property Protection***

We cannot predict whether the patent applications we pursue will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide any proprietary protection from competitors. Even if our pending patent applications are granted as issued patents, those patents, as well as any patents we license from third parties, may be challenged, circumvented or invalidated by third parties. As mentioned above, two granted patents, EP2981822 and EP3368069, are currently the subject of ongoing opposition proceedings before the EPO. While there are currently no contested proceedings or third-party claims relating to any of the other patents described above, we cannot provide any assurances that we will not have such proceedings or third-party claims at a later date.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the U.S., the patent term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during FDA regulatory review process. The Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug or biologic may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug or biologic or provide an additional period of protection for the approved pharmaceutical product following expiry of the patent. In the future, if our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the U.S. Patent and Trademark Office in the U.S. and the national patent offices in Europe, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

In addition to our reliance on patent protection for our inventions, product candidates and research programs, we also rely on trade secret protection for our confidential and proprietary information. For example, certain elements of our proprietary platform may be based on unpatented trade secrets that are not publicly disclosed. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

### **Manufacturing**

We do not own or operate facilities for clinical drug manufacturing, storage, distribution or quality testing. Currently, all of our clinical manufacturing is outsourced to third-party manufacturers. As our development programs expand and we build new process efficiencies, we expect to continually evaluate this strategy with the objective of satisfying demand for registration trials and, if approved, the manufacture, sale and distribution of commercial products.

## **Antibody Discovery**

We have built and internalized antibody display and discovery capability, however at times we may continue to rely on third parties to conduct antibody discovery and optimization based on criteria and specifications provided by us. Certain antibody discovery and optimization vendors require us to enter into a license with them for the right to use antibodies discovered by them in humans or for commercial purposes. Such license could include substantial milestone payments and royalties to the extent we choose to use an antibody discovered by such vendor. On March 12, 2019, we exercised an option to receive such a license from Adimab pursuant to our Adimab Agreement. Please see the description above in “License Agreements – Adimab Agreement” for more details on the terms of this agreement.

## **Competition**

The biotechnology and pharmaceutical industries are characterized by rapid evolution of technologies, fierce competition, and strong defense of intellectual property. While we believe that our product candidates, discovery programs, technology, knowledge, experience and scientific resources provide us with competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others.

Any product candidates that we successfully develop and commercialize could compete with currently approved therapies and new therapies that may become available in the future. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our products.

In the SMA market, there are three approved SMN-directed treatments and no approved muscle-directed treatments for SMA to date. We believe that it will take several treatment approaches to holistically treat SMA. The SMA drug development pipeline reflects that, wherein existing companies are looking to enhance their current offering or SMA portfolio, newer companies to the field, such as Scholar Rock, are researching novel approaches to target systems and processes adversely impacted by SMA to help slow the disease progression.

In October 2021, Roche announced the initiation of a Phase 2/3 clinical trial to investigate RO7204239, an anti-myostatin antibody targeting the muscles in SMA patients. This announcement follows the approval of Roche’s SMN directed treatment. We may face direct competition from products within the muscle-directed therapy category in the future as the SMA market evolves to these new treatment approaches.

In terms of indirect competition, existing companies like Novartis continue plans to study an alternate formulation of their existing gene therapy (OAV101) after a partial clinical trial hold last year. Biogen continues expanding their SMA pipeline with the recent licensing of another antisense oligonucleotide (BIIB115) that may have the potential for extending dosing intervals, in addition to their Phase 1 investigational agent (BIIB110) that is intended to work in part through inhibition of the myostatin signaling pathway. In addition, Cytokinetics, Inc. has completed a Phase 2 clinical trial with reldesemtiv, a fast-skeletal muscle troponin activator (“FSTA”) in SMA.

Our competitors for SRK-181 may include other companies developing cancer immunotherapies to be used in combination with CPI therapy. Novartis’s NIS793, an anti-TGF- $\beta$  IgG2 monoclonal antibody licensed from Xoma, is currently in a Phase 3 clinical trial for the treatment of metastatic pancreatic ductal carcinoma (mPDAC) in combination with chemotherapy as well as multiple early-stage clinical studies in a variety of solid tumor types and myelofibrosis.

Other companies, including Merck KGaA, Merck (acquired Tilos Therapeutics), Roche, Sanofi S.A., Bristol Meyers Squibb (acquired Forbuis), Gilead and AbbVie Inc. are developing therapies for cancer immunotherapy in combination with CPI therapy, that are intended to work, at least in part, through inhibition of the TGF $\beta$  signaling pathway.

Our competitors may also include companies that are or will be developing therapies for the same therapeutic areas that we are targeting within our early pipeline, including other neuromuscular disorders, cancer and fibrosis.

Many of the companies against which we may compete have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products. These competitors also compete with us in recruiting and retaining

qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

### **Government Regulation**

Government authorities in the U.S. at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, such as apitegromab, SRK-181 and any future product candidates. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

#### ***U.S. Biological Product Development***

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (“FDCA”), and its implementing regulations and biologics under the FDCA, the Public Health Service Act (“PHSA”), and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA’s refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Apitegromab, SRK-181, and any future product candidates regulated as biologics must be approved by the FDA through a Biologics License Application (“BLA”), process before they may be legally marketed in the U.S. The process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice (“GLP”) requirements;
- Manufacture of drug substance and drug product in accordance with applicable regulations, including manufacturing activities performed in accordance with good manufacturing practice (“GMP”) requirements;
- Submission to the FDA of an investigational new drug (“IND”) application, which must become effective before human clinical trials may begin;
- Approval by an institutional review board (“IRB”) or independent ethics committee at each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice (“GCP”) requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission of a BLA to the FDA;
- A determination by the FDA within 60 days of its receipt of a BLA to accept the filing for review;

- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the biologic will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the biologic's identity, strength, quality and purity;
- Potential FDA audit of the clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the biologic in the U.S.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for apitegromab, SRK-181 and any future product candidates will be granted on a timely basis, or at all.

### ***Preclinical Studies and IND***

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies.

An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin. Some long-term preclinical testing may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

### ***Clinical Trials***

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all patients provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may be combined or overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate.
- Phase 2 clinical trials generally involve studies in disease-affected patients to evaluate proof of concept and/or determine the dosing regimen(s) for subsequent investigations. At the same time, safety and further PK and PD information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

#### ***FDA Review Process***

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational



product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the U.S.

Under the Prescription Drug User Fee Act (“PDUFA”) as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted BLAs before it accepts them for filing, and may request additional information rather than accepting the BLA for filing. The FDA must make a decision on accepting a BLA for filing within 60 days of receipt, and such decision could include a refusal to file (“RTF”) by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth review of the BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months, from the filing date, in which to complete its initial review of an original BLA and respond to the applicant, and six months from the filing date of an original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates a BLA, it will issue an Approval Letter or a Complete Response Letter. An Approval Letter authorizes commercial marketing of the biologic with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

### ***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making the product available in the U.S. for this type of disease or condition will be recovered from sales of the product.

After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan



exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if our product is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union ("EU") has similar, but not identical, requirements and benefits.

### ***Rare Pediatric Disease Designation***

The FDA grants Rare Pediatric Disease designation for serious and life-threatening diseases that primarily affect children ages 18 years or younger and fewer than 200,000 individuals in the United States. Eligibility for a priority review voucher may be issued upon approval of a biologics license application ("BLA") or New Drug Application for therapies developed to treat such rare pediatric diseases. Priority review vouchers may be redeemed to obtain priority review for any subsequent marketing application or be sold or transferred.

### ***Expedited Development and Review Programs***

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that meet certain criteria. Specifically, new drugs and biologics are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for Fast Track status any time before receiving BLA approval, but ideally no later than the pre-BLA meeting. Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biologic designated for priority review in an effort to facilitate the review.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM"), that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, for products being considered for accelerated approval, the FDA currently requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period. If the FDA concludes that a drug or biologic shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the product. If the FDA determines that the conditions of approval are not being met, the FDA can withdraw its accelerated approval for such drug or biologic.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as Fast Track designation, plus intensive guidance from the FDA to ensure an efficient drug development program.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

### ***Pediatric Information***

Under the Pediatric Research Equity Act (“PREA”), as amended, a BLA or supplement to a BLA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (“PSP”) within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

### ***Post-marketing Requirements***

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as “off-label use”) and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. Prescription drug and biologic promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy (“REMS”) to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Newly discovered or developed safety or effectiveness data may require changes to a drug’s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, including a REMS or the conduct of post-marketing studies to assess a newly discovered safety issue. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws, as well as applicable tracking and tracing requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved BLA, including recall.

### ***Other Regulatory Matters***

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the U.S. in addition to the FDA, including the Centers for Medicare & Medicaid Services (“CMS”), other divisions of the Department of Health and Human Services (“HHS”), the Department of Justice, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

### ***Other Healthcare Laws***

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. In the U.S., these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

- The Anti-Kickback Statute, which makes it illegal for among other things, any person or entity, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by individual imprisonment, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.
- The federal civil and criminal false claims laws, including the False Claims Act (“FCA”), which prohibits individuals or entities (including prescription drug manufacturers) from knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government. The government may deem manufacturers to have “caused” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off label. Claims which include items or services resulting from a violation of the Anti-Kickback Statute are false or fraudulent claims for purposes of the FCA. Our future marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our product and any future product candidates, are subject to scrutiny under these laws.
- The Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which created additional federal criminal statutes that prohibit among other things, knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and their respective implementing regulations, which impose, among other things, specified requirements on covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates, which include individuals or entities that perform services for covered entities involving the creation, use, maintenance or disclosure of, individually identifiable health information, relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.
- The U.S. Physician Payments Sunshine Act (the “Sunshine Act”), enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the “ACA”), which impose new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program, for certain payments and “transfers of value” provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), non-physician providers (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope and apply regardless of payor. Such laws are enforced by various state agencies and through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant federal government compliance guidance, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and restrict marketing practices or require disclosure of marketing expenditures. Some state and local laws require the registration of pharmaceutical sales representatives.
- Many states in which we operate have laws that protect the privacy and security of sensitive and personal information. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts. Where state laws are more protective than HIPAA, we must comply with the state laws we are subject to, in addition to HIPAA. In certain cases, it may be necessary to modify our planned operations and procedures to comply with these more stringent state laws. Further, in some cases where we process sensitive and personal information of individuals from numerous states, we may find it necessary to comply with the most stringent state laws applicable to any of the information. For example, the California Consumer Privacy Act (the “CCPA”), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households, went into effect on January 1, 2020. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General will commence enforcement actions against violators beginning July 1, 2020. While there is currently an exception for protected health information that is subject to HIPAA, as currently written, the CCPA may impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is

possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, disgorgement, exclusion of drugs from participation in state and federal healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time and resource consuming and can divert a company's attention from the business.

### ***Current and Future Healthcare Reform Legislation***

In the U.S. and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

In the U.S., for example, in March 2010, the ACA was enacted. The ACA, among other things:

- subjects biological products to potential competition by lower cost biosimilars;
- addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations;
- establishes annual fees and taxes on manufacturers of certain branded prescription drugs;
- expands healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, establishes new government investigative powers and enhanced penalties for non-compliance;
- creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% as of January 1, 2019, pursuant to the Bipartisan Budget Act of 2018) point of sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expands eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expands the entities eligible for discounts under the PHS Act's pharmaceutical pricing program, also known as the 340B Drug Pricing Program;
- creates new requirements to report financial arrangements with physicians and teaching hospitals, commonly referred to as the Physician Payments Sunshine Act;

- creates a new requirement to annually report the identity and quantity of drug samples that manufacturers and authorized distributors of record provide to physicians;
- creates a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishes the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Some of the provisions of the ACA have been subject to judicial challenges as well as efforts to repeal, replace or otherwise modify them or to alter their interpretation or implementation. For example:

- The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Selection Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation’s automatic reduction to several government programs. In concert with subsequent legislation, this includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2030. However, pursuant to the Coronavirus Aid, Relief and Economy Security Act (“CARES Act”), and subsequent legislation, these Medicare sequester reductions will be suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Then, a 1% payment reduction will occur beginning April 1, 2022 through June 30, 2022, and the 2% payment reduction will resume on July 1, 2022.
- The American Taxpayer Relief Act of 2012 reduced Medicare payments to several types of health care providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years, among other things.
- The Tax Cuts and Jobs Act of 2017 (“Tax Act”), includes a provision that eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, commonly referred to as the “individual mandate,” effective January 1, 2019.
- The Bipartisan Budget Act of 2018 (“BBA”), among other things, amends the Medicare statute, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole” by raising the manufacturer discount under the Medicare Part D coverage gap discount program to 70% (as of January 1, 2019).
- In 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.
- In addition to these legislative efforts, on June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court’s decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021, which was subsequently extended through August 15, 2021, during which consumers can enroll in coverage (or adjust existing enrollment) in states with marketplaces served by the HealthCare.gov platform. State-based marketplaces operating their own platform have the option to take similar actions in their states. The executive order also directed certain federal agencies to review and



reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Additional legislative challenges, regulatory changes and judicial challenges related to the ACA remain possible.

Additionally, there has been increasing legislative, regulatory, and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

- At the federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration’s policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs the HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA’s implementing regulations.
- In addition, on November 20, 2020, CMS issued an interim final rule to implement a “Most Favored Nation” demonstration project to test Medicare Part B reimbursement of certain separately payable drugs or biologics identified by CMS as having the highest annual Medicare Part B spending via an alternative payment methodology based on international reference prices. However, on December 29, 2021 CMS rescinded the Most Favored Nations rule.
- Additionally, on November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026.

Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

In addition, there have been changes related to Medicare Part B reimbursement for drugs purchased under the 340B drug pricing program. In 2018, CMS implemented a reduction in reimbursement for Medicare Part B drugs obtained under the 340B program from Average Sales Price (ASP) +6% to ASP -22.5%. This reduction has been challenged in federal court, and in July 2021 the Supreme Court has agreed to hear this case. CMS has indicated that it will continue to evaluate Medicare Part B reimbursement for 340B-purchased drugs.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including by imposing price or patient assistance constraints, restrictions on certain product access, marketing cost disclosure and other transparency measures, and, in some cases, measures designed to encourage importation of pharmaceutical products from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will



be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

#### ***Packaging and Distribution in the U.S.***

If our products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

#### ***Other U.S. Environmental, Health and Safety Laws and Regulations***

We may be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

#### ***U.S. Patent Term Restoration and Marketing Exclusivity***

Depending upon the timing, duration and specifics of FDA approval of apitegromab, SRK-181 and any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch Waxman Amendments. The Hatch

Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

An abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009 ("BPCI Act"). This amendment to the PHS Act, in part, attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the U.S. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA issued "Written Request" for such a trial.

### **European Union Drug Development**

In the EU, our future products also may be subject to extensive regulatory requirements. As in the U.S., medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the U.S., the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

In April 2014, the EU adopted the Clinical Trials Regulation EU No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The main characteristics of the new Clinical Trials Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However,

overall related timelines will be defined by the Clinical Trials Regulation. The Clinical Trial Regulation will have a transition period of three years from the date it became effective.

In the EU the Pediatric Committee (“PDCO”) of the EMA must approve the pediatric investigation plan (“PIP”) prior to filing a Marketing Authorization Application (“MAA”), unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP. The PIP outlines the pharmaceutical company’s strategy for investigation of the new medicinal product in the pediatric population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the EC, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of any supplementary protection certificate (“SPC”), provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to 2 years before the SPC expires. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

#### ***European Union Expedited Review and Development***

PRIME, or PRIority MEDicine, is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need and provides accelerated assessment of products representing substantial innovation where the MAA will be made through the centralized procedure. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a major therapeutic advantage over existing treatments or benefits patients without treatment options. Products from small-and medium-sized enterprises (“SMEs”) may qualify for earlier entry into the PRIME scheme than larger companies. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. The receipt of PRIME designation does not change the standards for approval but may expedite the development or approval process. Where, during the course of development, a product no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

#### ***European Union Drug Marketing***

Much like the Anti-Kickback Statute prohibition in the U.S., the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is typically governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician’s employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

#### ***European Union Drug Review and Approval***

In the EU, medicinal products can only be commercialized after obtaining a Marketing Authorization (“MA”). There are two types of MAs.

Centralized MAs, which are issued by the EC through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use (“CHMP”) of the EMA, are valid throughout the EU, and in the additional Member States (Iceland, Liechtenstein and Norway) of the EEA. The centralized procedure is mandatory for certain

types of products, such as medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (i.e., gene therapy, somatic cell therapy or tissue engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the EU Member States and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU Member State, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the reference Member State (“RMS”). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics (“SmPC”), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU Member States make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

A paediatric-use marketing authorization (“PUMA”) is available for medicines which are already authorized, no longer covered by an SPC or patent that qualifies as an SPC and which are to be exclusively development for use in children. A PUMA is a dedicated MA covering the indication and formulation of a medicinal product developed exclusively for use in the paediatric population, where such development has been in accordance with an approved PIP. There are various incentives to apply for a PUMA, including access to the centralized procedure even where the product would otherwise fall outside the mandatory scope of this procedure.

#### ***European Union Data and Market Exclusivity***

In the EU, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity, if granted, prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator’s preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted, and the innovator’s data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained an MA based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

### ***European Union Orphan Designation and Exclusivity***

In the EU, the EMA's Committee for Orphan Medicinal Products ("COMP"), grants orphan designation to promote the development of products that are (1) intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (2) either (a) affecting no more than five in 10,000 persons in the EU when the application is made, or (b) where it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or, if a method exists, the product would be a significant benefit to those affected by the condition.

In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal product approval during which time no "similar medicinal product" may be placed on the market. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This period may be reduced to six years if the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan designation must be requested before submitting an application for marketing approval. We will be required to apply for the maintenance of the orphan designation granted to apitegromab for the treatment of SMA at the time of applying for an MA. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the EU Member States, plus Norway, Liechtenstein and Iceland.

### ***European General Data Protection Regulation***

Since we conduct clinical trials in the EEA, we are subject to additional European data privacy laws. The General Data Protection Regulation, (EU) 2016/679 ("GDPR"), became effective on May 25, 2018, and deals with the processing of personal data and on the free movement of such data. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal data (such as health and other sensitive data,) relating to identifiable individuals and transferring such information outside the EEA, including to the U.S., providing details to those individuals regarding the processing of their personal information, keeping personal information secure, obtaining consent of the individuals to whom the personal data relates, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Given the limited enforcement of the GDPR to date, we face uncertainty as to the exact interpretation of the new requirements on our trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

National laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, thereby implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty. In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR

ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

In the event we continue to conduct clinical trials in the EEA, we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA, in particular to the U.S., in compliance with European data protection laws. On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU/EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU/EEA (and not subject to the GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the EU Data Protection Directive. The UK is not subject to the EC's new standard contractual clauses but has published a draft version of a UK-specific transfer mechanism, which, once finalized, will enable transfers from the UK. Following a ruling from the Court of Justice of the European Union, in *Data Protection Commissioner v Facebook Ireland Limited and Maximilian Schrems* ("Schrems II"), Case C-311/18 ("Schrems II"), companies relying on standard contractual clauses to govern transfers of personal data to third countries (in particular the United States) will need to assess whether the data importer can ensure sufficient guarantees for safeguarding the personal data under GDPR. This assessment includes assessing whether third party vendors can also ensure these guarantees. We will be required to implement these new safeguards when conducting restricted data transfers under the EU and UK GDPR and doing so will require significant effort and cost. We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or pharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national clients or pharmaceutical partners to continue to use our products and solutions due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or pharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

### **Regulation in the United Kingdom**

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit, and the UK formally left the EU on January 31, 2020. There was a transition period during which EU pharmaceutical laws continued to apply to the UK, which expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently largely aligns with EU regulations, however it is possible that these regimes will diverge in the future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

### **Clinical Trials**

The UK has implemented the now repealed Clinical Trials Directive 2001/20/EC into national law through the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended). The extent to which the regulation of



clinical trials in the UK will mirror the new Clinical Trials Regulation that has come into effect is not yet known, however the Medicines and Healthcare products Regulatory Agency (“MHRA”), the UK medicines regulator, has opened a consultation on a set of proposals designed to improve and strengthen the UK clinical trials legislation. Such consultation is open until 14 March 2022.

### **Orphan Designation**

Since January 1, 2021, a separate process for orphan drug designation to the EU process has been applied to Great Britain. There is now no pre-marketing authorization orphan designation (as there is in the EU) in Great Britain and the application for orphan designation will be reviewed by the MHRA at the time of an application for a UK or Great Britain MA. The criteria for orphan designation remain the same as in the EU, except that they apply to Great Britain only (e.g., there must be no satisfactory method of diagnosis, prevention or treatment of the condition in Great Britain, as opposed to the EU).

### **Rest of the World Regulation**

For other countries outside of the UK, the EU and the U.S., such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### **Additional Laws and Regulations Governing International Operations**

If we further expand our operations outside of the U.S., we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act (“FCPA”) prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the U.S., it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The U.S. Securities and Exchange Commission (“SEC”) also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA’s accounting provisions.



## Coverage and Reimbursement

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition.

In the U.S. no uniform policy of coverage and reimbursement for drugs or biological products exists, and one payor's determination to provide coverage and adequate reimbursement for a product does not assure that other payors will make a similar determination. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products candidates, if approved, will be made on a payor by payor basis. The level of coverage and reimbursement for products can differ significantly from payor to payor. One payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. Decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products candidates, if approved, will be made on a payor by payor basis. The coverage determination process may be a time consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs.

A third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. The containment of healthcare costs has become a priority of federal, state and foreign governments and payors, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products.

Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Additional federal programs apply to pharmaceutical companies that affect coverage and reimbursement for drug products. For example, the Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price ("AMP") to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, creating a new method by which rebates owed by are calculated for drugs that are inhaled, infused, instilled, implanted or injected, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of

Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the “MMA”) established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children’s hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low priced and high priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the U.S. and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries.

## Human Capital

Our employees are relentlessly focused on the discovery and development of innovative medicines in which signaling by protein growth factors plays a fundamental role. Our people are our most important asset, embodying our values such as discovering the joy in science, in collaboration and in making a difference in the lives of patients, families and our communities. We are guided by our core values to create a collaborative, flexible, agile, empowering, and silo-free culture so that we can move with speed and urgency to deliver high-impact medicines to patients with devastating diseases.

**Employees.** As of March 1, 2022, we had 145 full-time employees, of which 110 employees are engaged in research and development activities and 35 are engaged in general and administrative activities. All of our employees are based in the U.S. and a majority are based in Massachusetts. During 2021, we enhanced our capabilities by adding 23 new full-time employees. The new employees were hired to support a variety of functions and key initiatives, including extending our research, clinical and pre-clinical pipeline development, with hires in clinical development and operations, research, and general and administrative functions. We anticipate continuing to add depth and new capabilities in key areas of our business. None of our employees is represented by a labor union or covered by a collective bargaining agreement, and we believe our relationship with our employees is good.

**Career Development and Growth.** We emphasize employee development and training. To empower employees to unleash their potential individually and as a team, we invest in our employees by providing development opportunities, and the necessary resources to support their success, including coaching, management and leadership training, presentation workshops and paid conference attendance. The diversity of our employees and their skillsets also offers a unique opportunity for us to learn from each other's experiences.

**Compensation and Benefits.** Our competitive compensation programs are designed to align the compensation of our employees with our performance and to provide the proper incentives to attract, retain and motivate employees to achieve superior results. The structure of our compensation programs balances incentive earnings for both short-term and long-term performance. We provide employee salaries that are competitive within our industry based on position, skill level, experience and knowledge. Additionally, we offer equity to each of our employees to align the interests of our employees with the company's mission.

We are committed to providing comprehensive benefit options and it is our intention to offer benefits that will allow our employees and their families to live healthier and more secure lives. Some examples of the benefits we offer are: medical insurance including prescription drug benefits, dental insurance, vision insurance, accident insurance, life insurance, disability insurance, health savings accounts, flexible spending accounts, wellness programs, access to mental health support and benefits, identity theft insurance and pet insurance.

**Employee Engagement.** We routinely conduct confidential employee engagement surveys to obtain feedback on a variety of topics, including culture, values, diversity and inclusion, career development, employee satisfaction and tenure, and execution of our company strategy. These survey results are reviewed by our executive team so that we can continue to continue to increase employee satisfaction and improve the well-being of our employees. We value and encourage fostering mechanisms and opportunities for two-way dialogue. We actively strive to operationalize feedback provided by employees in ways that align with our business and culture. We are also committed to communication and transparency, using multiple forums and channels to allow for the sharing of appropriate, timely information to all employees.

**Health & Safety.** Ensuring the safety and wellbeing of our employees and communities is of the utmost importance to us, particularly in light of COVID-19. What we have seen as a result of the pandemic is that flexibility is top of mind and a key consideration. At the start of the pandemic, we immediately formed a task force to keep up to date on federal, state and local mandates as well as the evolving science and communicate with our employees on a regular basis. We've offered daily onsite testing, masks at no cost to our employees and visitors and when necessary, conduct internal contract tracing.

The need to shift to working from home, has refocused our work model. We've helped employees set up home offices, provided them access to tools to perform their jobs remotely, provided ergonomic assessments of their working environments, and helped them address IT connectivity. We've also found ways to continue to foster collaboration and community through events like virtual trivia nights, scavenger hunts, coffee chats, charitable giving and lunch-n-learns, that we would normally do in person.

**Diversity & Inclusion (“D&I”):** We believe that fostering diversity and inclusion is a business imperative which supports and encourages individuals to show up as their whole selves. Investing in meaningful D&I work enhances culture and employee experience. We are committed to creating and maintaining a diverse, inclusive and safe work environment. As we grow and mature, we look forward to establishing programs that infuse D&I within the business, identify barriers that impact recruitment, development and retention of underrepresented employees, identify educational content, communicate the value and impact of D&I on goals and objectives, all while continuing to focus on hiring diverse talent at all levels of the company. Our ability to innovate and meet people's needs is strongest when all voices are heard and valued.

## **COVID-19 Pandemic**

In March 2020, the World Health Organization declared the outbreak of a novel coronavirus, or COVID-19, as a pandemic (the “COVID-19 pandemic”), which continues to spread throughout the U.S. and worldwide. We could be materially and adversely affected by the risks, or the public perception of the risks, related to an epidemic, pandemic, outbreak, or other public health crisis, such as the COVID-19 pandemic. The ultimate extent of the impact of any epidemic, pandemic, outbreak, or other public health crisis on our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of such epidemic, pandemic, outbreak, or other public health crisis and actions taken to contain or prevent the further spread, including the development and deployment of any vaccine program. Accordingly, we cannot predict the extent to which our business, including our clinical trials, financial condition and results of operations will be affected. As a result of the COVID-19 pandemic, we have experienced disruptions that have impacted our business, preclinical studies and clinical trials, including disruptions or restrictions on our ability to access and monitor certain clinical trial sites, restrictions on clinical trial participants' ability to access our clinical trial sites and delays in enrollment. Some clinical trial participants have missed or experienced delays in receiving doses of study drug and completing their clinical trial assessments. For example, four patients (one in Cohort 2 and three in Cohort 3) of the TOPAZ clinical trial each missed three doses of apitegromab over the course of the 12-month treatment period due to COVID-19-related site access restrictions. This has affected our clinical trials and could result in further impacts, including delays in or adverse impacts to data readouts from our clinical trials, delays in our ability to identify and enroll patients in current or future clinical trials and decisions by enrolled patients to discontinue from our clinical trials due to COVID-19 related concerns. While our laboratory operations have resumed to near-normal capacity, we may continue to experience challenges in procuring materials and supplies, as well as research services from our vendors in a consistently timely manner due to COVID-19 related supply chain issues. Some of our third-party manufacturers have diverted resources or manufacturing capacity to accommodate the development or manufacture of COVID-19 vaccines. Although this has not had an impact on our ability to produce sufficient quantities of apitegromab or SRK-181 for our clinical trials, we continue to work closely with our third-party manufacturers to mitigate potential impacts to our clinical supply chain. In addition, delays in the development of COVID-19 vaccines or the deployment of vaccines which are approved or otherwise authorized for emergency use, a recurrence or “subsequent waves” of COVID-19 cases, or the discovery of vaccine-resistant COVID-19 variants could cause other widespread or more severe impacts. We continue to monitor developments as we adjust to the disruptions and evaluate the uncertainties relating to the COVID-19 pandemic.

## **Facilities**

Our corporate headquarters and operations are located in Cambridge, Massachusetts.

In March 2015, we entered into a lease of laboratory and office space at 620 Memorial Drive in Cambridge, Massachusetts. Our amended lease expires in September 2023 and we have an option to extend the lease term for five additional years. In October 2020, we entered into a Sublease agreement with Orna Therapeutics, Inc. to lease this space for the period February 1, 2021 through August 31, 2023, unless terminated earlier.

In November 2019, we entered into a lease of laboratory and office space at 301 Binney Street in Cambridge, Massachusetts to be used as our new corporate headquarters. The expiration date is in August 2025 and we have the option to extend the term by two years. We relocated our headquarters to 301 Binney Street in 2021.

We believe that our facilities at 301 Binney Street are adequate to meet our current needs, and that suitable additional space will be available as and when needed.

### **Legal Proceedings**

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any material legal proceedings.

### **Website Access to Reports**

We are subject to the informational requirements of the Exchange Act and are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at [www.sec.gov](http://www.sec.gov). We also maintain a website at <http://www.scholarrock.com>. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information that is posted on or is accessible through our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered part of this or any other report that we file with or furnish to the SEC.

### **Item 1A. Risk Factors**

*Careful consideration should be given to the following risk factors, together with all other information set forth in this Annual Report on Form 10-K ("Annual Report"), including our consolidated financial statements and related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations," and in other documents that we file with the Securities and Exchange Commission (the "SEC"), in evaluating Scholar Rock Holding Corporation and our subsidiaries (collectively, the "Company", "we", or "our") and our business, before investing in our common stock. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The market price of our common stock could decline if one or more of these risks or uncertainties were to occur, which may cause you to lose all or part of the money you paid to buy our common stock. The risk factors described below disclose both material and other risks, and are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations. Certain statements below are forward-looking statements. See "Special Note Regarding Forward-Looking Statements" in this Annual report.*

#### **Summary of the Material Risks Associated with Our Business**

Our business is subject to numerous risks and uncertainties that you should be aware of before making an investment decision, including those highlighted in the section entitled "Risk Factors." These risks include, but are not limited to, the following:

##### Risks Related to Product Development and Regulatory Approval

- Product development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of apitegromab, SRK-181, or any future product candidates.

- Our business may be materially and adversely affected by pandemics such as the ongoing COVID-19 pandemic. The COVID-19 pandemic has had, and will likely continue to have, an impact on our business and operations, including clinical trial data and activities.
- The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Success of a product candidate in an early-stage clinical trial may not be replicated in later-stage clinical trials.
- Interim, initial and preliminary results from our clinical trials that we announce or publish from time to time may change (e.g. from positive efficacy results to poor or negative efficacy results) as more patient data become available and are subject to additional audit, validation and verification procedures that could result in material changes in the final data.
- The data from our clinical trials, including from any future clinical trials conducted by us or any of our collaborators, may reveal significant adverse events not seen in our preclinical studies or earlier clinical trials and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
- We rely on third parties to conduct our clinical trials and to conduct certain aspects of our preclinical studies. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with legal and regulatory requirements, we may be delayed or unable to receive regulatory approval of or commercialize any potential product candidates, and our business could be materially harmed.
- The regulatory approval process for our product candidates in the U.S., EU, UK and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.
- The FDA, EMA or regulatory authorities in other jurisdictions may disagree with our development plans and we may fail to receive or be delayed in receiving regulatory approval of our product candidates.
- We have received Orphan Drug designation from the FDA for apitegromab for the treatment of SMA and the EC granted Orphan Medicinal Product designation to apitegromab for the treatment of SMA. We may seek Orphan Drug designation from regulatory authorities in other jurisdictions for apitegromab and Orphan Drug designation from the FDA, EC or regulatory authorities in other jurisdictions for our future product candidates. In any of these instances, we may not receive the requested designation or we may be unable to realize the benefits associated with Orphan Drug designation, including the potential for market exclusivity.
- Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to develop our product pipeline and receive regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

#### Risks Related to Manufacturing and Supply

- Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials, and, if approved, commercial materials, may become limited or interrupted or may not be of satisfactory quantity or quality.

#### Risks Related to Our Business and Operations

- We will need to continue to grow our organization, including our personnel, systems and relationships with third parties, in order to develop our drug candidates.
- Our executives and highly skilled technical and managerial personnel are critical to our business. If we lose key personnel, have transition in management, or if we fail to recruit additional highly skilled personnel, our ability to further develop apitegromab and SRK-181, and our operations may be impaired.

- Failure by us or any of our employees, independent contractors, consultants, commercial partners or vendors to comply with applicable laws and regulations could negatively affect our business and operations.

#### Risks Related to Intellectual Property

- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- We depend on intellectual property licensed from third parties. Failure to comply with our obligations under any of these licenses or termination of any of these licenses could result in the loss of significant rights, which would harm our business.

#### Risks Related to Our Financial Condition and Capital Requirements

- We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.

#### Risks Related to Our Common Stock

- Our stock price is volatile and various factors could make our stock less attractive to investors.

### **Risks Related to Product Development and Regulatory Approval**

***Product development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of apitegromab, SRK-181, or any future product candidates.***

To receive the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to receive marketing approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a Biologics License Application (“BLA”) to the FDA, a Marketing Authorisation Application (“MAA”) to the EMA, MHRA, and similar marketing applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates.

We may experience delays in initiating, progressing or completing our clinical trials. We also may experience numerous unforeseen events during, or as a result of, any clinical trials in process or any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize apitegromab, SRK-181 or any future product candidates, including:

- delay or inability to reach agreement with the FDA or comparable foreign regulatory authorities on acceptable clinical trial design, conduct or statistical analysis plan;
- any orders from local, state or federal governments or clinical trial site policies resulting from the COVID-19 pandemic that determine essential and non-essential functions and staff, which may impact the ability of site staff to conduct assessments, or result in delays to the conduct of the assessments, as part of our clinical trial protocols, or the ability to enter assessment results into clinical trial databases in a timely manner;



- regulators, Institutional Review Boards (“IRBs”) or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective Contract Research Organizations (“CROs”), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure by our collaborators to provide us with an adequate and timely supply of product that complies with the applicable quality and regulatory requirements for a combination trial;
- collaborators may provide insufficient funding for a clinical trial program, delay or stop a clinical trial, abandon a product candidate or clinical trial program, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- clinical trials of any product candidates may fail to show safety and effectiveness, or produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower or more challenging than we anticipate or subjects may drop out of these clinical trials or fail to return for post treatment follow-up at a higher rate than we anticipate;
- challenges in identifying or recruiting sufficient study sites or investigators for clinical trials;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- there may be delays related to the impact of the spread of COVID-19 coronavirus on the FDA’s ability to continue its normal operations;
- clinical study sites or clinical investigators may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- limitations on our or our CROs’ ability to access and verify clinical trial data captured at clinical study sites through monitoring and source document verification;
- the cost of clinical trials of a product candidate may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates;
- our failure to establish an appropriate safety profile for a product candidate based on clinical or preclinical data for such product candidate and/or data emerging from other molecules in the same class as our product candidate;
- the FDA, EMA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial;

- evolution in the standard of care or changes in applicable governmental regulations or policies during the development of a product candidate that require amendments to ongoing clinical trials and/or the conduct of additional preclinical studies or clinical trials; and
- lack of adequate funding to complete a clinical trial.

We could also encounter delays if a clinical trial is placed on clinical hold, suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, the competent authorities and/or ethics committees of the EU Member States or other regulatory authorities, if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board (“DSMB”) for such trial, or on account of changes to federal, state, or local laws. A suspension or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, competent authorities and/or ethics committees of the EU Member States or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA, EMA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. For example, we anticipate some of our future trials to, in part, utilize an open-label trial design, and our ongoing DRAGON Phase 1 clinical trial for SRK-181 in cancer immunotherapy and our ongoing extension phase of the TOPAZ Phase 2 clinical trial for apitegromab in Type 2 and Type 3 SMA, in part, utilize an open-label trial design. An open-label trial is one where both the patient and investigator know whether the patient is receiving the test article or either an existing approved drug or placebo. Open-label trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label studies are aware that they are receiving treatment. Open-label trials may be subject to a patient bias, for example, if patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Open-label trials also may be subject to an investigator bias where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The potential sources of bias in clinical trials as a result of open-label design may not be adequately mitigated and may cause any of our trials that utilize such design to fail and additional trials may be necessary to support future marketing applications. In addition, other types of trials (including randomized, double-blind, parallel arm studies), particularly if smaller in size or if limited to one study, are also subject to potential sources of bias and limitations that may exaggerate any therapeutic effect or falsely identify a positive efficacy signal, or conversely, fail to detect an efficacy signal when in fact there may actually be a positive therapeutic effect. Further, the FDA, EMA or other regulatory authorities may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. The unpredictability caused by turnover at the FDA, EMA or other regulatory authorities could increase the risk of such change in the requirements for approval, which could impact our ability to receive approval, or could otherwise delay our clinical development programs and harm our business, financial condition and results of operations.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

***Our business may be materially and adversely affected by pandemics such as the ongoing COVID-19 pandemic. The COVID-19 pandemic has had, and will likely continue to have, an impact on our business and operations.***

The ongoing COVID-19 pandemic is evolving, continues to spread globally, and to date has led to the implementation of various responses, including government-imposed quarantines, closure of non-essential business, work-from-home directives, travel restrictions, physical distancing, shelter-in-place orders and other public health safety measures. Despite recent progress in the administration of vaccines, both the outbreak of recent variants, including Delta and Omicron, and the related containment and mitigation measures that have been put into place across the globe, have had an adverse impact on the global economy and our business, the severity and duration of which are uncertain. The COVID-19 pandemic continues to have a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services may be slow to return to pre-pandemic levels, if they return to pre-pandemic levels. In response to the COVID-19 pandemic, many of our employees are continuing to work remotely outside of our offices. Additionally, while our laboratory operations resumed to near-normal capacity, we may continue to experience challenges in procuring materials and supplies in a consistently timely manner due to COVID-19-related supply chain issues. We rely on third-party manufacturers to manufacture apitegromab and SRK-181. The demand for COVID-19 vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots needed for apitegromab or SRK-181. If any of our third-party manufacturers is adversely impacted by the COVID-19 pandemic or if they divert resources or manufacturing capacity to accommodate the development or manufacture of COVID-19 coronavirus vaccines, our supply chain may be disrupted, limiting our ability to supply apitegromab or SRK-181 for our clinical trials. As a result of the COVID-19 pandemic, we have experienced, and may continue to experience, disruptions that impact our business, preclinical studies and clinical trials.

Our clinical trials include sites located in regions that have been affected by the COVID-19 pandemic and many sites have instituted policies regarding operations. Some factors from the COVID-19 pandemic that could adversely affect enrollment in, as well as conduct, progress, continuation and completion of our clinical trials include:

- the diversion of healthcare resources away from the conduct of clinical trial matters to focus on COVID-19 pandemic concerns, including the administration of COVID-19 vaccines, which could negatively affect the attention of physicians serving as our clinical trial investigators, the hospitals serving as our clinical trial sites and the hospital staff supporting the conduct of our clinical trials;
- the continued impact from COVID-19 on healthcare providers, patients and personnel, which may vary considerably from jurisdiction to jurisdiction, as well as on local restrictions and practices, including the complexities of having to understand and navigate multiple sets of protocols and the accessibility and rates of vaccinations, and effectiveness of vaccinations in various geographies;
- limitations on travel and quarantine requirements that interrupt key trial activities, such as clinical trial site initiations, our ability and the ability of our CROs to access and monitor clinical trial sites, and new clinical trial site policies resulting from the COVID-19 pandemic that determine essential and non-essential functions and staff, which may impact the ability of site staff to conduct assessments, or result in delays to the conduct of the assessments, as part of our clinical trial protocols, or the ability to enter assessment results into clinical trial databases in a timely manner, or that limit the ability of a patient to participate in a clinical trial or delay access to product candidate dosing or assessments;
- patients may be unable or unwilling to participate further (or may have to limit participation, including missing certain scheduled doses of the investigational product) in our clinical trials;
- skipping or delays in product candidate dosing or assessments as part of a clinical trial that could adversely affect clinical trial data readouts, including efficacy and safety results;
- skipping or delays in the administration of background therapies of patients in a clinical trial, such as SMN upregulator therapy for SMA or anti-PD-(L)1 therapy for cancer, or other background care that could adversely affect clinical trial data readouts, including efficacy and safety results;
- interruption in global shipping affecting the transport of clinical trial materials, such as product candidates used in our trials; and

- employee absenteeism or furlough days that delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

If a patient participating in one of our clinical trials contracts COVID-19 (which may occur without detection or diagnosis), this could negatively impact the data readouts from these trials; for example, the patient may be unable to participate further (or may have to limit participation) in our clinical trial, the patient may show a different efficacy assessment than if the patient had not been infected, or such patient could experience an adverse event that could be attributed to our drug product. If a patient participating in any of our clinical trials receives COVID-19 vaccination, it is unknown whether or how the vaccination may impact the data readouts from our clinical trial, such as efficacy and safety. The global outbreak of COVID-19 continues to evolve and the conduct of our trials may be adversely affected, despite efforts to mitigate this impact.

Some clinical trial participants have missed or experienced delays in receiving doses of study drug and completing their clinical trial assessments. For example, as of the TOPAZ Phase 2 twelve-month top-line data readout, four patients in the clinical trial each missed three doses of apitegromab due to COVID-19-related site access restrictions. Additionally, enrollment in the DRAGON Phase 1 clinical trial in immuno-oncology has been slower than originally projected due to the travel restrictions imposed in areas affected by the COVID-19 pandemic and where certain clinical trial sites for this study are located. Disruptions and delays resulting from the COVID-19 pandemic could result in additional impacts on our ongoing, as well as future, clinical trials, including delays in or adverse impacts to data readouts (e.g. poor or negative efficacy results, adverse safety signal, reduced amounts of data available or data confounding) from our clinical trials and delays in our ability to identify and enroll patients in current or future clinical trials. As an example of impacts upon our development programs, the COVID-19 pandemic could lead to a negative or poor result in the Phase 3 trial of apitegromab in SMA and rejection for product approval by regulatory authorities, a delay in a potential regulatory filing for product approval, the requirement for additional clinical trial(s) beyond the currently planned program (e.g., if the amount of data from our Phase 3 trial is deemed by regulatory authorities as insufficient or confounded due to COVID-19 impacts), or other adverse outcomes.

The extent to which the COVID-19 pandemic continues to impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity and duration of the COVID-19 pandemic and the actions to contain the COVID-19 coronavirus or treat its impact, among others.

***Our clinical development strategy depends on the continued use and availability of certain third-party approved drug therapies.***

Apitegromab and SRK-181 are our two clinical-stage product candidates. Certain patients remaining in the open-label extension portion of our TOPAZ Phase 2 clinical trial are receiving apitegromab in conjunction with an approved SMN upregulator therapy such as nusinersen. These patients are reliant on the continued use and availability of such therapies. In addition, patients in our SAPPHIRE Phase 3 clinical trial are receiving apitegromab in conjunction with an approved SMN upregulator therapy. These patients are reliant on the continued use and availability of such therapies. If access to an approved SMN upregulator therapy such as nusinersen or risdiplam becomes limited or is unavailable, we may be forced to pause or stop our TOPAZ extension or SAPPHIRE trials, or the medical condition of patients may be affected which could negatively affect the efficacy and safety results for apitegromab in the trial or reduce the amount of data or confound the data from this trial. We have also initiated the DRAGON Phase 1 clinical trial of SRK-181 in patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibody therapies. Certain patients in this clinical trial are receiving SRK-181 in conjunction with an approved anti-PD-(L)1 therapy such as pembrolizumab. If access to the approved anti-PD-(L)1 therapy becomes limited or is unavailable, we may not be able to enroll, or may be delayed in enrolling patients or may be forced to pause or stop our DRAGON Phase 1 clinical trial, or the medical condition of patients may be affected which could negatively affect the efficacy and safety results for SRK-181 in the trial. Any delay or suspension of our clinical trials would significantly and adversely affect our business prospects.

***The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Success of a product candidate in an early-stage clinical trial may not be replicated in later-stage trials.***

The results of preclinical studies and early-stage clinical trials may not be predictive of the results of future, later-stage clinical trials. Preclinical studies and early-stage clinical trials are primarily designed to study PK and PD, understand the side effects of product candidates, and evaluate various doses and dosing schedules. Our current or future product candidates may demonstrate different chemical, biological and pharmacological properties in patients than they do in laboratory studies or may interact with human biological systems in unforeseen or harmful ways. Product candidates in later-stages of clinical trials may fail to show desired pharmacological properties or produce positive safety and efficacy results despite having progressed through preclinical studies and early-stage clinical trials. We completed a Phase 1 trial for apitegromab in healthy adult volunteers and the TOPAZ Phase 2 proof-of-concept trial for the treatment of patients with Type 2 and Type 3 SMA. In April 2021, we announced positive twelve-month top-line results from the TOPAZ Phase 2 clinical trial and from June to October 2021, we announced supportive data from additional exploratory analyses at various medical congresses. In January 2022, we initiated our SAPPHIRE Phase 3 clinical trial of apitegromab for the treatment of patients with Type 2 and Type 3 SMA. In November 2021, we presented interim clinical data from Part A of our DRAGON Phase 1 trial in cancer immunotherapy, at the Society for Immunotherapy of Cancer's Annual Meeting. We cannot assure you that the DRAGON Phase 1 trial or any other future clinical trials of SRK-181 or apitegromab will show positive results. There can be no assurance that any of our current clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There can also be no assurance that any of our future clinical trials will show similar results to our earlier clinical trials or support further development or registration of any of our product candidates. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

***Interim, initial or preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to additional audit, validation and verification procedures that could result in material changes in the final data.***

From time to time, we may publish interim, initial or preliminary data, including interim top-line results or initial or preliminary results from our clinical trials. Any interim, initial or preliminary data and other results from our clinical trials may materially change as more patient data become available. Preliminary, initial, interim or top-line results also remain subject to audit, validation and verification procedures that may result in the final data being materially different from the interim, initial or preliminary data we previously published. As a result, interim, initial or preliminary data may not be predictive of final results and should be viewed with caution until the final data are available. We may also arrive at different conclusions, or considerations may qualify such results, once we have received and fully evaluated additional data. For example, in November 2021, we presented preliminary and initial clinical data from Part A of our DRAGON Phase 1 trial for SRK-181 in cancer immunotherapy at the Society of Immunotherapy of Cancer's Annual Meeting. Data from our DRAGON Phase 1 trial will continue to be reported while the trial is ongoing and tumor response data will be based on assessments by site investigators. Central reads for the tumor responses are also being conducted, with a comprehensive review of the central reads to be performed once completed within and/or across the cohorts. Differences between preliminary, initial or interim data and final data could adversely affect our business.

***The data from our clinical trials, including from any future clinical trials conducted by us or any of our collaborators, may reveal significant adverse events not seen in our preclinical studies or earlier clinical trials and may result in a safety profile or undesirable side effects that could inhibit or limit regulatory approval or market acceptance of any of our product candidates.***

If significant adverse events or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. Patients in our clinical trials may develop levels of anti-drug antibodies which could limit the potential efficacy of our product candidates or trigger hypersensitivity reactions or other adverse effects. We, the FDA, the competent authorities and/or ethics committees of the EU Member States or other applicable regulatory authorities, or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects or patients in such trials are being exposed to unacceptable health risks or adverse side effects.

Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. The side effects could result in a number of potentially significant negative consequences, including:

- regulatory authorities may refuse to grant market approval to a product candidate or withdraw approvals of such product;
- we may suspend marketing of such product;
- regulatory authorities may require additional warnings on the label for such product;
- we may be required to develop a Risk Evaluation and Mitigation Strategy (“REMS”) for such a product, or if a REMS is already in place, to incorporate additional requirements under the REMS, or to develop a similar strategy as required by a comparable foreign regulatory authority;
- we may be required to conduct additional post-market studies;
- we could be sued and held liable for harm caused to subjects or patients; or
- our reputation may suffer.

Any of these developments could adversely affect our prospects for receiving or maintaining approval for our product candidates and/or inhibit market acceptance of any approved product and could materially harm our business, financial condition and prospects.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including due to the COVID-19 pandemic. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial’s primary endpoints;
- the willingness or availability of patients to participate in our trials (including due to the COVID-19 pandemic);
- the number and location of participating trial sites;
- the proximity of patients to trial sites and any limitations on travel or access to trial sites (including due to the COVID-19 pandemic);
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians’ and patients’ perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop-out of the trials before completion of their involvement in the study.

For example, we are initially developing apitegromab for the treatment of SMA, a rare disease, affecting an estimated 30,000 to 35,000 patients in the U.S. and Europe. As a result, we may encounter difficulties enrolling patients in our clinical trials for apitegromab due, in part, to the small size of this patient population. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Additionally, patients may opt out of participation in clinical trials in favor of treatment with FDA-approved therapies, or therapies approved in the EU or other foreign jurisdictions.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our future clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

***We rely on third parties to conduct our clinical trials and certain aspects of our preclinical studies. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with legal and regulatory requirements, we may be delayed or unable to receive regulatory approval of or commercialize apitegromab, SRK-181 or any future product candidates, and our business could be materially harmed.***

We depend upon third parties to conduct certain aspects of our preclinical studies and to conduct our clinical trials, under agreements with universities, medical institutions, CROs, strategic partners and others. We often have to negotiate budgets and contracts with such third parties, and if we are unsuccessful or if the negotiations take longer than anticipated, this could result in delays to our development timelines and increased costs.

We rely especially heavily on third parties over the course of our clinical trials, and, as a result, have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their individual employment policies or compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with Good Clinical Practice (“GCP”) requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in civil monetary penalties, adverse publicity and civil and criminal sanctions. The FDA and National Institutes of Health recently signaled the government’s willingness to begin enforcing these registration and reporting requirements against non-compliant clinical trial sponsors.

Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violate federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies or clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our preclinical studies and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical



trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they cannot perform their contractual duties or obligations due to the impacts of the COVID-19 pandemic on their operations or at the sites they are overseeing, if they need to be replaced or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, receive regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

***The regulatory approval process for our product candidates in the U.S., EU and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.***

The research, testing, manufacturing, labeling, approval, sale, import, export, marketing, promotion and distribution of drug products, including biologics, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities outside the U.S. We are not permitted to market any biological product in the U.S. until we receive a biologics license from the FDA. We have not previously submitted a BLA to the FDA or similar marketing application to comparable foreign authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection.

The FDA may seek independent advice from a panel of experts, referred to as an Advisory Committee, on complex or novel issues that may be presented in an application, including issues related to the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to receive approval of any product candidates that we develop based on the completed clinical trials.

Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions at which such trials are being conducted, or the FDA, the competent authorities and/or ethics committees of the EU Member States or other regulatory authorities, or recommended for suspension or termination by the DSMB for such trial, due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, competent authorities of the EU Member States or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the prospects for regulatory approval and commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

***The FDA, EMA or regulatory authorities in other jurisdictions may disagree with our development plans and we may fail to receive or be delayed in receiving regulatory approval of apitegromab, SRK-181 and future product candidates.***

FDA approval of a new biologic or drug generally requires dispositive data from two (and in some cases, one) adequate and well-controlled pivotal Phase 3 clinical trials of the biologic or drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete.

The results of our clinical trials may not support approval. Our product candidates could fail to receive regulatory approval for many reasons, including the following, among other reasons:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- the results of clinical trials may not meet the level of statistical significance or adequacy in the robustness or amount of data required by the FDA, EMA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to receive regulatory approval in the U.S. or elsewhere;
- the FDA, competent authorities of the EU Member States or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If we believe the clinical trial data support doing so, we may seek to pursue BLA approval in the United States or marketing authorization in jurisdictions outside the United States for one or more of our product candidates based on results of interim analyses of our pivotal trials, rather than submitting such applications after the relevant pivotal trials have been completed. We cannot assure you that the FDA, EMA or other regulatory authorities will agree with this approach or that these regulatory authorities will find the results from a single pivotal trial or of an interim analysis (such as that from a single pivotal trial or multiple trials) sufficient to meet the standards for approval or marketing authorization; and if they do not, the prospects for regulatory approval and commercialization of our product candidates may be delayed or harmed.

***We have received Orphan Drug designation from the FDA for apitegromab for the treatment of SMA and the EC granted Orphan Medicinal Product designation to apitegromab for the treatment of SMA. We may seek Orphan Drug designation from regulatory authorities in other jurisdictions for apitegromab and Orphan Drug designation from the FDA, EC or regulatory authorities in other jurisdictions for our future product candidates. In any of these instances, we may not receive the requested designation or we may be unable to realize the benefits associated with Orphan Drug designation, including the potential for market exclusivity.***

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if, among other things, it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be

recovered from sales in the U.S. In the EU, after a recommendation from the EMA's Committee for Orphan Medicinal Products ("COMP"), the EC grants orphan designation to promote the development of products that are (a) intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU, or (b) for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the medicinal product in the EU would generate sufficient return to justify the necessary investment in developing the medicinal product. Additionally, the orphan designation requires that there is no satisfactory method of diagnosis, prevention or treatment of the condition authorized for marketing in the EU, or, if such a method exists, the medicinal product must be of significant benefit to those affected by the condition. Any Orphan Drug designation that we are granted for our product candidates in the U.S. or in the EU would not assure Orphan Drug designation of those product candidates in any other jurisdiction. Orphan Drug designation neither shortens the development time or regulatory review time of a product candidate, nor gives the product candidate any advantage in the regulatory review or approval process (other than as discussed below).

In the U.S., Orphan Drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity for that indication. Orphan drug exclusivity means the FDA may not approve another application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan designation entitles a party to scientific assistance regarding necessary tests and trials, financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following grant of marketing authorization for the medicinal product if the criteria for orphan designation continue to be met before the grant of the marketing authorization. This period may be reduced to six years if the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

We have received Orphan Drug designation from the FDA for apitegromab for the treatment of SMA, and following the EMA's COMP's positive opinion, the EC designated apitegromab as an orphan medicinal product for the treatment of SMA. Even if we receive orphan drug exclusivity, the benefit of that exclusivity may be limited if we seek approval for an indication broader than the orphan-designated indication or could be revoked under certain circumstances, for example if the FDA later determines that the request for designation was materially defective or that we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we receive orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition during the exclusivity period because different drugs with different active moieties can be approved for the same condition, and the same product can be approved for different uses. Also, in the U.S., even after an orphan drug is approved and receives orphan drug exclusivity, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug, including because it has been shown to be clinically superior to the drug with exclusivity because it is safer, more effective or makes a major contribution to patient care. In the EU, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior; or
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

***We have received Rare Pediatric Disease designation for apitegromab for the treatment of SMA. However, a marketing application for apitegromab, if approved, may not meet the eligibility criteria for a rare pediatric disease priority review voucher.***

We have received Rare Pediatric Disease designation for apitegromab for the treatment of SMA. Designation of a biologic as a product for a rare pediatric disease does not guarantee that a BLA for such biologic will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the Federal Food, Drug, and Cosmetic Act (“FDCA”), we will need to request a rare pediatric disease priority review voucher in our original BLA for apitegromab. The FDA may determine that a BLA for apitegromab, if approved, does not meet the eligibility criteria for a rare pediatric disease priority review voucher, including for the following reasons:

- SMA no longer meets the definition of a rare pediatric disease;
- apitegromab contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in an application;
- the BLA is not deemed eligible for priority review;
- the BLA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population; or
- the BLA seeks approval for a different adult indication than the rare pediatric disease for which apitegromab is designated.

The authority for the FDA to award rare pediatric disease priority review vouchers for biologics after September 30, 2024 is currently limited to biologics that receive Rare Pediatric Disease designation on or prior to September 30, 2024, and the FDA may only award rare pediatric disease priority review vouchers through September 30, 2026. If the BLA for apitegromab is not approved on or prior to September 30, 2026 for any reason, it will not be eligible for a priority review voucher. However, it is possible the authority for the FDA to award rare pediatric disease priority review vouchers will be further extended by Congress.

***We have received Fast Track designation from the FDA and PRIME designation from the EMA for apitegromab for the treatment of SMA. We may seek Breakthrough Therapy designation or Fast Track designation from the FDA or PRIME designation from the EMA for other product candidates in the future, and we may not be successful in receiving such designations, or if received, such designation may not actually lead to a faster development or regulatory review or approval process.***

We may seek Breakthrough Therapy designation or Fast Track designation or PRIME designation for certain of our product candidates.

A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products that have been designated as breakthrough therapies are eligible for more frequent interaction and communication between the FDA and the sponsor, which can help to identify the most efficient path for clinical development, as well as rolling review. Products designated as breakthrough therapies by the FDA may also be eligible for (but are not assured) accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one

or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the breakthrough designation.

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for Fast Track designation. Products receiving a Fast Track designation are eligible for more frequent interaction and communication with FDA and rolling review. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In May 2021, the FDA granted Fast Track designation for apitegromab for the treatment of SMA.

In March 2021, the EMA granted PRIME designation to apitegromab for the treatment of SMA. PRIME, or PRIority MEDicine, is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a major therapeutic advantage over existing treatments or benefits patients without treatment options. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. The receipt of PRIME designation for apitegromab for the treatment of SMA may not result in a faster development process, review or approval compared to products considered for approval under conventional regulatory agency procedures and does not assure ultimate approval by the EMA.

***Receiving and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in receiving or maintaining regulatory approval of our product candidates in other jurisdictions.***

Receiving and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to receive or maintain regulatory approval in any other jurisdiction, but a failure or delay in receiving regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in other jurisdictions. Even if the FDA grants marketing approval of a product candidate, the EC, the competent authorities of EU Member States or comparable regulatory authorities in foreign jurisdictions may not approve the manufacturing, marketing and promotion of the product candidate in other countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U.S., including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the U.S. have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Receiving foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

***Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.***

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements, including requirements related to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping,

import, export, conduct of post-marketing studies and submission of safety, efficacy and other post-marketing information. In addition, we will be subject to continued compliance with current Good Manufacturing Practice (“cGMP”) and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers’ facilities are required to comply with extensive FDA, EU and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to periodic review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA or other marketing application and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved uses for which the product may be marketed or contain requirements for potentially costly post-market testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- permanent injunctions and consent decrees, including the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for their approved indications and in a manner consistent with their FDA-approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of unapproved uses and a company that is found to have improperly promoted unapproved uses may be subject to significant liability.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may face enforcement action and our business may be harmed.

***Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.***

If apitegromab, SRK-181 or any future product candidate we develop receives marketing approval, whether as a single agent or in conjunction with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. For example, doctors may deem it sufficient to treat patients with SMA with an SMN upregulator such as nusinersen, and therefore will not be willing to utilize apitegromab in conjunction with such SMN upregulator. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the amount, scope and nature of the clinical data (and other forms of data) available;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

***Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to develop our product pipeline and receive regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.***

We have two product candidates, apitegromab and SRK-181, and may not nominate any other product candidates for any of our programs. Before we can commence clinical trials for any product candidate, we must complete extensive preclinical studies that support our planned INDs in the U.S., or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical studies and cannot predict if the FDA, EMA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA, the competent authorities and/or ethics committees in the EU Member States or other regulatory authorities allowing clinical trials to begin.



Conducting preclinical testing can be a lengthy, time-consuming and expensive process. The time required for such testing may vary substantially according to the type, complexity and novelty of the program, and can be several years or more per program. Delays associated with programs for which we are conducting preclinical testing and studies, such as on account of interruptions or delays in preclinical studies at laboratories or other institutions due to the COVID-19 pandemic, may cause us to incur additional operating expenses. We also may be affected by delays associated with the preclinical testing and studies of certain programs that are the responsibility of our collaborators or our potential future collaborators over which we have limited or no control. The commencement and rate of completion of preclinical studies for a product candidate may be delayed by many factors, including, for example, challenges in reaching consensus with regulatory agencies regarding the scope of the necessary preclinical study program and/or appropriate preclinical study designs.

***The UK's withdrawal from the EU could increase the regulatory burden of product development and authorization in the UK and EU.***

On June 23, 2016, the UK held a referendum in which a majority of voters approved an exit from the EU, or Brexit, and the UK formally left the EU on January 31, 2020. There was a transition period during which EU pharmaceutical laws continued to apply to the UK, which expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns in the most part with EU regulations, however it is possible that these regimes will diverge in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. For example, the new Clinical Trials Regulation which became effective in the EU on January 31, 2022 and provides for a streamlined clinical trial application and assessment procedure covering multiple EU Member States has not been implemented into UK law, and a separate application will need to be submitted for clinical trial authorization in the UK. The long-term effects of Brexit will depend in part on how the terms of the TCA continue to take effect in practice and the terms of any further agreements the UK makes with the EU. Such a withdrawal from the EU is unprecedented, and it is unclear how the restrictions on the UK's access to the European single market for goods, capital, services and labor, or single market, and the wider commercial, legal and regulatory environment, will impact our future operations and clinical activities in the UK in the long term.

**Risk Related to Manufacturing and Supply**

***Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials, and, if approved, commercial materials, may become limited or interrupted or may not be of satisfactory quantity or quality.***

We rely on third-party contract manufacturers to manufacture some of our preclinical product candidate supplies and rely on third-party contract manufacturers to manufacture all of our clinical trial product supplies and, if approved, will rely on third-party contract manufacturers to manufacture all of our commercial product supplies, including all of our drug substance, vialing, labeling, and packaging. We do not own manufacturing facilities for producing any clinical trial or commercial product supplies. There can be no assurance that our preclinical, clinical development, and, if approved, commercial product supplies will not be limited or interrupted, including as a result of the COVID-19 pandemic, or that our product supplies will be of satisfactory quality or continue to be available at acceptable prices. For example, we rely on a single source supplier for the manufacture of drug substance for apitegromab and SRK-181, and this supplier also manufactures parts of the COVID-19 vaccine that may be subject to the priorities and allocations authority under the Defense of Production Act of 1950 whereby a contract to manufacture the COVID-19 vaccine could take precedence over any manufacturing we have contracted with this supplier. In addition, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of apitegromab, SRK-181 or future product candidates will depend on the severity and duration of the spread of COVID-19, and the actions undertaken to contain

COVID-19 or treat its effects. Any replacement of our current drug substance contract manufacturer would require significant resources, lead time and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMP. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, such as due to the COVID-19 pandemic, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third-party and a feasible alternative may not exist. These factors would increase our reliance on the original manufacturer or require us to obtain a license from such manufacturer in order to have another third-party manufacture our product candidates. If we must change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for apitegromab, SRK-181 or any future product candidate. To the extent that we have existing, or in the future enter into, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third-party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials for apitegromab, SRK-181 or of future product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for apitegromab, SRK-181 or future product candidates;
- loss of the cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of apitegromab, SRK-181 or future product candidates; and
- in the event of approval to market and commercialize apitegromab, SRK-181 or a future product candidate, an inability to meet commercial demands for our products.

In addition, we contract with fill and finishing providers which we believe have the appropriate expertise, facilities and scale to meet our needs. Failure to maintain compliance with cGMP can result in a contractor receiving FDA sanctions, which can impact our ability to operate or lead to delays in any clinical development programs. We believe that our current fill and finish contractors are operating in accordance with cGMP, but we can give no assurance that the FDA, EMA, competent authorities of the EU Member States or other regulatory agencies will not conclude that a lack of compliance exists. In addition, any delay in contracting for fill and finish services, or failure of the contract manufacturer

to perform the services as needed, may delay any clinical trials, registration and launches, which could negatively affect our business.

***Our reliance on third parties, such as manufacturers and antibody discovery vendors, may subject us to risks relating to manufacturing scale-up and may cause us to undertake substantial obligations, including financial obligations.***

In order to continue to conduct later-stage clinical trials with apitegromab, SRK-181 or any of our future product candidates, or, if approved, produce commercial product, we will need to manufacture such product candidate in large quantities. We, or any manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality-control issues may arise during scale-up activities. If we, or any manufacturing partners, are unable to successfully scale-up the manufacture of our product candidates in sufficient quality and quantity, including as a result of the COVID-19 pandemic, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not received, which could significantly harm our business.

In addition, we rely, and intend to continue to rely, on third-party entities to conduct certain antibody discovery work based on criteria and specifications provided by us. Certain of our antibody discovery vendors may require us to enter into a license agreement with them or exercise an option in an existing agreement with them for the right to use antibodies discovered by them in humans or for commercial purposes. Such license or other agreements could include substantial milestone payments and royalties to the extent we choose to use an antibody discovered by such vendors. For example, under our Adimab Agreement, upon exercise of the development and option for the research program from which SRK-181 was generated, we paid to Adimab a non-creditable, nonrefundable option exercise fee; and on a Product (as defined in the Adimab Agreement)-by-Product basis, we will pay Adimab upon the achievement of various clinical and regulatory milestone events with total milestone payments not to exceed mid-teen millions in the aggregate for a given Product; for any Product that is commercialized, on a country-by-country and Product-by-Product basis, we are obligated to pay to Adimab a low-to-mid single-digit percentage of annual worldwide net sales of such Product during the applicable royalty period in each country. In addition, if we do not meet our obligations under such license or other agreements, the counterparties may have the ability to terminate the license or other agreements and we could lose the right to use the discovered antibodies, which could significantly and adversely impact our business.

### **Risks Related to Our Business and Operations**

***We will need to grow the size of our organization, and we may experience difficulties in managing this growth.***

As our clinical development plans and strategies continue to develop and expand, we expect we will need to hire additional managerial, clinical development, scientific, regulatory, and administrative personnel. Our ability to compete in the highly competitive oncology and immuno-oncology fields depends upon our ability to attract and retain highly qualified specialized personnel. If apitegromab and SRK-181 approach commercialization, we will also need to hire sales, marketing and other commercial personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our development efforts effectively, including the clinical and regulatory review process for apitegromab, SRK-181, and any future product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize apitegromab, SRK-181 and future product candidates, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on third parties, advisors and consultants to provide certain services, including clinical research organizations, contract manufacturers and companies focused on antibody development and discovery activities. There can be no assurance that the services of third parties, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the services provided is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to receive, or may be substantially delayed in receiving, regulatory approval of apitegromab, SRK-181 or future product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel in the biopharmaceutical space, especially those engaged in oncology and immuno-oncology. In this highly competitive market, there may be increased costs to attract and retain qualified personnel. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we have to offer. If we are not able to offer competitive compensation or appealing opportunities for high quality candidates, we may not be able to attract or retain qualified candidates and personnel. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize apitegromab, SRK-181 or any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

***Our executives and highly skilled technical and managerial personnel are critical to our business. If we lose key personnel, have transition in management, or if we fail to recruit additional highly skilled personnel, our ability to further develop apitegromab, SRK-181 and identify and develop new or next generation product candidates may be impaired.***

Our performance substantially depends on the performance of our management team. The unplanned loss of the services of any of our executives or highly skilled technical and managerial personnel could cause us to incur increased operating expenses and divert senior management resources in searching for replacements. These changes in our organization may have a disruptive impact on our ability to implement our strategy and could have a material adverse effect on our business, internal controls, financial condition and results of operations. Management transition inherently causes some loss of institutional knowledge, which can negatively affect strategy and operational execution during this phase. If we have additional changes to our executives or highly skilled technical and managerial personnel, we may be unable to successfully manage and grow our business, and our results of operations, execution of corporate goals, internal controls and financial condition could suffer as a result. The unplanned loss of the services of our executives or other personnel also could harm our reputation.

***Our internal computer systems, or those used by our contract research organizations, or other contractors or consultants, may fail or suffer security breaches.***

Despite the implementation of security measures, our internal computer systems and those of our existing and future CROs, and other contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. Our increased reliance on personnel working from home may increase our cyber security risk, create data accessibility concerns, and make us more susceptible to workforce and communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and other agencies and contractors. For example, the loss of preclinical or clinical data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of apitegromab and SRK-181 and to conduct clinical trials, and similar events relating to their computer systems could also have a material

adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of apitegromab, SRK-181 and future product candidates could be delayed.

***Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws and regulations of the FDA, EU Member States, EMA and other similar foreign regulatory bodies; provide true, complete and accurate information to the FDA, EMA and other similar foreign regulatory bodies; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the U.S. and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we receive FDA approval of apitegromab, SRK-181 or any future product candidates and begin commercializing those products in the U.S., our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, commercial partners and vendors, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, monetary fines, individual imprisonment, disgorgement, possible exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations, any of which could adversely affect our ability to operate our business, financial condition and results of operations.

***Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.***

Changes in statutes, regulations or the interpretation of existing statutes or regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; (iv) additional record-keeping requirements; or (v) changes to our pricing arrangements, or coverage of or reimbursement for our products. If any such changes were to be imposed, they could adversely affect the profitability and operation of our business. Changes in statutes, regulations, or the interpretation of existing statutes or regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; (iv) additional record-keeping requirements; or (v) changes to our pricing arrangements, or coverage of or reimbursement for our products. If any such changes were to be imposed, they could adversely affect the profitability and operation of our business. See the sections entitled, “Business — Government Regulation — Current and Future Healthcare Reform Legislation” and “Business – Government Regulation – Coverage and Reimbursement.”

It is possible that the ACA, as currently enacted or as it may be amended or otherwise modified in the future, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare or other healthcare funding, more rigorous coverage criteria, or new payment methodologies or otherwise affect the prices we may obtain for any of our product candidates for which we may receive regulatory approval. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from commercial payors. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be modified or invalidated. The continuing health care reform initiatives efforts of the government, insurance companies, managed care organizations and other payers of health care services to contain or

reduce costs of health care may adversely affect the demand for any product candidates for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability; and the level of taxes that we are required to pay.

***Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors in the U.S. and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act (“FCA”), which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information received in the course of patient recruitment for clinical trials. See the section entitled “Business – Government Regulation – Other Healthcare Laws.”

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. In addition, there has been a trend of increased state regulation of payments made to physicians for marketing. Some states mandate implementation of corporate compliance programs, along with the tracking and reporting of gifts, compensation, and other remuneration to physicians.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time and resource consuming and can divert a company’s attention from the business.

It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management’s attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.



***Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.***

We, our CROs, and any potential collaborators may be subject to strict and changing federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security) and policies and contractual obligations related to data privacy and security. In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our CROs and collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

We have conducted our TOPAZ Phase 2 clinical trial of apitegromab in the European Economic Area ("EEA"), plan to conduct our SAPPHERE Phase 3 clinical trial of apitegromab in the EEA and the UK, and may conduct future clinical trials in the EEA or the UK and therefore may be subject to additional privacy laws. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the U.S., providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, where required reporting security breaches involving personal data to the competent national data protection authority and affected individuals, where required, appointing data protection officers, where required conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the UK is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.



The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Given the new law, we face uncertainty as to the exact interpretation of the new requirements and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the law. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

EU Member States have adopted implementing national laws to implement the EU GDPR which may partially deviate from the EU GDPR and the competent authorities in the EU Member States may interpret GDPR obligations slightly differently from country to country, so that we do not expect to operate in a uniform legal landscape in the EU. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty.

We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. If we are investigated by a European or UK data protection authority, we may face fines and other penalties. Any such investigation or charges by European or UK data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or pharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national clients or pharmaceutical partners to continue to use our products and solutions due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or pharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the foregoing could materially harm our business, prospects, financial condition and results of operations.

In addition, many states in which we operate have laws that protect the privacy and security of sensitive and personal information. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts. Where state laws are more protective than HIPAA, we must comply with the state laws we are subject to, in addition to HIPAA. In certain cases, it may be necessary to modify our planned operations and procedures to comply with these more stringent state laws. Further, in some cases where we process sensitive and personal information of individuals from numerous states, we may find it necessary to comply with the most stringent state laws applicable to any of the information. For example, California recently enacted the California Consumer Privacy Act (“CCPA”), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. While there are currently exceptions for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. We continue to monitor the impact that the state consumer privacy and protection law, like the CCPA may have on our business activities. See the section entitled “Business – Government Regulation – European Data Collection and State Privacy Laws.”

***Additional laws and regulations governing international operations, including certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, could negatively impact or restrict our operations.***

If we further expand our operations outside of the U.S., we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act (“FCPA”) prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including

international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the U.S., it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities, and as a result, may be subject to lengthy and expensive litigation and excessive damages and we may not have, or be able to obtain, sufficient capital to pay such amounts. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.***

We face an inherent risk of product liability as a result of testing apitegromab, SRK-181 and any of our future product candidates in clinical trials and will face an even greater risk if we commercialize any products, if approved. For

example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- inability to bring a product candidate to the market;
- decreased demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate, if approved; and
- decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. We may be unable to obtain, or may obtain on unfavorable terms, additional clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

***Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold because of the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approvals on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestically and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches. Additionally, as of May 26, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or may defer action on the application until an inspection can be completed. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Additionally, regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

***Our current laboratory operations are concentrated in one location, and we or the third parties upon whom we depend, including our clinical trial sites and the manufacturing facilities of our third-party contract manufacturers, may experience business interruptions and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster, including earthquakes, outbreak of disease or other natural disasters.***

Our office and laboratory facilities are located in Cambridge, Massachusetts. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, the facilities at any clinical trial site, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of apitegromab, SRK-181 and future product candidates or interruption of our business operations. If a natural disaster, outbreak of disease, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. For example, the COVID-19 pandemic has already resulted in extended shutdowns of certain businesses and has had ripple effects to businesses around the world. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services may be slow to return to pre-pandemic levels. In response to the spread of COVID-19 many of our employees are continuing to work remotely outside of our offices. As a result of the COVID-19 pandemic, our ability to identify and enroll patients in current and future clinical trials may become more difficult and costly and data readouts from our clinical trials may be delayed or adversely impacted. The full extent to which the COVID-19 pandemic impacts our business or operations will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information which may emerge concerning the severity of the COVID-19 coronavirus and the actions to contain COVID-19 or treat its impact, among others.

Global events, including global health concerns, like the COVID-19 pandemic, could also result in social, economic, and labor instability in the countries in which we operate or where the third parties with whom we engage, including our clinical trial sites and manufacturing facilities of our third-party contract manufacturers, operate. Unforeseen global events, such as the armed conflict between Russia and Ukraine, could adversely impact our business. For example, we are conducting SAPPHIRE, our Phase 3 clinical trial of apitegromab in the US and EU, and regional instability caused by the armed conflict between Russia and Ukraine could adversely affect the conduct of our clinical trial. Such conflicts could lead to sanctions, embargoes, supply shortages, regional instability, geopolitical shifts, cyberattacks, other retaliatory actions, and adverse effects on macroeconomic conditions, currency exchange rates, and financial markets, which could adversely impact our operations and financial results, as well as those of third parties with whom we conduct business.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at our facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, the manufacturing facilities of our third-party contract manufacturers, or the sites where we conduct clinical trials or preclinical studies, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

***Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates profitably.***

The success of our product candidates, apitegromab, SRK-181 and future product candidates, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, apitegromab, SRK-181 or future product candidates or assure that coverage and reimbursement will be available for any product that we may develop. See the sections entitled “Business– Government Regulation – Coverage and Reimbursement” and “Business–Government Regulation–Current and Future Healthcare Reform Legislation.”

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid or national payor bodies (such as in European countries), and commercial payors is critical to new product acceptance.

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third party payors, Coverage and reimbursement for products can differ significantly from payor to payor. One payor’s decision to cover a particular

medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. Coverage and reimbursement for products may vary widely across national payors from country to country.

Payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain and maintain coverage and reimbursement for any product, we may need to conduct expensive evidence generation studies in order to demonstrate the medical necessity and cost-effectiveness of such a product, in addition to the costs required to obtain regulatory approvals. If payors do not consider a product to be cost-effective compared to current standards of care, they may not cover the product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to cover its costs or make a profit. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. Additional state and federal healthcare reform measures are expected to be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for certain pharmaceutical products or additional pricing pressures.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the U.S. with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products.

***EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states.***

We intend to seek approval to market our product candidates in both the U.S. and in selected foreign jurisdictions. If we receive approval in one or more foreign jurisdictions for apitegromab, SRK-181 or future product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of medicinal products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after receiving marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Much like the federal Anti-Kickback Statute prohibition in the U.S., the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the

national anti-inducement, advertising and anti-bribery laws of EU Member States. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be disclosed publicly. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including several EU Member States, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced Member States, can further reduce prices. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the U.S. and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of any of our product candidates in those countries would be negatively affected.

***We may seek to enter into collaborations in the future with third parties, including for apitegromab, SRK-181 or potential product candidates. If we are unable to enter into such collaborations, or if these collaborations are not successful, our business could be adversely affected.***

A part of our strategy is to evaluate and, as deemed appropriate, enter into additional collaborations or partnerships in the future when strategically attractive, including potentially with biotechnology or pharmaceutical companies. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into collaborations with other companies to provide us with important technologies, capabilities and funding for our programs and underlying technology.

Any future collaboration we enter into may pose a number of risks, including the following:

- collaborators may have significant discretion or decision-making authority in determining the efforts and resources that they will apply to the collaboration or that we are required to apply to the collaboration;
- collaborators may not perform their obligations as expected or in a manner satisfactory to us;
- we may commit to certain preclinical or clinical development or commercialization efforts as part of the collaboration that we are unable to meet or our collaborators may not be satisfied with our preclinical or clinical development or commercialization efforts;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;



- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates. For example, our collaboration with Gilead Sciences, Inc. that we entered into on December 19, 2018 was terminated on January 6, 2022.

If our collaborations do not result in the successful discovery, development and commercialization of product candidates or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such collaboration. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the biotechnology or pharmaceutical industry, including within the business and financial communities, could be adversely affected.

We face significant competition in seeking appropriate partners for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully partner our product candidates, potential partners must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations

among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into collaborations or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected. Even if we are successful in our efforts to establish new strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

### **Risks Related to Our Intellectual Property**

***Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.***

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the U.S. and/or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property and/or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or

all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products.

In addition, periodic maintenance fees on any issued patent are due to be paid to the U.S. Patent Office ("USPTO") and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can, in many cases, be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. Moreover, complications due to the COVID-19 pandemic may result in inadvertent lapse due to, for example, unexpected closures of the USPTO or foreign patent offices, delays in delivery of notifications relating to deadlines, or failure to timely and/or properly obtain signatures on necessary documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds or cells that are similar to the biological compositions of our product candidates but that are not covered by the claims of our patents;
- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;

- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the U.S.;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; and/or
- the patents of others may have an adverse effect on our business.

Our current owned patents and co-owned patents covering our proprietary technologies and our product candidates are expected to expire beginning in 2034 (owned) and November 2033 (co-owned) respectively, without taking into account any possible patent term adjustments or extensions. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the U.S. or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a material adverse effect on our business, results of operations, financial condition and prospects. We own and co-own pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from November 2033 through 2043, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

***We depend on intellectual property licensed from third parties. Failure to comply with our obligations under any of these licenses or termination of any of these licenses could result in the loss of significant rights, which would harm our business.***

We are dependent on patents, know-how and proprietary technology, including intellectual property rights licensed from others. We may be a party to license agreements pursuant to which we in-license key patents and patent applications for our product candidates. These licenses impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license. Any termination of licenses by third parties could result in our loss of significant intellectual property rights and could harm our ability to commercialize our product candidates.

We may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer

of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

***We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.***

Because our programs may involve additional product candidates that may require the use of additional proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently, and these rights may be held by others. We may develop products containing our compounds and pre-existing pharmaceutical compounds. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product

candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

***Changes in patent law in the U.S. and in ex-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

In addition, recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act (the “America Invents Act”), enacted in 2013, the U.S. moved from a “first to invent” to a “first to file” system. Under a “first to file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act, and many of the substantive changes to patent law, including the “first to file” provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Recent U.S. Supreme Court rulings have also narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. As a consequence, issued patents may be found to contain invalid claims according to the newly revised eligibility and validity standards. Additionally, some of our owned or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in proceedings before the USPTO, or during litigation, under the revised criteria which could also make it more difficult to obtain patents.

Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case *Amgen Inc. v. Sanofi*, the Federal Circuit held that a well characterized antigen is insufficient to satisfy the written description requirement of certain claims directed to a genus of antibodies that are solely defined by function. While the validity of a subset of patents at issue was subsequently upheld by a district court jury, uncertainty remains as to the legal question pertaining to the written description requirement under 35 USC §112 as it relates to functional antibodies. In the case of *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. We cannot predict how these decisions or any future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition.

***Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.***

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical

industries, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post-grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting clinical trials and other development activities in the U.S. is protected under the Safe Harbor exemption as set forth in 35 U.S.C. § 271. If and when apitegromab, SRK-181 or another one of our product candidates is approved by the FDA, that certain third-party may then seek to enforce its patent by filing a patent infringement lawsuit against us. While we are not aware of any claims of such a patent that could otherwise materially adversely affect commercialization of our product candidates, we may be incorrect in this belief, or we may not be able to prove it in a litigation. In this regard, patents issued in the U.S. by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held



invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms, or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, and/or pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

We may also choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an ex-parte re-exam, inter partes review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge the grant of a third-party's patent in opposition proceedings in the European Patent Office ("EPO") or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office, then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

***We may incur substantial costs as a result of litigation or other proceedings relating to our patents or the patents of our licensors, and we may be unable to protect our rights to our products and technology.***

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims against a third party(ies), which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. There is also the risk that, even if the validity of our patents or the patents of our licensors is upheld, the court will refuse to stop the third-party on the ground that such third-party's activities do not infringe our owned or in-licensed patents. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

In some situations, we or our licensor, may not be able to detect infringement against our owned or in-licensed patents, as the case may be, which may be especially difficult for manufacturing processes or formulation patents. Even if we or our licensors detect infringement by a third-party of our owned or in-licensed patents, we or our licensors, as the case

may be, may choose not to pursue litigation against or settlement with the third-party. If we, or our licensors, later sue such third-party for patent infringement, the third-party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us or our licensors to enforce our owned or in-licensed patents, as the case may be, against such third-party.

***Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.***

If we or one of our licensing partners initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include inter parties review, ex parte re-examination, post-grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). For example, EP3368069 and EP2981822 are currently subject to opposition proceedings. Such proceedings are expensive and could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

In addition, because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, because patent applications in PCT member jurisdictions are typically not published until 18 months after the earliest filing, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products, compositions, methods of use, or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the U.S. If we or one of our licensors is a party to an interference proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

For applications filed under pre-AIA, interference proceedings declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S.

***We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.***

We have limited intellectual property rights outside the U.S. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign

countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the U.S. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products and/or methods of medical treatment, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Patent terms may result in inadequate protection for our product candidates, and we may be unable to obtain patent term extensions and data exclusivity for our product candidates, resulting in material harm to our business.***

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, also known as the Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. The patent term restoration period is generally one-half of the time between the effective date of the IND or the date of patent grant (whichever is later) and the date of submission of the BLA, plus the time between the date of submission of the BLA and the date of FDA approval of the product. The patent holder must apply for restoration within 60 days of approval. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. We may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request.

Given the amount of time required for the development, testing and regulatory review of new product candidates, the patents protecting our product candidates might expire before or shortly after such candidates are commercialized. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours, which could materially harm our business, financial condition, results of operations, and prospects.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the U.S. are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

***Third parties may assert that our employees or consultants have wrongfully used, disclosed, or misappropriated their confidential information or trade secrets.***

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent

litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

#### **Risks Related to Our Financial Condition and Capital Requirements**

***We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.***

We are a biopharmaceutical company formed in 2012 and our operations to date have been focused on research and development of monoclonal antibodies that selectively inhibit activation of growth factors for therapeutic effect. We have not yet demonstrated the ability to progress any of our product candidates through clinical trials, we have no products approved for commercial sale and we have not generated any revenue from product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. For the twelve months ended December 31, 2021, we reported a net loss of \$131.8 million. As of December 31, 2021, we had an accumulated deficit of \$376.1 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates, apitegromab and SRK-181, and any future product candidates.

To become and remain profitable, we or any current or potential future collaborators must develop and eventually commercialize products with significant market potential and favorable pricing. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials, receiving marketing approval for product candidates, manufacturing, marketing and selling products for which we may receive marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

***We will require additional capital to fund our operations and if we fail to obtain necessary capital, we will not be able to complete the development and commercialization of apitegromab, SRK-181 and any future product candidates.***

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts of cash to conduct further research and development, including clinical trials for apitegromab and SRK-181 and preclinical studies and clinical trials for any future product candidates, to seek regulatory approvals for our product candidates and to launch and commercialize any products for which we receive regulatory approval. As of December 31, 2021, we had approximately \$253.0 million in cash, cash equivalents and marketable securities. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021, will be sufficient to fund our operating expenses and capital expenditure requirements into mid-2023. However, our

future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will in any event require additional capital in order to complete clinical development of any of our current programs. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Additionally, any program setbacks or delays due to changes in federal or state laws or clinical site or clinical vendor policies as a result of the COVID-19 pandemic could impact our programs and increase our expenditures. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, completion, costs and results of clinical trials for apitegromab and SRK-181 and preclinical studies and clinical trials for any future product candidates;
- the clinical development plans we establish for our product candidates;
- the number and characteristics of product candidates that we identify and develop;
- the terms of any collaboration, strategic alliance, or licensing agreements we are currently party to or may choose to enter into in the future;
- the impact of the COVID-19 pandemic on the initiation or completion of preclinical studies or clinical trials and the supply of our product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA, and other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of developing research cell lines and development and completion of commercial scale outsourced manufacturing activities; and
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

We do not have any committed external source of funds or other support for our development efforts other than pursuant to our license agreement with Janssen, which payments we may not receive in full or at all, and we cannot be certain that additional funding will be available on acceptable terms, or at all. Even if we receive the maximum payments under the license agreement with Janssen, the payments may not meet our current or future funding requirements. Until we can generate sufficient product or royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek collaborators for apitegromab, SRK-181 or any future product candidate at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of apitegromab, SRK-181 or one or more of our future product candidates or other research and development initiatives.



Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

***Changes in tax law could adversely affect our business and financial condition.***

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

***Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.***

As of December 31, 2021, we had net operating loss carryforwards for federal and state income tax purposes of \$302.1 million and \$300.2 million, respectively, which begin to expire in 2032, except for our post 2017 federal net operating loss carryforwards of \$251.6 million which do not expire. As of December 31, 2021, we also had available tax credit carryforwards for federal and state income tax purposes of \$22.5 million and \$4.2 million, respectively, which begin to expire in 2034 and 2024, respectively. Additionally, for taxable years beginning after December 31, 2021 the deductibility of such federal net operating losses is limited to 80% of our taxable income in any future taxable year. Under Section 382 of the Internal Revenue Code of 1986, as amended (the “Code”), changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Private placements and other transactions that have occurred since our inception, as well as our Initial Public Offering (“IPO”), may trigger such an ownership change pursuant to Section 382 of the Code. Any such limitation, whether as the result of our IPO, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years.

**Risks Related to Our Common Stock**

***The price of our stock is volatile, and you could lose all or part of your investment.***

Similar to the trading prices of the common stock of other biopharmaceutical companies, the trading price of our common stock is subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this Annual Report, these factors include:

- announcements of significant acquisitions, strategic collaborations or partnerships, joint ventures or capital commitments by us, our collaborators or our competitors;
- actual or anticipated variations in quarterly operating results or our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- changes in accounting practices; and
- significant lawsuits, including patent or stockholder litigation.



In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including as a result of the COVID-19 pandemic. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

***We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.***

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Furthermore, our ability to pay cash dividends is currently restricted by the terms of our credit facility with Oxford and SVB, and future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

***Our Board members, management, and their affiliates, own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.***

As of December 31, 2021, our executive officers, directors and their affiliates beneficially hold, in the aggregate, approximately 16.5% of our outstanding voting stock. These stockholders, acting together, are able to significantly influence all matters requiring stockholder approval. For example, these stockholders are able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

***We are an “emerging growth company” and a “smaller reporting company,” and we cannot be certain if the reduced reporting requirements applicable to emerging growth and smaller reporting companies will make our common stock less attractive to investors.***

We are an Emerging Growth Company (“EGC”), as defined in the Jumpstart Our Business Startups Act (the “JOBS Act”), enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (“Sarbanes-Oxley Act”);
- reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements;
- exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements; and
- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management's Discussion and Analysis of Financial Condition and Results of Operations” disclosure.

We will remain an emerging growth company until the earlier of (1) December 31, 2023 (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.07 billion or (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-

affiliates to exceed \$700 million as of the last business date of our most recently completed second fiscal quarter, and (4) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

We are also a “smaller reporting company” as defined in the Exchange Act, and have elected to take advantage of certain of the scaled disclosures available to smaller reporting companies.

***We expect to continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.***

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. These rules and regulations have significantly increased our legal and financial compliance costs and we anticipate that these activities will become more time-consuming and costly over time.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting, and, once we are no longer an EGC or a “smaller reporting company”, we will be required to furnish an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction to the trading price of our common stock in the financial markets due to a loss of confidence in the reliability of our financial statements.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.***

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an

EGC or a “smaller reporting company”, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years following the completion of our IPO and will qualify as a “smaller reporting company” if the market value of our common stock held by non-affiliates is below \$250 million (or \$700 million if our annual revenue is less than \$100 million) as of June 30 in any given year. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

***We have broad discretion in the use of our existing cash, cash equivalents and marketable securities and may not use them effectively.***

Our management has broad discretion in the application of our existing cash, cash equivalents and marketable securities. Because of the number and variability of factors that will determine our use of our existing cash and cash equivalents, their ultimate use may vary substantially from their currently intended use. Our management might not apply our existing cash and cash equivalents in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business.

***Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing

or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

***If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.***

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

***We may be subject to securities litigation, which is expensive and could divert management attention.***

The market price of our common stock may be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

***Our amended and restated bylaws contain certain exclusive forum provisions requiring that substantially all disputes between us and our stockholders be resolved in certain judicial forums, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our amended and restated bylaws contain a provision by virtue of which, unless we consent in writing to the selection of an alternative forum, the U.S. District Court for the District of Massachusetts will be the exclusive forum for any complaint asserting a cause of action arising under the Securities Act. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions, however, stockholders cannot and will not be deemed to have waived compliance with federal securities laws and the rules and regulations thereunder. We have chosen the U.S. District Court for the District of Massachusetts as the exclusive forum for such causes of action because our principal executive offices are located in Cambridge, Massachusetts. Some companies that have adopted similar federal district court forum selection provisions are currently subject to a suit in the Court of Chancery of the State of Delaware brought by stockholders who assert that the federal district court forum selection provision is not enforceable. While the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our federal forum selection provision, and we may incur additional costs of litigation should such enforceability be challenged. If the federal forum selection provision is otherwise found inapplicable to, or unenforceable in respect of, one or more of the specified actions or proceedings, we may incur additional costs, which could have an adverse effect on our business, financial condition or results of operations. We recognize that the federal district court forum selection clause may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the Commonwealth of Massachusetts. Additionally, the choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs

associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

Our corporate headquarters and operations are located in Cambridge, Massachusetts. In March 2015, we entered into a lease of laboratory and office space at 620 Memorial Drive in Cambridge, Massachusetts. Our amended lease expires in September 2023 and we have an option to extend the lease term for five additional years. This space has been sublet beginning February 1, 2021.

In November 2019, we entered into a lease of laboratory and office space at 301 Binney Street in Cambridge, Massachusetts to be used as our new corporate headquarters. We were involved in the construction and design of the space. The expiration date is in August 2025 and we have the option to extend the term by two years. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional space will be available as and when needed.

**Item 3. Legal Proceedings**

From time to time, we are subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this Annual Report, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

**Item 4. Mine Safety Disclosures**

Not applicable.

## PART II

### **Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**

#### **Market Information**

Our common stock is traded on the Nasdaq Global Select Market under the symbol “SRRK”. Trading of our common stock commenced on May 24, 2018, following the completion of our IPO. Prior to that time, there was no established public trading market for our common stock.

#### **Stockholders**

As of March 2, 2022, there were approximately 10 stockholders of record of our common stock. This number does not include beneficial owners whose shares are held in street name.

#### **Dividends**

We have never declared or paid any dividends to our stockholders since our inception and we do not plan to declare or pay cash dividends in the foreseeable future. We currently anticipate that we will retain all available funds and any future earnings for the operation and expansion of our business. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend on, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

#### **Equity Compensation Plans**

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

#### **Unregistered Sales of Securities**

Not applicable.

#### **Issuer Purchases of Equity Securities**

None.

### **Item 6. Reserved**

Not applicable.

## Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

*The information contained in this section has been derived from our consolidated financial statements and should be read together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities and Exchange Act of 1934, as amended, the "Exchange Act" and are subject to the "safe harbor" created by those sections. In particular, statements contained in this Annual Report on Form 10-K that are not historical facts, including, but not limited to statements regarding our future expectations, plans and prospects, including without limitation, our expectations regarding the potential of the TGFβ program, the potential of apitegromab as a therapy in SMA and the timeline for and progress in developing apitegromab, the potential of SRK-181 as a cancer immunotherapy and the timeline for and progress in developing SRK-181, and liquidity, constitute forward-looking statements and are made under these safe harbor provisions. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "could," "seek," "intends," "plans," "estimates," "anticipates," or other comparable terms. Forward-looking statements involve inherent risks and uncertainties, which could cause actual results to differ materially from those in the forward-looking statements. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. We urge you to consider the risks and uncertainties discussed in greater detail under the heading "Risk Factors" elsewhere in this Annual Report on Form 10-K in evaluating our forward-looking statements. We have no plans to update our forward-looking statements to reflect events or circumstances after the date of this report. As a result of many factors, including those factors set forth under the heading "Risk Factors" elsewhere in this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of serious diseases in which signaling by protein growth factors plays a fundamental role. Our novel understanding of the molecular mechanisms of growth factor activation enabled us to develop a proprietary platform for the discovery and development of monoclonal antibodies that locally and selectively target the precursor, or latent, forms of growth factors. By targeting the signaling proteins at the cellular level and acting in the disease microenvironment, we believe we may avoid the historical dose-limiting safety challenges associated with inhibiting growth factors for therapeutic effect. We believe our focus on biologically validated growth factors may facilitate a more efficient development path.

We have a productive scientific platform and are building our portfolio of novel product candidates with the aim of transforming the lives of patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer, and fibrosis. We have discovered and progressed the development of:

- Apitegromab, an inhibitor of the activation of latent myostatin, for the treatment of SMA. We also believe apitegromab could have potential in the treatment of other myostatin-related disorders.
- SRK-181, an inhibitor of the activation of latent TGFβ1, for the treatment of cancers that are resistant to anti-PD-(L)1 antibody therapies.
- Potent and selective inhibitors of the activation of TGFβ for the treatment of fibrotic diseases. We are advancing multiple antibody profiles toward product candidate selection including antibodies that selectively inhibit the activation of latent TGFβ1 in the context of fibrotic extracellular matrix and that avoid perturbing TGFβ1 presented by cells of the immune system.
- Additional discovery and early preclinical programs related to the selective modulation of growth factor signaling, including BMP6 and other growth factors.

Our first product candidate, apitegromab (formerly SRK-015), is a highly selective, fully human, monoclonal antibody with a unique mechanism of action that results in inhibition of the activation of the growth factor, myostatin, in skeletal muscle. Apitegromab is being developed as a potential first muscle-directed therapy for the treatment of SMA. We are



conducting SAPPHERE, a pivotal Phase 3 clinical trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA (which is estimated to represent the majority of the current prevalent SMA patient population in the U.S. and Europe). Apitegromab was evaluated in the Company's TOPAZ Phase 2 proof-of-concept clinical trial for the treatment of patients with Type 2 and Type 3 SMA. Positive 12-month top-line results were announced in April 2021 showing apitegromab's transformative potential (see "Topaz Twelve-Month Analysis" in Item 1. Business). From June to October 2021, we announced supportive data from additional exploratory analyses from the TOPAZ Phase 2 clinical trial at various medical congresses, including the Cure SMA virtual conference, the World Muscle Society virtual congress, the Child Neurology Society annual meeting, and the World Congress of Neurology. The FDA granted Fast Track designation, Rare Pediatric Disease designation and Orphan Drug Designation to apitegromab for the treatment of SMA in May 2021, August 2020 and March 2018, respectively. The EMA granted PRIME designation in March 2021 and the EC granted Orphan Medicinal Product designation in December 2018 to apitegromab for the treatment of SMA.

We have identified multiple other diseases for which the selective inhibition of the activation of myostatin may offer therapeutic benefit, including additional patient populations in SMA (such as Type 1 SMA and ambulatory SMA) and indications outside of SMA.

Our second product candidate, SRK-181, is being developed for the treatment of cancers that are resistant to CPI therapies, such as anti-PD-1 or anti-PD-L1 antibody therapies. SRK-181 is a highly selective inhibitor of the activation of latent TGF $\beta$ 1 that is being investigated in our DRAGON Phase 1 proof-of-concept clinical trial in patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibodies. This two-part clinical trial consists of a dose escalation portion (Part A) and a dose expansion portion evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody therapy (Part B). Part B encompasses five cohorts, including urothelial carcinoma, cutaneous melanoma, non-small cell lung cancer, clear cell renal cell carcinoma and other solid tumors and commenced in 2021. Initial clinical data from Part A were presented in November 2021 at the SITC 36<sup>th</sup> Annual Meeting.

Utilizing our proprietary platform, we have multiple early stage and preclinical programs directed against targets that are known to be important in serious diseases, including neuromuscular disorders, cancer and fibrosis. We are discovering and generating selective and differentiated monoclonal antibodies against difficult targets by 1) applying our structural insights and antibody discovery expertise, 2) prioritizing human biology, and 3) embedding translational thinking early in the research and development process.

Since inception, we have incurred significant operating losses. Our net losses were \$131.8 million and \$86.5 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of \$376.1 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. In addition, we anticipate that our expenses will increase in connection with our ongoing activities, as we:

- continue development activities for apitegromab, including the ongoing extension phase of our TOPAZ Phase 2 clinical trial and conduct of our SAPPHERE Phase 3 pivotal clinical trial in SMA and associated drug supply;
- continue research and development activities for SRK-181, including the conduct of our DRAGON Phase 1 proof of concept clinical trial;
- continue to discover, validate and develop additional product candidates through the use of our proprietary platform;
- maintain, expand and protect our intellectual property portfolio;
- hire additional research, development and business personnel; and
- continue to build the infrastructure to support our operations as a public company.

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If we successfully complete clinical development and obtain regulatory approval for apitegromab, SRK-181 or any of our future product candidates, we may generate revenue in the future from product sales. In addition, if we obtain regulatory approval for apitegromab, SRK-181 or any of our future product candidates,

we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution activities.

### **COVID-19 Pandemic**

In March 2020, the World Health Organization declared the outbreak of a novel coronavirus, or COVID-19, as a pandemic (the “COVID-19 pandemic”), which continues to spread throughout the U.S. and worldwide. We could be materially and adversely affected by the risks, or the public perception of the risks, related to an epidemic, pandemic, outbreak, or other public health crisis, such as the COVID-19 pandemic. The ultimate extent of the impact of any epidemic, pandemic, outbreak, or other public health crisis on our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of such epidemic, pandemic, outbreak, or other public health crisis and actions taken to contain or prevent the further spread, including the development and deployment of any vaccine program. Accordingly, we cannot predict the extent to which our business, including our clinical trials, financial condition and results of operations will be affected. As a result of the COVID-19 pandemic, we have experienced disruptions that have impacted our business, preclinical studies and clinical trials, including disruptions or restrictions on our ability to access and monitor certain clinical trial sites, restrictions on clinical trial participants’ ability to access our clinical trial sites and delays in enrollment. Some clinical trial participants have missed or experienced delays in receiving doses of study drug and completing their clinical trial assessments. For example, four patients (one in Cohort 2 and three in Cohort 3) of the TOPAZ clinical trial each missed three doses of apitegromab over the course of the 12-month treatment period due to COVID-19-related site access restrictions. This has affected our clinical trials and could result in further impacts, including delays in or adverse impacts to data readouts from our clinical trials, delays in our ability to identify and enroll patients in current or future clinical trials and decisions by enrolled patients to discontinue from our clinical trials due to COVID-19 related concerns. While our laboratory operations have resumed to near-normal capacity, we may continue to experience challenges in procuring materials and supplies, as well as research services from our vendors in a consistently timely manner due to COVID-19 related supply chain issues. Some of our third-party manufacturers have diverted resources or manufacturing capacity to accommodate the development or manufacture of COVID-19 vaccines. Although this has not had an impact on our ability to produce sufficient quantities of apitegromab or SRK-181 for our clinical trials, we continue to work closely with our third-party manufacturers to mitigate potential impacts to our clinical supply chain. In addition, delays in the development of COVID-19 vaccines or the deployment of vaccines which are approved or otherwise authorized for emergency use, a recurrence or “subsequent waves” of COVID-19 cases, or the discovery of vaccine-resistant COVID-19 variants could cause other widespread or more severe impacts. We continue to monitor developments as we adjust to the disruptions and evaluate the uncertainties relating to the COVID-19 pandemic.

### **Financial Operations Overview**

#### **Revenue**

No revenues have been recorded from the sale of any commercial product. Revenue generation activities have been limited to collaborations, containing research services and the issuance of a license. Currently, revenue is being recognized related to the Gilead Collaboration Agreement which was executed on December 19, 2018 (the “Effective Date”), and we began recognizing associated revenue in 2019. Under the Gilead Collaboration Agreement, Gilead had exclusive options to license worldwide rights to product candidates that emerged from three of the Company’s TGF $\beta$  programs (each a “Gilead Program”). Each option could have been exercised by Gilead at any time from the Effective Date through a date that is 90 days following the expiration of the Research Collaboration Term for a given Gilead Program (no later than March 19, 2022), or until termination of the Gilead Program, whichever is earlier (the “Option Exercise Period”). On January 6, 2022, Gilead agreed that its option exercise period for all programs has been terminated.

Revenue associated with the research and development and license performance obligations relating to the Gilead Programs was recognized as revenue using an input method as the research and development services were provided over the research term, which ended in December 2021. The input method was based on the costs incurred on each Gilead Program and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurred over time. In management’s judgment, this input method was the best measure of progress towards

satisfying the performance obligations. We evaluated the measure of progress each reporting period and, if necessary, adjusted the measure of performance and related revenue recognition. The estimate of remaining costs had been highly subjective, as the research was novel, therefore efforts to be successful may have been significantly different than the estimated costs made at each balance sheet date. To date, we have recognized all revenue associated with the service period of the collaboration. The amounts received that have not yet been recognized as revenue are recorded in deferred revenue on our consolidated balance sheet and represent \$33.2 million in deferred revenue associated with the material rights provided by the options. Gilead agreed that its option exercise period for all programs terminated in January 2022, we expect to recognize the remaining revenue in the first quarter of 2022.

### ***Operating Expenses***

#### **Research and Development**

Research and development expenses consist primarily of costs incurred for our research and development activities, including our product candidate discovery efforts, preclinical studies, manufacturing, and clinical trials under our research programs, which include:

- employee-related expenses, including salaries, benefits and equity-based compensation expense for our research and development personnel;
- expenses incurred under agreements with third parties that conduct research and development and preclinical activities on our behalf;
- expenses incurred under agreements related to our clinical trials, including the costs for investigative sites and CROs, that conduct our clinical trials;
- manufacturing process-development, manufacturing of clinical supplies and technology-transfer expenses;
- consulting and professional fees related to research and development activities;
- costs of purchasing laboratory supplies and non-capital equipment used in our internal research and development activities;
- costs related to compliance with clinical regulatory requirements; and
- facility costs and other allocated expenses, which include expenses for rent and maintenance of facilities, insurance, depreciation and other supplies.

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable advance payments for research and development goods and services to be received in the future from third parties are deferred and capitalized. The capitalized amounts are expensed as the related services are performed.

A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis after a clinical product candidate has been identified. However, we do not allocate our internal research and development expenses, consisting primarily of employee related costs, depreciation and other indirect costs, on a program-by-program basis as they are deployed across multiple projects.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials, as well as the associated clinical trial material requirements. We expect research and development costs to increase for the foreseeable future as our product candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

The successful development of apitegromab, SRK-181 and any future product candidates is uncertain. Accordingly, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of apitegromab, SRK-181 and any future product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of our product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the scope, progress, outcome and costs of our preclinical development activities, clinical trials and other research and development activities;
- establishing an appropriate safety profile;
- successful enrollment in and completion of clinical trials, including on account of the COVID-19 pandemic and its impact at clinical trial sites;
- whether our product candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, if any;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- significant and changing government regulation;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of the products following any regulatory approval.

A change in the outcome of any of these variables with respect to the development of apitegromab, SRK-181 or any of our future product candidates could significantly change the costs and timing associated with the development of that product candidate.

#### **General and Administrative**

General and administrative expenses consist primarily of employee-related expenses, including salaries, benefits and equity-based compensation expenses for personnel in executive, finance, business development, investor relations, legal, information technology and human resources functions. Other significant general and administrative expenses include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting, consulting services, and corporate expenses.

We anticipate that our general and administrative expenses will increase in the future as our business expands to support expected growth in research and development activities, including the continued progression of our product candidates through development stages, as we hope to approach marketing and commercialization. These increases will likely include increased costs related to the hiring of additional personnel, as well as fees to outside consultants, among other expenses. We also anticipate continued expenses associated with being a public company, including costs for audit, legal, regulatory and tax-related services, director and officer insurance premiums and investor relations costs.

#### ***Other Income (Expense), Net***

Other income (expense), net consists primarily of interest expense incurred on our credit facility entered into in October 2020, including amortization of debt discount and debt issuance costs, partially offset by interest income earned on our cash, cash equivalents and marketable securities.

## Results of Operations

### Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of consolidated operations for the years ended December 31, 2021 and 2020 (in thousands, except percentages):

	Year Ended December 31,		Change	
	2021	2020	\$	%
Revenue	\$ 18,816	\$ 15,403	\$ 3,413	22.2 %
Operating expenses:				
Research and development	108,468	74,062	34,406	46.5 %
General and administrative	40,269	28,219	12,050	42.7 %
Total operating expenses	148,737	102,281	46,456	45.4 %
Loss from operations	(129,921)	(86,878)	(43,043)	49.5 %
Other income (expense), net	(1,878)	395	(2,273)	(575.4)%
Net loss	\$ (131,799)	\$ (86,483)	\$ (45,316)	52.4 %

### Revenue

Revenue was \$18.8 million for the year ended December 31, 2021 compared to \$15.4 million for the year ended December 31, 2020, an increase of \$3.4 million, or 22.2%. The revenue for both of these periods was related to the Gilead Collaboration Agreement executed in December 2018. Revenue associated with the research and development and license performance obligations relating to the Gilead Programs was recognized as the research and development services were provided using a cost input method. The increase in revenue was attributable to the change in progress of the programs period over period as well as changes in estimates of the total costs expected to be incurred. The \$33.2 million deferred revenue balance as of December 31, 2021 is related to material rights that is expected to be recognized as revenue in the first quarter of 2022, as Gilead agreed in January 2022 that its option exercise period for all programs had been terminated.

### Operating Expenses

#### Research and Development

Research and development expense was \$108.5 million for the year ended December 31, 2021 compared to \$74.1 million for the year ended December 31, 2020, an increase of \$34.4 million, or 46.5%. The following table summarizes our research and development expense for the years ended December 31, 2021 and 2020 (in thousands, except percentages):

	Year Ended December 31,		Change	
	2021	2020	\$	%
External costs by program:				
Apitegromab (SRK-015)	\$ 38,141	\$ 19,213	\$ 18,928	98.5 %
SRK-181	13,999	16,397	(2,398)	(14.6)%
Other early programs and unallocated costs	7,378	6,058	1,320	21.8 %
Total external costs	59,518	41,668	17,850	42.8 %
Internal costs:				
Employee compensation and benefits	32,487	22,590	9,897	43.8 %
Facility and other	16,463	9,804	6,659	67.9 %
Total internal costs	48,950	32,394	16,556	51.1 %
Total research and development expense	\$108,468	\$ 74,062	\$ 34,406	46.5 %

The increase in research and development expense was primarily attributable to the following:

- An increase in our external research and development costs of \$17.9 million, which primarily consisted of:
  - \$18.9 million increase in costs associated with apitegromab, due primarily to costs related to clinical drug supply manufacturing, including clinical trial material and process development work;
  - \$1.3 million increase in costs in other early development candidates and unallocated costs, which is mostly related to expense associated with the purchase of our customized antibody display library from Specifica;
  - \$2.4 million decrease in costs associated with SRK-181, as we incurred more clinical drug supply manufacturing costs in 2020 in preparation for our DRAGON Phase 1 clinical trial, which was initiated during the first quarter of 2020.
- \$16.6 million increase in internal research and development costs, which was primarily driven by an increase in employee compensation and benefits costs, associated with increased headcount, equity-based compensation and related overhead as we continued to expand our research and development functions in addition to an increase in facility costs due to our new office and laboratory space at 301 Binney Street in Cambridge, Massachusetts.

We expect our research and development expenses to increase as we continue to advance the development of our product candidates, including apitegromab through the extension phase of our TOPAZ Phase 2 clinical trial and preparation and conduct of our SAPPHERE Phase 3 pivotal clinical trial in SMA, and SRK-181, through our DRAGON Phase 1 clinical trial. However, as described above in “*COVID-19 Pandemic*”, the ultimate extent of the impact of the COVID-19 pandemic on our results of operations will depend on future developments, which are highly uncertain. Accordingly, we cannot fully predict the extent to which our business and results of operations will be affected.

#### **General and Administrative**

General and administrative expense was \$40.3 million for the year ended December 31, 2021 compared to \$28.2 million for the year ended December 31, 2020, an increase of \$12.1 million or 42.8%. The increase in general and administrative expense was primarily attributable to an increase of \$7.6 million in employee compensation and benefits, related to increased headcount and equity-based compensation, an increase of \$1.9 million in professional fees and an increase of \$1.5 million in facility costs due to our new office space at 301 Binney Street in Cambridge, Massachusetts.

We anticipate that our general and administrative expenses will increase in the future as our business expands to support our expected growth in research and development activities, including the continued development of our product candidates. However, as described above in “*COVID-19 Pandemic*”, the ultimate extent of the impact of the COVID-19 pandemic on our results of operations will depend on future developments, which are highly uncertain. Accordingly, we cannot fully predict the extent to which our business and results of operations will be affected.

#### ***Other Income (Expense), Net***

The change in other income (expense), net was primarily attributable to an increase in interest expense related to the Loan and Security Agreement, as well as a decrease in income earned on our investment portfolio associated with lower interest rates during the year ended December 31, 2021, as compared to the year ended December 31, 2020.

#### **Liquidity and Capital Resources**

##### ***Sources of Liquidity***

Since our inception, we have not generated any product revenue and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations to date primarily with proceeds from the sale of our convertible preferred stock and units in private placements before our IPO, and sale of our common stock through our IPO, to Gilead in an exempt private placement, through a secondary public offering in June 2019, through a follow-on offering completed in November 2020, through an at-the-market (“ATM”) sale in October 2021, as well as payments from our research collaborations and the Loan and Security Agreement entered into in October 2020.

The following table provides information regarding our total cash, cash equivalents and marketable securities at December 31, 2021 and December 31, 2020 (in thousands):

	December 31, 2021	December 31, 2020
Cash and cash equivalents	\$ 212,835	\$ 160,358
Marketable securities	40,159	180,673
Total cash, cash equivalents and marketable securities	<u>\$ 252,994</u>	<u>\$ 341,031</u>

During the year ended December 31, 2021, our cash, cash equivalents and marketable securities balance decreased by approximately \$88.0 million. The decrease was primarily due to cash used to operate our business, including payments related to, among other things, research and development and general and administrative expenses as we continued to invest in our primary product candidates and supported our internal research and development efforts, capital purchases, and interest payments on our debt, partially offset by proceeds of \$13.1 million through an ATM sale, \$25.0 million from Tranche 2 of the Loan and Security Agreement, as well as proceeds from stock option exercises.

In October 2021, we sold 500,000 shares of our common stock through an ATM sale, pursuant to the Open Market Sale Agreement<sup>SM</sup> with Jefferies, LLC, and received \$13.1 million in net proceeds, after underwriting fees.

In October 2020, we entered into an underwriting agreement relating to the issuance and sale of an aggregate of 3,717,948 shares of our common stock at \$39.00 per share and pre-funded warrants to purchase 2,179,487 shares of our common stock. The price of each pre-funded warrant was \$38.9999, which equals the per share public offering price for the common shares less the \$0.0001 exercise price for each such pre-funded warrant. Total gross proceeds of the transaction was \$230.0 million. The offering closed on November 2, 2020 and we received approximately \$215.9 million in net proceeds, after deducting underwriting discounts and commissions and estimated offering expenses.

In October 2020, we entered into the Loan and Security Agreement (the “Loan and Security Agreement”) with Oxford and SVB (each, a “Lender” and collectively, the “Lenders”), providing up to \$50.0 million of borrowings, of which \$25.0 million from Tranche 1 was advanced in October 2020 and \$25.0 million from Tranche 2 was received in December 2021.

In June and July 2019, we sold 3,450,000 shares of our common stock through an underwritten public offering. As a result of the offering, we received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately \$48.3 million.

In December 2018, we entered into the Gilead Collaboration Agreement, pursuant to which we conducted research and pre-clinical development activities relating to the diagnosis, treatment, cure, mitigation or prevention of diseases, disorders or conditions, other than in the field of oncology in accordance with a pre-determined research plan. Pursuant to the Gilead Collaboration Agreement, Gilead made non-refundable payments of \$80.0 million, including an upfront payment and an equity investment. In December 2019, we achieved a \$25.0 million preclinical milestone for the successful demonstration of efficacy in preclinical *in vivo* proof-of-concept studies, and subsequently received the associated payment in January 2020.



### **Cash Flows**

The following table provides information regarding our cash flows for the years ended December 31, 2021 and 2020 (in thousands):

	<b>Year Ended December 31,</b>	
	<b>2021</b>	<b>2020</b>
Net cash used in operating activities	\$ (126,789)	\$ (60,271)
Net cash provided by (used in) investing activities	134,315	(63,498)
Net cash provided by financing activities	44,951	247,819
Net increase in cash, cash equivalents and restricted cash	<u>\$ 52,477</u>	<u>\$ 124,050</u>

#### **Net Cash Used in Operating Activities**

Net cash used in operating activities was \$126.8 million for the year ended December 31, 2021, and consisted of our net loss of \$131.8 million, changes in our assets and liabilities of \$28.4 million, partially offset by non-cash adjustments of \$33.5 million. The changes in our assets and liabilities includes a \$18.8 million change in deferred revenue related to the Gilead collaboration. The non-cash adjustments are primarily from equity-based compensation.

Net cash used in operating activities was \$60.3 million for the year ended December 31, 2020, and consisted of our net loss of \$86.5 million partially offset by changes in our assets and liabilities of \$11.2 million and non-cash adjustments of \$15.0 million. The changes in our assets and liabilities includes the reduction of accounts receivable due to the \$25.0 million of cash received from Gilead in January 2020 from the preclinical milestone that was achieved in December 2019 and a \$15.4 million change in deferred revenue related to the Gilead collaboration. The non-cash adjustments are primarily from equity-based compensation.

#### **Net Cash Provided by (Used in) Investing Activities**

Net cash provided by investing activities was \$134.3 million for the year ended December 31, 2021, compared to net cash used in investing activities of \$63.5 million for the year ended December 31, 2020. Net cash provided by and used in investing activities for both periods was primarily associated with transactions involving our marketable securities as well as capital expenditures.

#### **Net Cash Provided by Financing Activities**

Net cash provided by financing activities was \$45.0 million for the year ended December 31, 2021, compared to \$247.8 million for the year ended December 31, 2020. Net cash provided by financing activities for the year ended December 31, 2021 consisted primarily of the second \$25.0 million drawdown from our Loan and Security Agreement, \$13.1 million in net proceeds from the sale of our common stock in an ATM sale completed in October 2021, as well as \$6.9 million in proceeds from stock option exercises.

Net cash provided by financing activities for the year ended December 31, 2020 consisted primarily of \$215.9 million in net proceeds from the sale of our common stock in a follow-on offering completed in November 2020 as well as the first \$25.0 million drawdown from our Loan and Security Agreement, in addition to \$7.3 million in proceeds from stock option exercises.

### **Funding Requirements**

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development for, continue and initiate later stage clinical trials for, continue to develop and optimize our manufacturing processes for, and seek marketing approval for, our product candidates, including apitegromab and SRK-181, and any of our future product candidates. In addition, if we obtain marketing approval for apitegromab, SRK-181 or any of our future product candidates, we expect to incur significant commercialization expenses related to product sales,

marketing, manufacturing and distribution. Furthermore, we expect to continue to incur costs associated with operating as a public company.

We expect that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into mid-2023. However, we will require additional capital in order to complete clinical development for each of our current programs. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the costs and timing of developing our product candidates, apitegromab and SRK-181, including our SAPPHIRE Phase 3 pivotal clinical trial for apitegromab in SMA, the extension phase of our TOPAZ Phase 2 clinical trial for apitegromab and the DRAGON Phase 1 clinical trial for SRK-181, and the costs and timing of conducting future preclinical studies and clinical trials, including on account of the COVID-19 pandemic and its impact at clinical trial sites;
- the costs of future manufacturing of apitegromab, SRK-181 and any other product candidates; including impacts from the COVID-19 pandemic and its impact at our contract manufacturers;
- the scope, progress, results and costs of discovery, preclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs of identifying and developing, or in-licensing or acquiring, additional product candidates and technologies;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements, license agreements, or other agreements we might have at such time;
- the costs of seeking marketing approvals for our product candidates that successfully complete clinical trials, if any;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and research and development activities;
- the costs of expanding our infrastructure and facilities to accommodate our growing employee base, including adding equipment and physical infrastructure to support our research and development; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, common stockholder

ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of a common stockholder. Additional debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

### **Critical Accounting Estimates**

This management's discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgements about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this report, we believe that the following accounting estimates are those most critical to the judgments used in the preparation of our consolidated financial statements. They involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our finance condition or result of operations.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced. In certain instances, we prepay for services to be provided in the future. These amounts are expensed as the services are performed.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid

balance accordingly. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

The accrued research and development expenses at the end of each year are generally paid during the following year and therefore the same estimates and assumptions do not continue to exist each year, although, as described above, the method and procedures to develop those estimates and assumptions are generally consistent.

### **Revenue Recognition**

No revenues have been recorded from the sale of any commercial product. Revenue generation activities have been limited to collaborations, containing research services and the issuance of a license. Currently, revenue is being recognized related to the Gilead Collaboration Agreement which was executed in December 2018. We began recognizing associated revenue in 2019 over the period that research is performed under the collaboration. We account for revenue under ASC Topic 606, Revenue from Contracts with Customers (“ASC 606”).

Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, we perform the following five steps: (i) identification of the contract(s) with the customer, (ii) identification of the promised goods or services in the contract and determination of whether the promised goods or services are performance obligations, (iii) measurement of the transaction price, (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to our customer.

#### **Identification of the Contract(s) with the Customer**

We account for a contract with a customer that is within the scope of ASC 606 when all of the following criteria are met: (i) the arrangement has been approved by the parties and the parties are committed to perform their respective obligations, (ii) each party's rights regarding the goods or services to be transferred can be identified, (iii) the payment terms for the goods or services to be transferred can be identified, (iv) the arrangement has commercial substance and (v) collection of substantially all of the consideration to which we will be entitled in exchange for the goods or services that will be transferred to the customer is probable.

#### **Identification of the Performance Obligations**

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when: (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, we consider factors such as the stage of development of the underlying intellectual property, the capabilities of our customer to develop the intellectual property on their own and whether the required expertise is readily available. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The identification of material rights requires judgments related to the determination of the value of the underlying license relative to the option exercise price, including assumptions about technical feasibility and the probability of developing a candidate that would be subject to the option rights.

### **Determination of the Transaction Price**

We estimate the transaction price based on the amount of consideration we expect to receive for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, we evaluate the amount of the potential payments and the likelihood that the payments will be received. We utilize either the most likely amount method or expected value method to estimate the transaction price based on which method better predicts the amount of consideration expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

We evaluate whether development, regulatory, and commercial milestone payments are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, we re-evaluate the probability of achievement of such milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue and earnings in the period of adjustment.

For sales-based royalties, including milestone payments based on the level of sales, we determine whether the sole or predominant item to which the royalties relate is a license. When the license is the sole or predominant item to which the sales-based royalty relates, we recognize revenue at the later of: (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any sales-based royalty revenue resulting from our arrangement.

### **Allocation of Transaction Price**

We allocate the transaction price based on the estimated standalone selling price. We must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. We utilize key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Estimating costs for research and development programs is subjective as we estimate the costs anticipated to successfully complete the research performance obligations. As the research is novel, efforts to be successful may be significantly different than the estimated costs at the beginning of the contract. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amounts we would expect to receive for satisfying each performance obligation.

### **Recognition of Revenue**

We utilize judgment to determine whether the performance obligation is satisfied over time or at a point in time. We determine the appropriate method of measuring progress performance obligations satisfied over time for purposes of recognizing revenue, such as by using an input method based on costs incurred compared to the costs expected to be incurred in the future to satisfy the performance obligation. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The estimated remaining costs is highly subjective, as the research is novel, therefore efforts to be successful may be significantly different than the estimated costs made at the balance sheet date. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we will recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license.

We receive payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our right to consideration is unconditional.

As it relates to the Gilead Collaboration Agreement, the Company has recognized the revenue related to the research and development services based on a cost input method over the research term for each respective Gilead Program. We evaluated the measure of progress each reporting period and, if necessary, adjusted the measure of performance and related revenue recognition. The estimate of remaining costs was highly subjective, as the research was novel, and efforts to be successful may have been significantly different than the estimated costs made at each balance sheet date.

#### **Recent Accounting Pronouncements**

We have reviewed all recently issued standards and have determined that, other than Recently Issued Accounting Pronouncements as disclosed in Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, such standards will not have a material impact on our financial statements or do not otherwise apply to our operations.

#### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk.**

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act of 1934, as amended (the “Exchange Act”), and are not required to provide the information required under this item.

#### **Item 8. Financial Statements and Supplementary Data**

Our financial statements, together with the report of our independent registered public accounting firm, appear in this Annual Report beginning on page F-1.

#### **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

#### **Item 9A. Controls and Procedures.**

##### **Management’s Evaluation of our Disclosure Controls and Procedures**

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’s rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our interim chief executive officer (principal executive officer) and chief financial officer (principal financial officer), has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our interim chief executive officer and chief financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date. We continue to review and document our disclosure controls and procedures, including our internal controls and procedures for financial reporting, and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our systems evolve with our business.

##### **Management’s Annual Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a-15(f) and 15d-15(d) under the Exchange Act. Our internal control system was designed to provide reasonable assurance to our management and our Board regarding the preparation and

fair presentation of published financial statements. All internal control systems, no matter how well designed have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, our management used the criteria set forth in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013 (“COSO criteria”). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021. This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for “emerging growth companies”.

**Changes in Internal Controls Over Financial Reporting**

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the year ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information.**

None.

**Item 9C. Foreign Jurisdictions that Prevent Inspections**

Not applicable.



### **PART III**

#### **Item 10. Directors, Executive Officers, and Corporate Governance**

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

#### **Item 11. Executive Compensation**

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

#### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

#### **Item 13. Certain Relationships and Related Transactions and Director Independence**

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

#### **Item 14. Principal Accountant Fees and Services**

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

**PART IV****Item 15. Exhibits, Financial Statements and Schedules**

## (a)(1) Financial Statements.

Our consolidated financial statements and notes thereto, together with the Reports of Independent Registered Public Accounting Firm are included in Item 8 of this Annual Report on Form 10-K commencing on page F-1.

## (a)(2) Financial Statement Schedules.

All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

## (a)(3) Exhibits.

The following exhibits are included in this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 (and are numbered in accordance with Item 601 of Regulation S-K):

<u>Number</u>	<u>Description</u>	<u>Form</u>	<u>File No.</u>	<u>Exhibit No.</u>	<u>Filing Date</u>
3.1	<a href="#">Amended and Restated Certificate of Incorporation of the Registrant</a>	S-1/A	333-224493	3.2	May 8, 2018
3.2	<a href="#">Amendment to Amended and Restated Certificate of Incorporation of the Registrant</a>	S-1/A	333-224493	3.1.1	May 14, 2018
3.3	<a href="#">Amended and Restated By-laws of the Registrant</a>	S-1/A	333-224493	3.4	May 8, 2018
4.1	<a href="#">Investors' Rights Agreement among the Registrant and certain of its stockholders, dated December 22, 2017</a>	S-1	333-224493	4.1	April 27, 2018
4.2	<a href="#">Specimen Stock Certificate evidencing shares of common stock</a>	S-1/A	333-224493	4.2	May 14, 2018
4.3	<a href="#">Amended and Restated Warrant to Purchase Stock, by and between Silicon Valley Bank and the Registrant, dated December 22, 2017</a>	S-1	333-224493	4.3	April 27, 2018
4.4*	<a href="#">Description of Capital Stock</a>	10-K	001-38501	4.4	March 12, 2020
10.1+	<a href="#">2017 Stock Option and Incentive Plan and forms of award agreements thereunder</a>	S-1	333-224493	10.1	April 27, 2018
10.2+	<a href="#">2018 Stock Option and Incentive Plan and forms of award agreements thereunder</a>	S-1/A	333-224493	10.2	May 14, 2018
10.3+	<a href="#">Senior Executive Cash Incentive Bonus Plan</a>	S-1/A	333-224493	10.3	May 8, 2018
10.4+	<a href="#">2018 Employee Stock Purchase Plan</a>	S-1/A	333-224493	10.4	May 14, 2018
10.5+	<a href="#">Form of Indemnification Agreement</a>	S-1/A	333-224493	10.5	May 14, 2018
10.6†	<a href="#">Exclusive License Agreement by and between the Registrant, and Children's Medical Center, dated as December 16, 2013</a>	S-1	333-224493	10.6	April 27, 2018
10.10+	<a href="#">Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement, by Nagesh K. Mahanthappa, dated October 10, 2012</a>	S-1	333-224493	10.10	April 27, 2018

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10.11+	<a href="#">Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement, by Yung H. Chyung, M.D., dated February 2, 2016</a>	S-1	333-224493	10.11	April 27, 2018
10.12†	<a href="#">Option and License Agreement by and between the Registrant and Janssen Biotech, Inc., dated as of December 17, 2013</a>	S-1	333-224493	10.13	April 27, 2018
10.13	<a href="#">Lease Agreement by and between 620 Memorial Leasehold LLC and the Registrant, dated March 5, 2015, as amended by the First Amendment dated February 22, 2016 and the Second Amendment dated February 22, 2018</a>	S-1	333-224493	10.14	April 27, 2018
10.14+	<a href="#">Form of Employment Agreement to be entered into by and between Yung H. Chyung, M.D., and the Registrant.</a>	S-1/A	333-224493	10.17	May 14, 2018
10.15††	<a href="#">Master Collaboration Agreement, dated December 19, 2018, by and between the Registrant and Gilead Sciences, Inc.</a>	8-K/A	001-38501	10.1	December 24, 2018
10.16††	<a href="#">Form of License Agreement.</a>	8-K/A	001-38501	10.2	December 24, 2018
10.17	<a href="#">Share Purchase Agreement, dated December 19, 2018, by and between Scholar Rock Holding Corporation and Gilead Sciences, Inc.</a>	8-K/A	001-38501	10.3	December 24, 2018
10.18	<a href="#">Registration Rights Agreement, dated December 19, 2018, by and among the Registrant, Gilead Sciences, Inc. and Scholar Rock Holding Corporation stockholder signatories named therein.</a>	8-K/A	001-38501	10.4	December 24, 2018
10.19	<a href="#">Irrevocable Registration Rights Waiver and Amendment, dated December 19, 2018, by and among the Registrant, Gilead Sciences, Inc. and Scholar Rock Holding Corporation stockholder signatories named therein.</a>	8-K/A	001-38501	10.5	December 24, 2018
10.20	<a href="#">Amended and Restated Collaboration Agreement, dated March 12, 2019, by and between Scholar Rock, Inc. and Adimab, LLC</a>	8-K	001-38501	10.1	March 13, 2019
10.21	<a href="#">Lease Agreement by and between BMR-Rogers Street LLC and Scholar Rock, Inc., dated November 5, 2019.</a>	10-Q	001-38501	10.2	November 12, 2019
Schedules have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedules will be furnished supplementally to the Securities and Exchange Commission upon request.					
10.22+	<a href="#">Employment Agreement, dated July 14, 2020, by and between Scholar Rock, Inc. and Stuart A. Kingsley.</a>	8-K	001-38501	10.1	July 16, 2020
10.23+	<a href="#">Employment Agreement, dated July 14, 2020, by and between Scholar Rock, Inc. and Edward H. Myles.</a>	8-K	001-38501	10.2	July 16, 2020

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10.24+	<a href="#">Consulting Agreement, dated July 16, 2020, by and between Scholar Rock, Inc. and Nagesh K. Mahanthappa.</a>	8-K	001-38501	10.3	July 16, 2020
10.25	<a href="#">Loan and Security Agreement, dated October 16, 2020, by and among the Registrant, Scholar Rock, Inc., Oxford Finance LLC and Silicon Valley Bank.</a>	10-K	001-38501	10.26	March 9, 2021
10.26+	<a href="#">Employment Agreement, dated May 23, 2018, by and between Scholar Rock, Inc. and Gregory Carven, as amended.</a>	10-K	001-38501	10.27	March 9, 2021
10.27*	<a href="#">First Amendment to Loan and Security Agreement, dated November 16, 2021, by and among the Registrant, Scholar Rock, Inc., Oxford Finance LLC and Silicon Valley Bank.</a>				
10.28+	<a href="#">Employment Agreement by and between Scholar Rock, Inc. and Nagesh Mahanthappa dated July 30, 2021.</a>	8-K	001-38501	10.1	August 3, 2021
10.29+	<a href="#">Separation Agreement, dated August 4, 2021, by and between Scholar Rock, Inc. and Stuart A. Kingsley.</a>	10-Q	001-38501	10.2	August 10, 2021
21.1*	<a href="#">Subsidiaries of the Registrant</a>				
23.1*	<a href="#">Consent of Independent Registered Public Accounting Firm.</a>				
24.1*	<a href="#">Power of Attorney (included on the signature page to this report).</a>				
31.1*	<a href="#">Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				
31.2*	<a href="#">Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>				
32.1**	<a href="#">Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>				
101.INS	XBRL Instance Document				
101.SCH	XBRL Taxonomy Extension Schema				

101.CAL	Document XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

104\* Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.)

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\* Filed herewith.

\*\* Furnished herewith and not deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, the Exchange Act, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

+ Indicates a management contract or compensatory plan.

† Confidential treatment has been granted for certain portions of this exhibit. These portions have been omitted and filed separately with the SEC.

†† Portions of this exhibit have been omitted pursuant to a request for confidential treatment that will be separately filed with the SEC.

**Item 16. Form 10-K Summary**

Not applicable.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

### SCHOLAR ROCK HOLDING CORPORATION

Date: March 7, 2022

By: /s/ Nagesh K. Mahanthappa  
Nagesh K. Mahanthappa  
Interim Chief Executive Officer and President  
(Principal Executive Officer)

Date: March 7, 2022

By: /s/ Edward H. Myles  
Edward H. Myles  
Chief Operating Officer & Chief Financial  
Officer (Principal Financial and Accounting  
Officer)

## POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Nagesh K. Mahanthappa and Edward H. Myles, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his true and lawful attorney-in-fact and agent to act in his name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Nagesh K. Mahanthappa</u> Nagesh K. Mahanthappa	Interim Chief Executive Officer and President (Principal Executive Officer)	March 7, 2022
<u>/s/ Edward H. Myles</u> Edward H. Myles	Chief Operating Officer & Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2022
<u>/s/ David Hallal</u> David Hallal	Chairman of the Board of Directors	March 7, 2022
<u>/s/ Kristina Burow</u> Kristina Burow	Director	March 7, 2022
<u>/s/ Jeffrey S. Flier</u> Jeffrey S. Flier	Director	March 7, 2022
<u>/s/ Michael Gilman</u> Michael Gilman	Director	March 7, 2022
<u>/s/ Amir Nashat</u> Amir Nashat	Director	March 7, 2022
<u>/s/ Akshay Vaishnaw</u> Akshay Vaishnaw	Director	March 7, 2022
<u>/s/ Joshua Reed</u> Joshua Reed	Director	March 7, 2022



**SCHOLAR ROCK HOLDING CORPORATION**  
**Index to Financial Statements**

<a href="#">Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)</a>	F-2
<a href="#">Consolidated Balance Sheets</a>	F-3
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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Scholar Rock Holding Corporation

### Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Scholar Rock Holding Corporation (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

### Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.

Boston, Massachusetts  
March 7, 2022

**SCHOLAR ROCK HOLDING CORPORATION**  
**CONSOLIDATED BALANCE SHEETS**

(In thousands, except share and per share data)

	December 31, 2021	December 31, 2020
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 212,835	\$ 160,358
Marketable securities	40,159	180,673
Prepaid expenses and other current assets	12,325	3,373
Total current assets	265,319	344,404
Property and equipment, net	9,564	8,121
Operating lease right-of-use asset	25,442	32,261
Restricted cash	2,498	2,498
Other long-term assets	1,622	1,021
Total assets	<u>\$ 304,445</u>	<u>\$ 388,305</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 4,434	\$ 3,409
Accrued expenses	17,456	14,958
Operating lease liability	7,407	5,366
Short-term debt	1,577	—
Deferred revenue	33,193	18,816
Other current liabilities	230	15
Total current liabilities	64,297	42,564
Long-term portion of operating lease liability	19,652	27,093
Long-term debt	48,422	24,680
Other long-term liabilities	—	5
Long-term portion of deferred revenue	—	33,193
Total liabilities	<u>132,371</u>	<u>127,535</u>
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized at December 31, 2021 and December 31, 2020; no shares issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock, \$0.001 par value; 150,000,000 shares authorized; 35,209,099 and 34,152,470 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	35	34
Additional paid-in capital	548,204	505,069
Accumulated other comprehensive loss	(35)	(2)
Accumulated deficit	(376,130)	(244,331)
Total stockholders' equity	<u>172,074</u>	<u>260,770</u>
Total liabilities and stockholders' equity	<u>\$ 304,445</u>	<u>\$ 388,305</u>

The accompanying notes are an integral part of these consolidated financial statements.

**SCHOLAR ROCK HOLDING CORPORATION**  
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**

(In thousands, except share and per share data)

	Year Ended December 31,	
	2021	2020
Revenue	\$ 18,816	\$ 15,403
Operating expenses:		
Research and development	108,468	74,062
General and administrative	40,269	28,219
Total operating expenses	<u>148,737</u>	<u>102,281</u>
Loss from operations	(129,921)	(86,878)
Other income (expense), net	(1,878)	395
Net loss	<u>\$ (131,799)</u>	<u>\$ (86,483)</u>
Net loss per share, basic and diluted	<u>\$ (3.59)</u>	<u>\$ (2.81)</u>
Weighted average common shares outstanding, basic and diluted	<u>36,711,833</u>	<u>30,734,109</u>
Comprehensive loss:		
Net loss	\$ (131,799)	\$ (86,483)
Other comprehensive loss:		
Unrealized loss on marketable securities	(33)	(39)
Total other comprehensive loss	<u>(33)</u>	<u>(39)</u>
Comprehensive loss	<u>\$ (131,832)</u>	<u>\$ (86,522)</u>

The accompanying notes are an integral part of these consolidated financial statements.

**SCHOLAR ROCK HOLDING CORPORATION**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**

(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balance at December 31, 2019</b>	<b>29,792,922</b>	<b>\$ 30</b>	<b>\$ 270,682</b>	<b>\$ 37</b>	<b>\$ (157,848)</b>	<b>\$ 112,901</b>
Unrealized loss on marketable securities	—	—	—	(39)	—	(39)
Sale of common shares and pre-funded warrants, net of issuance costs	3,717,948	4	215,918	—	—	215,922
Exercise of warrants	6,961	—	—	—	—	—
Restricted shares forfeited during the period	(42,010)	—	—	—	—	—
Exercise of stock options	676,649	—	7,294	—	—	7,294
Equity-based compensation expense	—	—	11,175	—	—	11,175
Net Loss	—	—	—	—	(86,483)	(86,483)
<b>Balance at December 31, 2020</b>	<b>34,152,470</b>	<b>\$ 34</b>	<b>\$ 505,069</b>	<b>\$ (2)</b>	<b>\$ (244,331)</b>	<b>\$ 260,770</b>
Unrealized loss on marketable securities	—	—	—	(33)	—	(33)
Sale of common shares, net of issuance costs	500,000	—	13,095	—	—	13,095
Exercise of stock options	556,629	1	6,891	—	—	6,892
Equity-based compensation expense	—	—	23,149	—	—	23,149
Net loss	—	—	—	—	(131,799)	(131,799)
<b>Balance at December 31, 2021</b>	<b>35,209,099</b>	<b>\$ 35</b>	<b>\$ 548,204</b>	<b>\$ (35)</b>	<b>\$ (376,130)</b>	<b>\$ 172,074</b>

The accompanying notes are an integral part of these consolidated financial statements.

**SCHOLAR ROCK HOLDING CORPORATION**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

(In thousands)

	Year Ended December 31,	
	2021	2020
<b>Cash flows from operating activities:</b>		
Net loss	\$ (131,799)	\$ (86,483)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,627	1,491
Amortization of debt discount and debt issuance costs	335	58
Loss on disposal of property and equipment	24	28
Equity-based compensation	23,149	11,175
Amortization/accretion of investment securities	918	(162)
Non-cash operating lease expense	6,397	2,380
Change in operating assets and liabilities:		
Accounts receivable	—	25,000
Prepaid expenses and other current assets	(8,530)	(3,361)
Other assets	(601)	(923)
Accounts payable	1,016	2,101
Accrued expenses	3,663	5,089
Operating lease liabilities	(5,400)	(1,261)
Deferred revenue	(18,816)	(15,403)
Other liabilities	228	—
Net cash used in operating activities	<u>(126,789)</u>	<u>(60,271)</u>
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(5,248)	(4,088)
Purchases of marketable securities	(60,437)	(200,110)
Maturities of marketable securities	200,000	140,700
Net cash provided by (used in) investing activities	<u>134,315</u>	<u>(63,498)</u>
<b>Cash flows from financing activities:</b>		
Proceeds from debt	24,984	24,622
Proceeds from sale of common shares and pre-funded warrants, net of issuance costs	13,095	215,922
Proceeds from stock option exercises	6,892	7,294
Other	(20)	(19)
Net cash provided by financing activities	<u>44,951</u>	<u>247,819</u>
Net increase in cash, cash equivalents and restricted cash	52,477	124,050
Cash, cash equivalents and restricted cash, beginning of period	162,856	38,806
Cash, cash equivalents and restricted cash, end of period	<u>\$ 215,333</u>	<u>\$ 162,856</u>
Supplemental disclosure of non-cash items:		
Property and equipment purchases in accounts payable and accrued expenses	\$ 212	\$ 1,368
Operating lease right-of-use asset obtained in exchange for operating lease obligation	\$ —	\$ 31,286
Supplemental cash flow information:		
Cash paid for interest	\$ 2,082	\$ 251

The accompanying notes are an integral part of these consolidated financial statements.

**SCHOLAR ROCK HOLDING CORPORATION**  
**Notes to Consolidated Financial Statements**

**1. Nature of the Business and Basis of Presentation**

***Organization***

Scholar Rock Holding Corporation (the “Company”) is a biopharmaceutical company focused on the discovery and development of innovative medicines for the treatment of serious diseases in which signaling by protein growth factors plays a fundamental role. The Company’s novel understanding of the molecular mechanisms of growth factor activation enabled the development of a proprietary platform for the discovery and development of monoclonal antibodies that locally and selectively target the precursor, or latent, forms of growth factors. The Company’s first product candidate, apitegromab (formerly SRK-015), is a highly selective, fully human, monoclonal antibody, with a unique mechanism of action that results in inhibition of the activation of the growth factor, myostatin, in skeletal muscle. Apitegromab is being developed as a potential first muscle-directed therapy for the treatment of spinal muscular atrophy (“SMA”). The Company is conducting SAPPHIRE, a pivotal Phase 3 clinical trial to evaluate the efficacy and safety of apitegromab in patients with non-ambulatory Type 2 and Type 3 SMA. The Company’s second product candidate, SRK-181, is being developed for the treatment of cancers that are resistant to checkpoint inhibitor (“CPI”) therapies, such as anti-PD-1 or anti-PD-L1 antibody therapies. SRK-181 is a highly selective inhibitor of the activation of latent transforming growth factor beta-1 (“TGFβ1”) that is being investigated in the Company’s DRAGON Phase 1 proof-of-concept clinical trial in patients with locally advanced or metastatic solid tumors that exhibit primary resistance to anti-PD-(L)1 antibodies. The DRAGON trial consists of two parts: Part A (dose escalation of SRK-181 as a single-agent or in combination with an approved anti-PD-(L)1 therapy) and Part B (dose expansion evaluating SRK-181 in combination with an approved anti-PD-(L)1 antibody therapy). Part B encompasses five cohorts, including urothelial carcinoma, cutaneous melanoma, non-small cell lung cancer, clear cell renal cell carcinoma and other solid tumors and commenced in 2021. Additionally, the Company continues to create a pipeline of product candidates to deliver novel therapies to underserved patients suffering from a wide range of serious diseases, including neuromuscular disorders, cancer, and fibrosis. The Company was originally formed in May 2012. Its principal offices are in Cambridge, Massachusetts.

Since its inception, the Company’s operations have focused on research and development of monoclonal antibodies that selectively inhibit activation of growth factors for therapeutic effect, as well as establishing the Company’s intellectual property portfolio and performing research and development activities. The Company has primarily financed its operations through various equity financings (Note 8), as well as research and development collaboration agreements and the Company’s debt facility (Note 12).

Revenue generation activities have been limited to two collaborations, both containing research services and the issuance of a license. The first agreement, executed in 2013, was with Janssen Biotech, Inc. (“Janssen”), a subsidiary of Johnson & Johnson. The second agreement (the “Gilead Collaboration Agreement”), executed in December 2018, was with Gilead Sciences, Inc. (“Gilead”). No revenues have been recorded from the sale of any commercial product.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, successful discovery and development of its drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and regulatory approval and market acceptance of the Company’s product candidates. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop its product candidates. The Company believes that its existing cash, cash equivalents, and marketable securities at December 31, 2021 will be sufficient to allow the Company to fund its current operations through at least a period of one year after the date these financial statements are issued.

***Basis of Presentation***

The consolidated financial statements include the accounts of Scholar Rock Holding Corporation and its wholly owned subsidiaries. All intercompany balances have been eliminated in consolidation.



These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S. (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

## 2. Summary of Significant Accounting Policies

### *Use of Estimates*

The preparation of financial statements in accordance with GAAP requires management to make estimates and judgments that may affect the reported amounts of assets and liabilities and related disclosures of contingent assets and liabilities at the date of the financial statements and the related reporting of revenues and expenses during the reporting period. Management bases its estimates on historical experience and on various assumptions that are believed to be reasonable under the circumstances. Actual results could differ from those estimates.

### *Concentration of Credit Risk and Off-Balance Sheet Risk*

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign-hedging arrangements. The Company follows an investment policy approved by the Board of Directors. Its primary objectives are the preservation of capital and maintenance of liquidity. The Company invests only in fixed income instruments denominated and payable in U.S. dollars including obligations of the U.S. government and its agencies and money market funds registered according to SEC Rule 2a-7 of the Investment Company Act of 1940. All securities must have a readily ascertainable market value, must be readily marketable and be U.S. dollar denominated.

### *Cash, Cash Equivalents and Restricted Cash*

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents are stated at cost, which approximates market value. At December 31, 2021 and 2020, cash equivalents include money market funds that invest primarily in U.S. government-backed securities and treasuries.

Restricted cash consists of letters of credit in the amount of \$2.5 million related to its leased facilities. The following table reconciles cash, cash equivalents and restricted cash per the balance sheet to the statement of cash flows (in thousands):

	<u>As of December 31,</u>	
	<u>2021</u>	<u>2020</u>
Cash and cash equivalents	\$ 212,835	\$ 160,358
Restricted cash	2,498	2,498
	<u>\$ 215,333</u>	<u>\$ 162,856</u>

### *Property and Equipment*

Property and equipment are recorded at cost. Expenditures for major renewals or betterments that extend the useful lives of property and equipment are capitalized; expenditures for maintenance and repairs are charged to expense as incurred.

Depreciation is calculated on a straight-line basis over the estimated useful lives of the related asset. Property and equipment are depreciated as follows:

	Estimated Useful Life (in Years)
Laboratory equipment	3 – 5
Computer equipment & software	3
Furniture & fixtures	5
Machinery & equipment	3 – 5
Leasehold improvements	Shorter of the useful life or remaining lease term

### ***Impairment of Long-Lived Assets***

Long-lived assets consist of property and equipment and right-of-use assets. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2021 or 2020.

### ***Leases***

The Company accounts for leases using ASC Topic 842, Leases (“ASC 842”). At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its estimated incremental borrowing rates, which are the rates incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

In accordance with the guidance in ASC 842, components of a lease should be split into three categories: lease components (e.g. land, building, etc.), non-lease components (e.g. common area maintenance, consumables, etc.), and non-components (e.g. property taxes, insurance, etc.). Then the fixed and in-substance fixed contract consideration (including any related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components. For operating leases, lease expense relating to fixed payments is recognized on a straight-line basis over the term and lease expense relating to variable payments is expensed as incurred.

### ***Fair Value Measurements***

ASC Topic 820, Fair Value Measurement (“ASC 820”), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company’s own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company’s assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions

in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1** — Quoted market prices in active markets for identical assets or liabilities.
- Level 2** — Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.
- Level 3** — Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair values requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

### ***Segment Information***

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment operating exclusively in the U.S.

### ***Revenue Recognition***

The Company accounts for revenue using the provisions of ASC Topic 606, Revenue from Contracts with Customers ("ASC 606"). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the contract(s) with the customer, (ii) identification of the promised goods or services in the contract and determination of whether the promised goods or services are performance obligations, (iii) measurement of the transaction price, (iv) allocation of the transaction price to the performance obligations, and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company accounts for a contract with a customer that is within the scope of ASC 606 when all of the following criteria are met: (i) the arrangement has been approved by the parties and the parties are committed to perform their respective obligations, (ii) each party's rights regarding the goods or services to be transferred can be identified, (iii) the payment terms for the goods or services to be transferred can be identified, (iv) the arrangement has commercial substance and (v) collection of substantially all of the consideration to which the Company will be entitled in exchange for the goods or services that will be transferred to the customer is probable.

The Company first evaluates license and/or collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC Topic 808, *Collaborative Arrangements*, based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. The Company accounts for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside of the scope of ASC 606. The Company's existing collaborations represent revenue arrangements.

For the arrangements or arrangement components that are subject to revenue accounting guidance, in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company

performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the standalone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to the Company's proprietary technology or a material right provided by a customer option, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling prices, the Company evaluates whether changes in the key assumptions used to determine its estimated stand-alone selling prices will have a significant effect on the allocation of arrangement consideration between performance obligations.

The Company estimates the transaction price based on the amount of consideration the Company expects to be received for transferring the promised goods or services in the contract. The consideration may include both fixed consideration and variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of the potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate the transaction price based on which method better predicts the amount of consideration expected to be received. If it is probable that a significant revenue reversal would not occur, the variable consideration is included in the transaction price.

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer. Promised goods or services are considered distinct when: (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own and whether the required expertise is readily available.

The Company allocates the transaction price based on the estimated standalone selling price. The Company must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Estimating costs for research and development programs is subjective as the Company estimates the costs anticipated to successfully complete the research performance obligations. As the research is novel, efforts to be successful may be significantly different than the estimated costs at the beginning of the contract. Certain variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated to each performance obligation are consistent with the amounts the Company would expect to receive for each performance obligation.

For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation in order to determine whether the combined performance obligation is satisfied over time or at a point in time. The Company determines the appropriate method of measuring progress of combined performance obligations satisfied over time for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The estimated remaining costs is highly subjective, as the research is novel, therefore efforts to be successful may be significantly different than the estimated costs made at the balance sheet date. If the license to the

Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company will recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. The Company receives payments from customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

*Exclusive Licenses* – If the license granted in the arrangement is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promise, whether the value of the license is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the arrangement.

*Research and Development Services* – The promises under the Company's collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. For performance obligations that include research and development services, the Company generally recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure, such as costs incurred. The Company evaluates the measure of progress each reporting period as described under *Exclusive Licenses* above. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are generally recorded as a reduction to research and development expense.

*Customer Options* – The Company's arrangements may provide a collaborator with the right to certain optional purchases, such as the right to license a target either at the inception of the arrangement or within a pre-defined option period. Under these agreements, fees may be due to the Company (i) at the inception of the arrangement as an upfront fee or payment or (ii) upon the exercise of an option to acquire a license. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount, and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

*Milestone Payments* – At the inception of each arrangement that includes milestone payments based on certain events, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to

be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company's efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

*Royalties* – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

For a complete discussion of accounting for collaboration revenues, see Note 13, *Agreements*.

#### ***Research and Development Expenses and Accruals***

Research and development expenses are expensed as incurred and consist of costs incurred in performing research and development activities, including compensation related expenses for research and development personnel, preclinical and clinical activities including cost of drug supply, overhead expenses including facilities expenses, materials and supplies, amounts paid to consultants and outside service providers, and depreciation of equipment. Upfront license payments related to acquired technologies which have not yet reached technological feasibility and have no alternative future use are also included in research and development expense.

The Company has entered into various research and development service arrangements under which vendors perform various services. The Company records accrued expenses for estimated costs incurred under the arrangements. When evaluating the adequacy of the accrued expenses, the Company analyzed the progress of the studies, trials or other services performed, including invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued expense balances at the end of each reporting period.

#### ***Equity-Based Compensation***

The Company accounts for equity awards, including restricted stock awards, restricted stock units, and common stock options, granted as equity award compensation in accordance with ASC Topic 718, Compensation — Stock Compensation ("ASC 718"). ASC 718 requires all stock-based payments to employees, which includes grants of employee equity awards, to be recognized as expense in the statements of operations based on their grant date fair values.

The fair value of each restricted stock award and restricted stock unit is based on the fair value of the Company's common stock less any purchase price, if applicable. The fair value of each stock option award is estimated using the Black-Scholes option-pricing model, which uses as inputs the fair value of the Company's common stock and certain subjective assumptions, including the expected stock price volatility, the expected term of the award, the risk-free rate, and expected dividends. Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information was available. The historical volatility is generally calculated based on a period of time commensurate with the expected term assumptions. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption. The Company uses the simplified method, under which the expected term is presumed to be the midpoint between the vesting date and

the end of the contractual term. The Company utilizes this method due to lack of historical exercise data and the plain nature of its stock-based awards. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on common stock.

Compensation expense related to equity awards to employees that are subject to graded vesting is recognized on a straight-line basis, based on the grant date fair value, over the requisite service period of the award, which is generally the vesting term. For awards subject to performance conditions, the Company recognizes equity award compensation expense using an accelerated recognition method over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

The Company classifies equity-based compensation expense in its consolidated statements of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

The Company accounts for forfeitures when they occur.

### ***Comprehensive Loss***

Comprehensive loss is the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss includes net loss and the change in accumulated other comprehensive income (loss) for the period. Accumulated other comprehensive loss consisted entirely of unrealized gains and losses on available-for-sale marketable securities during the period ending December 31, 2021 and 2020.

### ***Net Loss per Share***

The Company applies the two-class method to compute basic and diluted net loss per share because it has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (losses) available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all income (losses) for the period had been distributed. During periods of loss, there is no allocation required under the two-class method since the participating securities do not have a contractual obligation to fund the losses of the Company.

The Company calculates basic net loss per share by dividing net loss by the weighted average number of common shares outstanding, including pre-funded warrants and excluding restricted common stock. The Company calculates diluted net loss per share by dividing net loss by the weighted average number of common shares outstanding, as applicable, after giving consideration to the dilutive effect of restricted stock awards, restricted stock units, warrants, pre-funded warrants, and stock options that are outstanding during the period.

### ***Income Taxes***

Income taxes are recorded in accordance with ASC Topic 740, Income Taxes ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred income tax assets and liabilities are recognized based on future income tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities, and their respective income tax basis. Deferred income tax assets and liabilities are measured using enacted income tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions, as necessary. The tax benefits recorded are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is "more likely than not" to be realized following resolution of any uncertainty related to the tax benefit, assuming that the matter in question will be raised by the tax authorities.



The Company is open to examination by the Internal Revenue Service for the tax years ended December 31, 2013 to December 31, 2021. Since the Company is in a U.S. loss carryforward position, carryforward tax attributes generated in prior years may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years. The Company has not recorded any interest or penalties on any unrecognized tax benefits since its inception.

### **Marketable Securities**

The Company classifies its marketable securities as available-for-sale. Marketable securities with a remaining maturity date greater than one year are classified as non-current. Marketable securities are maintained by an investment manager and consist of U.S. treasury securities. Marketable securities are carried at fair value with the unrealized gains and losses included in accumulated other comprehensive loss as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the underlying marketable security.

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income (expense) within the statement of operations and comprehensive loss. During the years ended December 31, 2021 and 2020, no marketable securities were adjusted for other than temporary declines in fair value.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company would reduce the investment to fair value through a charge to the statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

### **Recently Issued Accounting Pronouncements**

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The standard requires that a financial asset or a group of financial assets measured at amortized cost basis to be presented at the net amount expected to be collected. Under current GAAP, a company only considered past events and current conditions in measuring an incurred loss. Under ASU 2016-13, the information that a company must consider is broadened in developing an expected credit loss estimate for assets measured either collectively or individually. The use of forecasted information incorporates more timely information in the estimate of expected credit loss. The guidance is applied using a modified retrospective, or prospective approach, depending on a specific amendment. In November 2019, the FASB deferred the effective date for smaller reporting companies to fiscal years beginning after December 15, 2022. The Company does not anticipate a material impact to its net financial position or disclosures as a result of the adoption of ASU 2016-13.

### 3. Fair Value of Financial Assets and Liabilities

The following tables summarize the assets and liabilities measured at fair value on a recurring basis at December 31, 2021 and 2020 (in thousands):

	Fair Value Measurements at December 31, 2021			
	Total	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market funds, included in cash and cash equivalents	\$ 188,493	\$ 188,493	\$ —	\$ —
Marketable securities:				
U.S. Treasury obligations	40,159	40,159	—	—
Total assets	<u>\$ 228,652</u>	<u>\$ 228,652</u>	<u>\$ —</u>	<u>\$ —</u>

	Fair Value Measurements at December 31, 2020			
	Total	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market funds, included in cash and cash equivalents	\$ 119,841	\$ 119,841	\$ —	\$ —
U.S. Treasury obligations, included in cash and cash equivalents	9,998	9,998	—	—
Marketable securities:				
U.S. Treasury obligations	180,673	180,673	—	—
Total assets	<u>\$ 310,512</u>	<u>\$ 310,512</u>	<u>\$ —</u>	<u>\$ —</u>

Cash, cash equivalents and marketable securities are Level 1 assets and include investments in money market funds and U.S. government securities that are valued using quoted market prices. Accordingly, money market funds and government funds are categorized as Level 1 as of December 31, 2021 and 2020. There were no transfers of assets between fair value measurement levels during the years ended December 31, 2021 and 2020.

The carrying amounts reflected in the balance sheets for prepaid expenses and other current assets, accounts payable, and accrued expenses approximate their fair values at December 31, 2021 and 2020, due to their short-term nature.

The Company believes the terms of its debt reflect current market conditions for an instrument with similar terms and maturity, therefore the carrying value of the Company's debt approximates its fair value based on Level 3 of the fair value hierarchy.

#### 4. Marketable Securities

The following table summarizes the Company's investments as of December 31, 2021 (in thousands):

	Amortized Cost	Gross Unrealized		Estimated Fair Value
		Gains	Losses	
Marketable securities available-for-sale:				
U.S. Treasury obligations	\$ 40,194	—	(35)	\$ 40,159
Total available-for-sale securities	\$ 40,194	\$ —	\$ (35)	\$ 40,159

The following table summarizes the Company's investments as of December 31, 2020 (in thousands):

	Amortized Cost	Gross Unrealized		Estimated Fair Value
		Gains	Losses	
Marketable securities available-for-sale:				
U.S. Treasury obligations	\$ 180,675	\$ 7	\$ (9)	\$ 180,673
Total available-for-sale securities	\$ 180,675	\$ 7	\$ (9)	\$ 180,673

The aggregate fair value of marketable securities with unrealized losses was \$30.2 million and \$45.7 million at December 31, 2021 and 2020, respectively. At December 31, 2021 and 2020, 3 investments and 5 investments, respectively, were in an unrealized loss position. All such investments have been in an unrealized loss position for less than a year and these losses are considered temporary. The Company has the ability and intent to hold these investments until a recovery of their amortized cost, which may not occur until maturity.

#### 5. Property and Equipment, Net

At December 31, 2021 and 2020, property and equipment consists of the following (in thousands):

	December 31, 2021	December 31, 2020
Laboratory equipment	\$ 9,497	\$ 5,359
Leasehold improvements	5,160	1,579
Computer equipment & software	1,080	461
Furniture & fixtures	995	224
Machinery & equipment	75	75
Construction in progress	48	5,282
	16,855	12,980
Less: Accumulated depreciation and amortization	(7,291)	(4,859)
	\$ 9,564	\$ 8,121

Depreciation and amortization expense was \$2.6 million and \$1.5 million for the years ended December 31, 2021 and 2020, respectively.

## 6. Accrued Expenses

At December 31, 2021 and 2020, accrued expenses consist of the following (in thousands):

	As of	
	December 31, 2021	December 31, 2020
Accrued external research and development expense	\$ 8,428	\$ 5,387
Accrued payroll and related expenses	7,147	6,663
Accrued professional and consulting expense	1,421	1,141
Accrued other	436	476
Accrued payable for property and equipment	24	1,291
	<u>\$ 17,456</u>	<u>\$ 14,958</u>

## 7. Preferred Stock

The Board of Directors or any authorized committee thereof is expressly authorized, to the fullest extent permitted by law, to provide by resolution or resolutions for, out of the unissued shares of Preferred Stock, the issuance of the shares of Preferred Stock in one or more series of such stock, and by filing a certificate of designations pursuant to applicable law of the State of Delaware, to establish or change from time to time the number of shares of each such series, and to fix the designations, powers, including voting powers, full or limited, or no voting powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualifications, limitations and restrictions thereof.

## 8. Common Stock

The Company has a sales agreement with Jefferies LLC (“Jefferies”) with respect to an at-the-market (“ATM”) offering program under which the Company may offer and sell, from time to time at its sole discretion, shares of its common stock having an aggregate offering price of up to \$150.0 million, through Jefferies as its sales agent. In an ATM offering, exchange-listed companies incrementally sell newly issued shares into the secondary trading market through a designated broker-dealer at prevailing market prices. On October 28, 2021, 500,000 shares of common stock were sold pursuant to the ATM, resulting in net proceeds of approximately \$13.1 million.

On October 28, 2020, the Company entered into an underwriting agreement relating to the issuance and sale of an aggregate of 3,717,948 shares of its common stock at \$39.00 per share and pre-funded warrants to purchase 2,179,487 shares of its common stock. The price of each pre-funded warrant was \$38.9999, which equals the per share public offering price for the common shares less the \$0.0001 exercise price for each such pre-funded warrant. Total gross proceeds of the transaction were \$230.0 million and net proceeds were \$215.9 million, after deducting underwriting discounts and commissions and offering expenses. The pre-funded warrants are exercisable at any time, do not expire, and meet the condition for equity classification and were therefore recorded as a component of stockholders’ equity within additional paid-in capital. No pre-funded warrants have been exercised as of December 31, 2021.

In June and July 2019, the Company sold 3,450,000 shares of its common stock, including the exercise of the overallotment option, through an underwritten public offering at a price of \$15.00 per share. The offering was made pursuant to the Company’s effective shelf registration statement on Form S-3. The Company received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately \$48.3 million.

### **Shares Reserved For Future Issuance**

As of December 31, 2021, the Company had reserved common shares as follows:

	<b>As of December 31, 2021</b>
Common shares reserved for exercise of pre-funded warrants	2,179,487
Common shares reserved for future issuance under the 2018 ESPP	1,137,373
Common shares reserved for exercise of outstanding stock options under the 2017 and 2018 Plans	3,743,400
Common shares reserved for future issuance under the 2018 Plan	2,394,091
Common shares reserved for unvested restricted stock units under the 2018 Plan	314,901
	<u>9,769,252</u>

## **9. Equity-Based Compensation**

### **Equity Plans**

As of December 31, 2021, the Company has three active equity plans, the 2018 Stock Option and Incentive Plan (the “2018 Plan”), the 2017 Stock Option and Incentive Plan (the “2017 Plan”), and the 2018 Employee Stock Purchase Plan (the “2018 ESPP”).

#### **2018 Stock Option and Incentive Plan**

The 2018 Plan was adopted by the Company’s Board of Directors on May 2, 2018, and approved by the Company’s stockholders on May 11, 2018. The 2018 Plan has replaced the 2017 Plan as no additional awards will be granted under that plan following the consummation of the IPO. At December 31, 2021 there were 2,394,091 shares available to grant under the 2018 Plan.

The 2018 Plan provides for the grant of equity-based incentive awards, including incentive stock options, non-qualified stock options, restricted stock awards, unrestricted stock awards and restricted stock units to the Company’s officers, employees, directors and other key persons (including consultants). Stock options and restricted stock units granted under the 2018 Plan to employees generally vest over four years. The shares of common stock underlying any awards that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2018 Plan will be added back to the shares of common stock available for issuance under the 2018 Plan.

The 2018 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2019, by 4% of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Board of Directors or compensation committee (the “Annual Increase”). These limits are subject to adjustment in the event of a stock split, stock dividend or other change in the Company’s capitalization.

#### **2017 Stock Option and Incentive Plan**

The 2017 Plan provides for the grant of incentive stock options, non-qualified stock options, restricted stock awards, unrestricted stock awards and restricted stock units. Stock options granted under the 2017 Plan to employees generally vest over four years. The shares of common stock underlying any awards that are forfeited, cancelled, repurchased or are otherwise terminated by the Company under the 2017 Plan will be added back to the shares of common stock available for issuance under the 2018 Plan.

**2018 Employee Stock Purchase Plan**

On May 2, 2018, the Board of Directors adopted the 2018 ESPP, and it was approved by the stockholders on May 11, 2018. At December 31, 2021 there were 1,137,373 shares available to grant under the 2018 ESPP and no shares had been issued. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2019 through January 1, 2028, by the lesser of (i) 353,614 shares of common stock, (ii) 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or (iii) such lesser number of shares as determined by the 2018 ESPP administrator. The number of shares reserved under the 2018 ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization.

**Total Equity-Based Compensation Expense**

The Company recorded equity-based compensation expense related to all equity-based awards, which was allocated as follows in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development expense	\$ 10,176	\$ 3,554
General and administrative expense	12,973	7,621
	<u>\$ 23,149</u>	<u>\$ 11,175</u>

Equity-based compensation during the year ended December 31, 2020 includes \$1.5 million related to the modification of certain equity awards.

The following table summarizes the Company's unrecognized equity-based compensation expense as of December 31, 2021:

	As of December 31, 2021	
	Unrecognized Expense (in thousands)	Weighted Average Remaining Period of Recognition (years)
Restricted Stock Units	12,079	3.3
Stock Options	45,364	2.4
	<u>\$ 57,443</u>	

**Restricted Stock Awards**

The following table summarizes the Company's restricted stock award activity for the current year:

	Number of Shares	Weighted Average Fair Value per Share at Issuance
Restricted stock awards as of December 31, 2020	57,969	\$ 5.77
Vested	(57,969)	\$ 5.77
Restricted stock awards as of December 31, 2021	<u>—</u>	<u>\$ —</u>

**Restricted Stock Units**

The following table summarizes the Company's restricted stock unit activity for the current year:

	<u>Number of Units</u>	<u>Weighted Average Grant Date Fair Value</u>
Restricted stock units as of December 31, 2020	—	\$ —
Granted	392,661	\$ 49.48
Forfeited	(77,760)	\$ 57.98
Restricted stock units as of December 31, 2021	<u>314,901</u>	\$ 47.38

**Stock Options**

The following table summarizes the Company's stock option activity for the current year:

	<u>Number of Shares</u>	<u>Weighted Average Exercise Price</u>	<u>Weighted Average Remaining Contractual Term (in years)</u>	<u>Aggregate Intrinsic Value (in thousands)</u>
Outstanding as of December 31, 2020	3,679,931	\$ 14.96	8.01	\$ 123,600
Granted	1,462,930	\$ 49.23		
Exercised	(556,629)	\$ 12.38		
Cancelled	(842,832)	\$ 29.12		
Outstanding as of December 31, 2021	<u>3,743,400</u>	\$ 25.55	8.06	\$ 26,272
Options exercisable as of December 31, 2021	1,544,062	\$ 18.42	7.18	\$ 14,851

Using the Black-Scholes option pricing model, the weighted average fair value of options granted during the year ended December 31, 2021 was \$36.08.

The following weighted average assumptions were used in determining the fair value of options granted in the years ended December 31, 2021 and 2020:

	<u>Year Ended December 31,</u>	
	<u>2021</u>	<u>2020</u>
Risk-free interest rate	0.86 %	0.92 %
Expected dividend yield	0.0 %	0.0 %
Expected term (years to liquidity)	6.22	6.21
Expected volatility	87.62 %	82.09 %



## 10. Income Taxes

The Company has not recorded a current or deferred tax provision for the years ended December 31, 2021 and 2020.

The effective income tax rate differed from the amount computed by applying the federal statutory rate to the Company's loss before income taxes as follows:

	For Year Ended December 31,	
	2021	2020
Tax effected at statutory rate	21.0 %	21.0 %
State taxes	6.8	6.8
Stock compensation	0.9	1.6
Non-deductible expenses	(1.6)	(2.4)
Federal research and development credits	6.5	7.9
Other	(1.5)	(0.5)
Change in valuation allowance	(32.1)	(34.4)
	<u>— %</u>	<u>— %</u>

Deferred tax assets (liabilities) consist of the following at December 31, 2021 and 2020 (in thousands):

	As of December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	\$ 82,403	\$ 46,112
Tax credits	25,800	17,423
Deferred revenue	9,035	14,194
Operating lease liability	7,365	9,196
Stock based compensation	4,751	1,892
Reserve and accruals	2,844	2,635
Total gross deferred tax assets	132,198	91,452
Valuation allowance	(124,233)	(81,980)
Total deferred tax assets	7,965	9,472
Total deferred tax liabilities:		
Operating lease right-of-use asset	(6,925)	(8,805)
Fixed and intangible assets	(1,040)	(667)
Total deferred tax liabilities	(7,965)	(9,472)
Total net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

### **Total Net Deferred Tax Assets**

Deferred tax assets are reduced by a valuation allowance if, based on the weight of available positive and negative evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2021 and 2020. The valuation allowance for deferred tax assets increased by \$42.3 million and \$29.7 million in 2021 and 2020, respectively. This increase mainly relates to the establishment of a valuation allowance against the Company's net domestic deferred tax assets in connection with net operating losses generated in each year and the additional tax credit carryforwards generated. As of December 31, 2021, the Company had approximately \$302.1 million and \$300.2 million of Federal and State operating loss carryforwards respectively, which begin to expire in 2032, except for the \$251.6 million of the Company's federal net operating loss carryforwards that do not expire. These loss carryforwards are available to reduce future taxable income, if any. These loss carryforwards are subject to review and possible adjustment by the appropriate taxing authorities. As of December 31, 2021, the Company also had federal and state credit carryovers of \$22.5 million and \$4.2 million, respectively. The amount of loss and credit carryforwards that may be utilized in any future period may

be limited based upon changes in the ownership of the Company's ultimate parent. Additionally, the deductibility of federal net operating losses generated after December 31, 2017 is limited to 80% of the Company's taxable income in any future taxable year.

The Company follows the provisions of ASC 740-10, "Accounting for Uncertainty in Income Taxes," which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. As of December 31, 2021 and 2020, the Company has not recorded any amounts for uncertain tax positions. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its statements of income.

## **11. Commitments and Contingencies**

### ***Operating Leases***

#### ***620 Memorial Facility Lease***

In March 2015, the Company entered into a 5-year lease of office and laboratory space for its corporate headquarters (the "Lease") at 620 Memorial Drive in Cambridge, Massachusetts. The Lease was amended in February 2018, to add an additional space (the "Expansion Space") at the current location and to extend the Lease term (the "Amended Lease"). The Amended Lease expires in September 2023. Annual rent payments, including the Expansion Space, increase from \$1.4 million to \$1.7 million over the term of the Amended Lease. Variable lease payments include the Company's allocated share of costs incurred and expenditures made by the landlord in the operation and management of the building. The Company has the option to extend the term of the Amended Lease for one additional term of 5 years commencing after the Amended Lease expires.

On October 5, 2020, the Company entered into a Sublease Agreement (the "Sublease") with Orna Therapeutics, Inc. (the "Subtenant") to sublease the space covered by the Amended Lease at 620 Memorial Drive, Cambridge, Massachusetts. The Sublease term commenced on February 1, 2021 and ends on August 31, 2023, unless terminated earlier. The Sublease provides for initial annual base rent of approximately \$1.9 million. The Subtenant is obligated to pay for certain costs, taxes and operating expenses, subject to certain exclusions. The Sublease is subordinate to that certain Indenture of Lease, dated March 5, 2015, by and between 620 Memorial Leasehold LLC and Scholar Rock, Inc., as amended.

#### ***301 Binney Facility Lease***

In November 2019, the Company entered into a lease of office and laboratory space at 301 Binney Street in Cambridge, Massachusetts to be used as its new corporate headquarters. The expiration date of the lease is in August 2025 and the Company has the option to extend the term by two years. The base rent is \$6.9 million per year, subject to an annual increase of 3.5%, and the Company was subject to a free-rent period through mid-August 2020. Variable lease payments include the Company's allocated share of costs incurred and expenditures made by the landlord in the operation and management of the building. The lease included incentives of \$14.1 million in the form of an allowance for tenant improvements related to the design and build out of the space. In connection with the lease, the Company has secured a letter of credit for \$2.3 million which renews automatically each year. The lease commencement date, for accounting purposes, was reached in September 2020.

Other information related to the Company’s leases (excluding the Company’s sublease income of \$2.3 million for the year ending December 31, 2021) is as follows (in thousands, except lease term and discount rate):

	<u>For Year Ended December 31, 2021</u>
<b>Lease Cost:</b>	
Operating lease cost	\$ 8,642
Variable lease cost	2,256
Total lease cost	<u>\$ 10,898</u>

	<u>For Year Ended December 31, 2021</u>
<b>Other information:</b>	
Operating cash flows used for operating leases	\$ 8,880
Weighted average remaining lease term	3.4
Weighted average incremental borrowing rate	7.5 %

The following is a maturity analysis of the annual undiscounted cash flows reconciled to the carrying value of the operating lease liabilities as of December 31, 2021 (in thousands):

<b>Year Ending December 31,</b>	
2022	9,183
2023	9,057
2024	8,051
2025	<u>4,498</u>
Total lease payments	30,789
Less imputed interest	<u>(3,730)</u>
Total operating lease liability	<u>\$ 27,059</u>
Short-term portion of operating lease liability	7,407
Long-term portion of operating lease liability	19,652

The Company recorded approximately \$8.6 million and \$3.2 million in rent expense (excluding sublease income) for the years ended December 31, 2021 and 2020, respectively.

### ***Specifica Antibody Library***

On December 20, 2019 (the “Effective Date”), the Company entered into a Library Development and Transfer Agreement with Specifica Inc. (“Specifica”), whereby Specifica is responsible for developing and delivering a customized antibody display library (the “Library”) for the Company to use to identify antibodies for further research, development, and commercialization. As of December 31, 2021 the Company has paid \$2.0 million of the total \$3.7 million in fees expected to be paid through 2023 related to the Library. As the return right has lapsed, all \$3.7 million in fees have been recognized as expense to date.

### ***Legal Proceedings***

The Company, from time to time, may be party to litigation arising in the ordinary course of its business. The Company was not subject to any material legal proceedings during the years ended December 31, 2021 and 2020.

## 12. Debt

On October 16, 2020 (the “Closing Date”) the Company entered into a Loan and Security Agreement with Oxford Finance LLC and Silicon Valley Bank (“SVB”) for \$50.0 million (the “Loan and Security Agreement”). Tranche 1 of \$25.0 million was funded on the Closing Date. The Company had an additional \$25.0 million in loan proceeds available through December 31, 2021 if certain criteria were met under Tranche 2. On November 16, 2021, the Company entered into Amendment No. 1 (the “Amendment”) to the Loan and Security Agreement to revise the Tranche 2 milestones to be when the Company has: (i) publicly announced the SAPPHIRE Phase 3 clinical trial design for apitegromab and registered such clinical trial with clinicaltrials.gov; and (ii) initiated Part B of the DRAGON Phase 1 clinical trial for SRK-181. Pursuant to the Amendment, Tranche 2 of \$25.0 million was funded in December 2021. The Loan and Security Agreement will mature on May 1, 2025 and requires interest only payments through November 2022, with principal payments commencing in December 2022. The interest rate on the unpaid principal will be the greater of the Wall Street Journal prime rate plus 4.60% or 7.85% per annum. Prepayment is permitted and may include either a 2% or 3% fee (of the principal amount being prepaid), depending on when the prepayment is made. The Company is also required to make a final payment equal to 4% of the original principal amount. The Company shall maintain cash in an SVB account equal to the lesser of 100% of the Company’s consolidated cash or 105% of the dollar amount of the outstanding debt.

The following table shows required payments (excluding interest), during the next five years on debt outstanding at December 31, 2021 (in thousands):

<b>Year Ending December 31,</b>	<b>Total future payments</b>
2022	1,667
2023	20,000
2024	20,000
2025	10,333
Total payments	\$ 52,000

The Company incurred costs on behalf of the lender recorded as a debt discount of \$0.3 million and incurred debt issuance costs of \$0.1 million, both of which are recorded as a deduction from the carrying amount of the debt and are being amortized as interest expense over the term of the loan. The final payment fee will be treated as an additional debt discount and accreted to the debt balance over the term.

For the years ended December 31, 2021 and 2020, the Company recorded total interest expense for the debt of \$2.1 million and \$0.4 million, respectively.

## 13. Agreements

### *Collaboration with Gilead*

On December 19, 2018 (the “Effective Date”), the Company entered into a three-year Master Collaboration Agreement (the “Gilead Collaboration Agreement”) with Gilead to discover and develop specific inhibitors of TGF $\beta$  activation focused on the treatment of fibrotic diseases. Under the collaboration, Gilead had exclusive options to license worldwide rights to product candidates that emerge from three of the Company’s TGF $\beta$  programs (each a “Gilead Program”). Pursuant to the Gilead Collaboration Agreement, the Company was responsible for antibody discovery and preclinical research through product candidate nomination, after which, upon exercising the option for a Gilead Program, Gilead would be responsible for the program’s preclinical and clinical development and commercialization. Such option could have been exercised by Gilead at any time from the Effective Date through a date that is 90 days following the expiration of the Research Collaboration Term for a given Gilead Program (no later than March 19, 2022), or until

termination of the Gilead Program, whichever is earlier (the “Option Exercise Period”). On January 6, 2022, Gilead agreed that its option exercise period for all programs has been terminated.

Revenue associated with the research and development and license performance obligations relating to the Gilead Programs is recognized as revenue as the research and development services are provided using an input method, according to the costs incurred on each Gilead Program and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurred over time. In management’s judgment, this input method was the best measure of progress towards satisfying the performance obligation. The amounts allocated to the three material rights will be recognized either upon exercise or termination of the respective options. The amounts received that have not yet been recognized as revenue are recorded in deferred revenue on the Company’s consolidated balance sheet.

A \$25.0 million preclinical milestone was achieved in December 2019 for the successful demonstration of efficacy in preclinical *in vivo* proof-of-concept studies. As a result, the associated \$25.0 million was included in the consideration transferred and proportionally allocated to the performance obligations, as it was probable that a future material reversal will not occur.

In the year ended December 31, 2021, the Company recognized \$18.8 million in revenue in the Company’s consolidated statements of operations and comprehensive loss under the Gilead Collaboration Agreement, all of which was included in deferred revenue at the beginning of the period. The Company has recognized the revenue related to the research and development services based on a cost input method over the research term for each respective Gilead Program, which ended in December 2021. The aggregate amount of the transaction price allocated to the Company’s unsatisfied performance obligations and recorded in deferred revenue at December 31, 2021 is \$33.2 million, which is fully attributable to the material rights. As Gilead agreed in January 2022, its option exercise period for all programs has been terminated. The Company will recognize the remaining deferred revenue in the first quarter of 2022.

#### 14. Net Loss per Share

The Company calculates basic net loss per share by dividing net loss by the weighted average number of common shares outstanding, excluding restricted common stock. The weighted average number of common shares used in the basic and diluted net loss per share calculation include the pre-funded warrants issued in connection with the Company’s November 2, 2020 follow-on offering as the warrants are exercisable at any time for nominal cash consideration. The Company has generated a net loss in all periods presented, so the basic and diluted net loss per share are the same, as the inclusion of the potentially dilutive securities would be anti-dilutive.

Basic and diluted net loss per share is calculated as follows (in thousands, except share and per share data):

	<u>Year Ended December 31, 2021</u>	<u>Year Ended December 31, 2020</u>
Net loss	\$ (131,799)	\$ (86,483)
Weighted average common shares outstanding, basic and diluted	36,711,833	30,734,109
Net loss per share, basic and diluted	\$ (3.59)	\$ (2.81)

The following table sets forth the outstanding common stock equivalents, presented based on amounts outstanding at each period end, that have been excluded from the calculation of diluted net loss per share for the periods indicated because their inclusion would have been anti-dilutive:

	<u>Year Ended December 31,</u>	
	<u>2021</u>	<u>2020</u>
Restricted stock awards	—	57,969
Restricted stock units	314,901	—
Stock options	3,743,400	3,679,931
	<u>4,058,301</u>	<u>3,737,900</u>

## **15. Retirement Plan**

The Company sponsors a 401(k) retirement plan, in which substantially all employees are eligible to participate upon employment. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. Effective, January 1, 2020, the Company adopted a policy to match 50% of the employee contributions to the 401(k) plan up to a maximum of 6% of the participating employee's eligible earnings, resulting in a maximum company match of 3% of the participating employee's eligible earnings subject to statutory limitations. The Company recognized \$0.7 million and \$0.5 million in expense related to the match during the years ended December 31, 2021 and 2020, respectively.

## FIRST AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS FIRST AMENDMENT to Loan and Security Agreement (this “**Amendment**”) is entered into as of November 16, 2021, by and among OXFORD FINANCE LLC, a Delaware limited liability company with an office located at 115 South Union Street, Suite 300, Alexandria, Virginia 22314 (“**Oxford**”), as collateral agent (in such capacity, “**Collateral Agent**”), the Lenders listed on Schedule 1.1 to the Loan Agreement (as defined below) or otherwise a party thereto from time to time including Oxford in its capacity as a Lender and SILICON VALLEY BANK, a California corporation with an office located at 3003 Tasman Drive, Santa Clara, CA 95054 (“**Bank**” or “**SVB**”) (each a “**Lender**” and collectively, the “**Lenders**”), and SCHOLAR ROCK HOLDING CORPORATION, a Delaware corporation (“**Parent**”) and SCHOLAR ROCK, INC., a Delaware corporation (together with Parent, individually and collectively, jointly and severally, “**Borrower**”) with an office located at 301 Binney Street, 3<sup>rd</sup> Floor, Cambridge, MA 02142.

A. WHEREAS, Collateral Agent, Borrower and Lenders have entered into that certain Loan and Security Agreement dated as of October 16, 2020 (as amended, supplemented or otherwise modified from time to time, the “**Loan Agreement**”) pursuant to which Lenders have provided to Borrower certain loans in accordance with the terms and conditions thereof; and

B. WHEREAS, Borrower has requested that Collateral Agent and Lenders modify the defined term Term B Milestone; and

C. WHEREAS, Borrower, the Lenders party to this Amendment (constituting the Required Lenders) and Collateral Agent desire to amend such defined term as provided herein and subject to the terms and conditions set forth herein.

### AGREEMENT

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Borrower, Lenders and Collateral Agent hereby agree as follows:

1. **Definitions.** Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. **Amendments to Loan Agreement.**

2.1 **Notices.** The address information for Borrower (but not the address information for Goodwin Procter LLP, which remains unchanged) in Section 10 of the Loan Agreement hereby is amended and restated in its entirety as follows:

SCHOLAR ROCK HOLDING CORPORATION  
301 Binney Street, 3rd Floor  
Cambridge, MA 02142  
Attn: Junlin Ho, SVP, Head of Legal  
Email: jho@scholarrock.com

2.2 **Definitions.** The following term and its definition in Section 13.1 of the Loan Agreement hereby are amended and restated in their entirety as follows:

“**Term B Milestone**” is Borrower’s delivery to Collateral Agent and the Lenders of evidence, satisfactory to Collateral Agent and the Lenders in their sole but reasonable discretion, that Borrower has both (i) publicly announced the Phase 3 clinical trial (SAPPHIRE) design for SRK-015 (Apitegromab) and registration of such clinical trial with clinicaltrials.gov and (ii) initiated the Part B of the DRAGON Phase 1 clinical trial for SRK-181 (as confirmed by public disclosure).

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### **3. Limitation of Amendment.**

**3.1** The amendment set forth above are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right, remedy or obligation which Lenders or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

**3.2** This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents are hereby ratified and confirmed and shall remain in full force and effect.

**4. Representations and Warranties.** To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

**4.1** Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date) and (b) no Event of Default has occurred and is continuing;

**4.2** Borrower has the power and due authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

**4.3** The organizational documents of Borrower delivered to Collateral Agent on the Effective Date, and updated pursuant to subsequent deliveries by or on behalf of the Borrower to the Collateral Agent, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

**4.4** The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not contravene (i) any material law or regulation binding on or affecting Borrower, (ii) any material contractual restriction with a Person binding on Borrower, (iii) any material order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (iv) the organizational documents of Borrower;

**4.5** The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, except as already has been obtained or made;

**4.6** This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

### **5. Release by Borrower.**

**5.1 FOR GOOD AND VALUABLE CONSIDERATION**, Borrower hereby forever relieves, releases, and discharges Collateral Agent and each Lender and their respective present or former employees, officers, directors, agents, representatives, attorneys, and each of them, from any and all claims, debts, liabilities, demands, obligations, promises, acts, agreements, costs and expenses, actions and causes of action, of every type, kind, nature, description or character whatsoever, whether known or unknown, suspected or unsuspected, absolute or contingent, arising out of or in any manner whatsoever connected with or related to facts, circumstances, issues, controversies or claims existing or arising from the beginning of time through and including the date of execution of this Amendment solely to the

extent such claims arise out of or are in any manner whatsoever connected with or related to the Loan Documents, the Recitals hereto, any instruments, agreements or documents executed in connection with any of the foregoing or the origination, negotiation, administration, servicing and/or enforcement of any of the foregoing (collectively “**Released Claims**”).

**5.2** By entering into this release, Borrower recognizes that no facts or representations are ever absolutely certain and it may hereafter discover facts in addition to or different from those which it presently knows or believes to be true, but that it is the intention of Borrower hereby to fully, finally and forever settle and release all matters, disputes and differences, known or unknown, suspected or unsuspected in relation to the Released Claims; accordingly, if Borrower should subsequently discover that any fact that it relied upon in entering into this release was untrue, or that any understanding of the facts was incorrect, Borrower shall not be entitled to set aside this release by reason thereof, regardless of any claim of mistake of fact or law or any other circumstances whatsoever. Borrower acknowledges that it is not relying upon and has not relied upon any representation or statement made by Bank with respect to the facts underlying this release or with regard to any of such party’s rights or asserted rights.

**5.3** This release may be pleaded as a full and complete defense and/or as a cross-complaint or counterclaim against any action, suit, or other proceeding that may be instituted, prosecuted or attempted in breach of this release. Borrower acknowledges that the release contained herein constitutes a material inducement to Collateral Agent and the Lenders to enter into this Amendment, and that Collateral Agent and the Lenders would not have done so but for Collateral Agent’s and the Lenders’ expectation that such release is valid and enforceable in all events.

**6. Effectiveness.** This Amendment shall be deemed effective as of the date hereof upon the due execution of this Amendment by the parties thereto.

**7. Counterparts.** This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument. Delivery by electronic transmission (e.g. “.pdf”) of an executed counterpart of this Amendment shall be effective as a manually executed counterpart signature thereof.

**8. Governing Law.** This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the State of New York.

***[Balance of Page Intentionally Left Blank]***

IN WITNESS WHEREOF, the parties hereto have caused this First Amendment to Loan and Security Agreement to be executed as of the date first set forth above.

**BORROWER:**

SCHOLAR ROCK HOLDING CORPORATION

By:           /s/          Edward          Myles

Name:                   Edward                  Myles

Title: Chief Financial Officer and Treasurer

SCHOLAR ROCK, INC.

By:           /s/          Edward          Myles

Name:                   Edward                  Myles

Title: Chief Financial Officer and Treasurer

**COLLATERAL AGENT AND LENDER:**

OXFORD FINANCE LLC

By:           /s/          Colette          H.          Featherly

Name:                   Colette                  H.                  Featherly

Title: Senior Vice President

**LENDER:**

SILICON VALLEY BANK

By:           /s/          Ryan          Roller

Name:                   Ryan                  Roller

Title:   Director



***[Signature Page to First Amendment to Loan and Security Agreement]***

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SUBSIDIARIES OF SCHOLAR ROCK HOLDING CORPORATION

**Subsidiary**

Scholar Rock, Inc.

Scholar Rock Securities Corporation

**Jurisdiction**

Delaware

Massachusetts



**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the following Registration Statements:

- (1) Registration Statement (Form S-3 Nos. 333-254057, 333-249715, and 333-231920) of Scholar Rock Holding Corporation,
- (2) Registration Statement (Form S-8 Nos. 333-238082 and 333-256065) pertaining to the 2018 Stock Option and Incentive Plan and 2018 Employee Stock Purchase Plan, of Scholar Rock Holding Corporation, and
- (3) Registration Statement (Form S-8 No. 333-225192) pertaining to the 2017 Stock Option and Incentive Plan, 2018 Stock Option and Incentive Plan, and 2018 Employee Stock Purchase Plan, of Scholar Rock Holding Corporation;

of our report dated March 7, 2022, with respect to the consolidated financial statements of Scholar Rock Holding Corporation, included in this Annual Report (Form 10-K) of Scholar Rock Holding Corporation for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 7, 2022

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**Certifications**

I, Nagesh K. Mahanthappa, certify that:

1. I have reviewed this Annual Report on Form 10-K of Scholar Rock Holding Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2022

/s/ Nagesh K. Mahanthappa

Nagesh K. Mahanthappa  
Interim Chief Executive Officer and President  
(Principal Executive Officer)

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**Certifications**

I, Edward H. Myles, certify that:

1. I have reviewed this Annual Report on Form 10-K of Scholar Rock Holding Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2022

/s/ Edward H. Myles

Edward H. Myles

Chief Operating Officer & Chief Financial Officer  
(Principal Financial and Accounting Officer)

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**CERTIFICATION PURSUANT TO**  
**18 U.S.C. SECTION 1350**  
**AS ADOPTED PURSUANT TO**  
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Scholar Rock Holding Corporation (the “Company”) for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), each of the undersigned officers of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to his or her knowledge, that:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

This certification is being provided pursuant to 18 U.S.C. 1350 and is not to be deemed a part of the Report, nor is it to be deemed to be “filed” for any purpose whatsoever.

Date: March 7, 2022

/s/ Nagesh K. Mahanthappa

Nagesh K. Mahanthappa

Interim Chief Executive Officer and President

Date: March 7, 2022

/s/ Edward H. Myles

Edward H. Myles

Chief Operating Officer & Chief Financial Officer

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