SCHOLAR ROCK

From New Insights to New Medicines

January 2019

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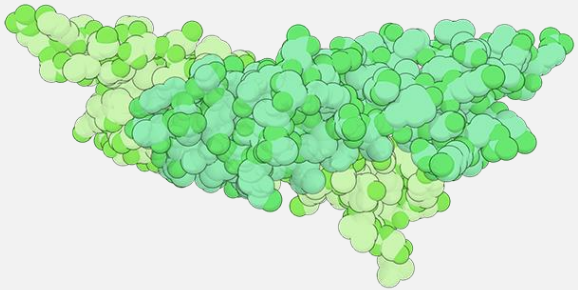
Various statements in this presentation concerning Scholar Rock's future expectations, plans and prospects, including without limitation, Scholar Rock's expectations regarding its strategy, its product candidate selection and development timing, including timing for the initiation of and reporting results from its clinical trials for its product candidates, its product candidate selection and development timing, its disease indication selection timing, its management team capabilities, and the ability of SRK-015 to affect the treatment of patients suffering from SMA either as a monotherapy or in conjunction with the current standard of care, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward looking statements. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Scholar Rock's ability to provide the financial support and resources necessary to identify and develop product candidates on the expected timeline, competition from others developing products for similar uses, Scholar Rock's ability to obtain, maintain and protect its intellectual property, Scholar Rock's dependence on third parties for development and manufacture of product candidates including to supply any clinical trials, and Scholar Rock's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives as well as those risks more fully discussed in the section entitled "Risk Factors" in the Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, which is on file with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in Scholar Rock's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Scholar Rock's views only as of today and should not be relied upon as representing its views as of any subsequent date. Scholar Rock explicitly disclaims any obligation to update any forward-looking statements unless required by law.

Nature's Growth Factor Activation Machinery

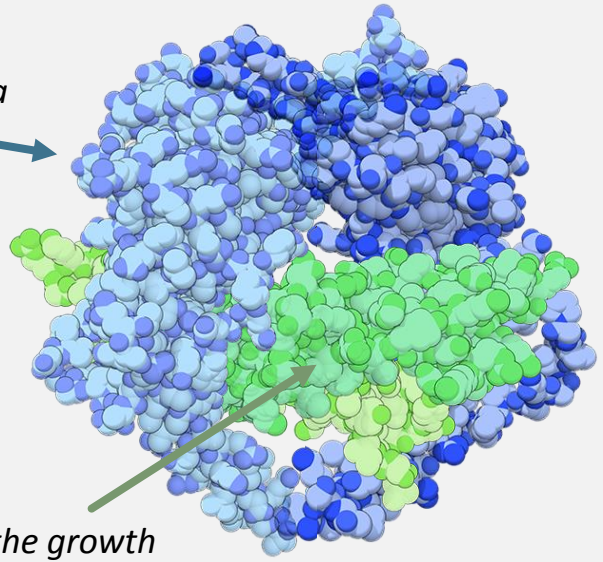
Mature TGFβ1

Active form of the growth factor



TGFβ1 Precursor Complex

TGFβ1 propeptide which forms a "cage"



Cage renders the growth factor inactive or "latent"

TGFβ Superfamily: More than 30 Related Growth Factors that Mediate Diverse Biological Processes

Shi, M., et al. Nature 474, 7351, 343-9 (2011)

Scholar Rock's Proprietary Solution to Traditional Challenges

Traditional Challenges:

- Focused on inhibiting the growth factor after activation and systemic release
- Have been limited by:
  - Structural similarities
  - Overlapping sets of related receptors
  - Diverse and overlapping physiological roles

Unique Mechanism of Growth Factor Regulation

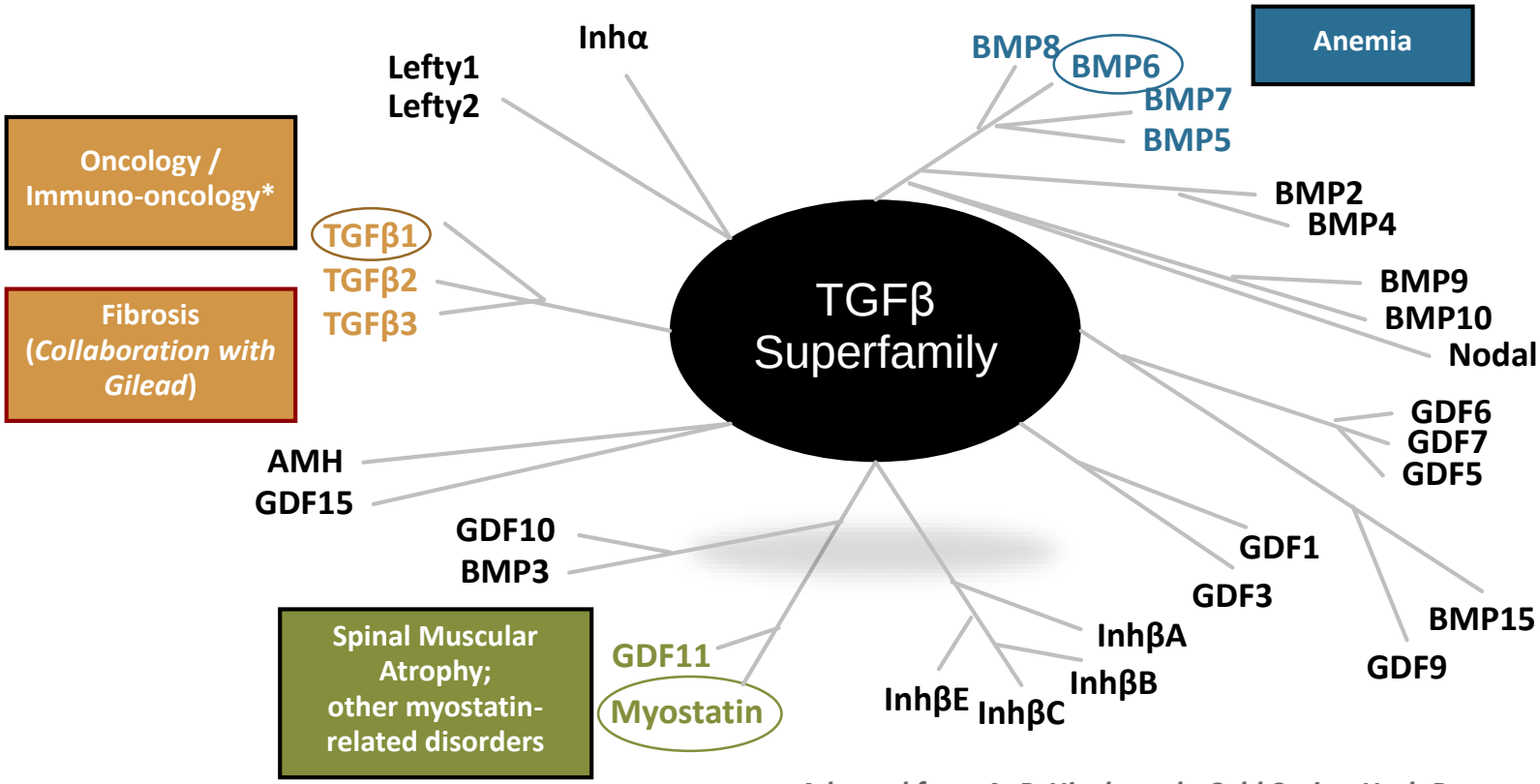
Exploits Scholar Rock's Structural Biology Insights

Offers Localization of Effect and High Selectivity

Well-established Modality (Monoclonal Antibodies)

Broad IP Portfolio Covering Compositions and Methods

The TGFβ Superfamily



Adapted from A. P. Hinck et al., Cold Spring Harb Perspect Biol (2016)

*Context-dependent latent TGFβ1 / GARP program licensed to Janssen Biotech, Inc.

Robust Pipeline Portfolio

Program / Target		Indication	Discovery / Early Preclinical	Preclinical	Phase 1	Phase 2	Rights / Partner	Next Anticipated Milestone
INTERNAL PROPRIETARY PROGRAMS								
SRK-015	Pro/Latent Myostatin	Spinal Muscular Atrophy						Ph1 Ongoing / Initiate Ph2 in 1Q19
	Pro/Latent Myostatin	Myostatin-Related Disorders						1H19 – Identify Next Indication
Latent TGFβ	Context-Independent Latent TGFβ1	Oncology/Immuno-oncology						1H19 – Nominate Product Candidate
	Context-Dependent Latent TGFβ1 / GARP & LRRC33	Oncology/Immuno-oncology						
	Context-Dependent Latent TGFβ1 / LRRC33	Oncology/Immuno-oncology						
BMP6	BMP6 Signaling Pathway	Anemia						
PARTNERED PROGRAMS								
Latent TGFβ	Context-Independent Latent TGFβ1	Fibrosis					*Gilead Sciences, Inc*	
	Context-Dependent Latent TGFβ1 / LTBP1 & LTBP3	Fibrosis					*Gilead Sciences, Inc*	
	Undisclosed Program	Fibrosis					*Gilead Sciences, Inc*	
	Context-Dependent Latent TGFβ1 / GARP	Oncology/Immuno-oncology					*Janssen Biotech, Inc*	

2018 Achievements

Capitalization and Collaboration:

- ✓ Raised $86M in gross proceeds from IPO in May
- ✓ Entered into strategic fibrosis collaboration with Gilead
  - $80M upfront and up to $1.45B in potential milestones

SRK-015 Clinical and Regulatory:

- ✓ Initiated Phase 1 trial of SRK-015 in May
- ✓ FDA granted and EMA adopted positive opinion on Orphan Drug Designation for SMA
- ✓ Published data showing benefits of inhibiting myostatin in mouse models of SMA in *Human Molecular Genetics*

TGFβ1 Inhibitor Discovery:

- ✓ Completed 28-day rat pilot toxicology study
- ✓ Achieved proof-of-concept with TGFβ1 inhibitor and anti-PD1 in mouse models of primary checkpoint resistance

2019 Milestones

Clinical Advancements for SRK-015:

- ❑ Announce interim results from Phase 1 in 1Q19
- ❑ Initiate Phase 2 POC study in patients with SMA in 1Q19
- ❑ Present Phase 1 results at a medical conference
- ❑ Continue to evaluate our selective inhibitors of the activation of myostatin in various disease models
- ❑ Identify next indication in 1H19

Preclinical Development of TGFβ1 Inhibitors:

- ❑ Continue to evaluate selective inhibitors of the activation of TGFβ1 in cancer immunotherapy models
- ❑ Nominate product candidate in TGFβ1 program by the end of 1H19
- ❑ Continue to advance active discovery programs for context-dependent inhibition of TGFβ1
- ❑ Conduct discovery and preclinical studies as part of Gilead collaboration

SRK-015: Inhibitor of Myostatin Activation

Potential First Muscle-Directed Therapy for SMA

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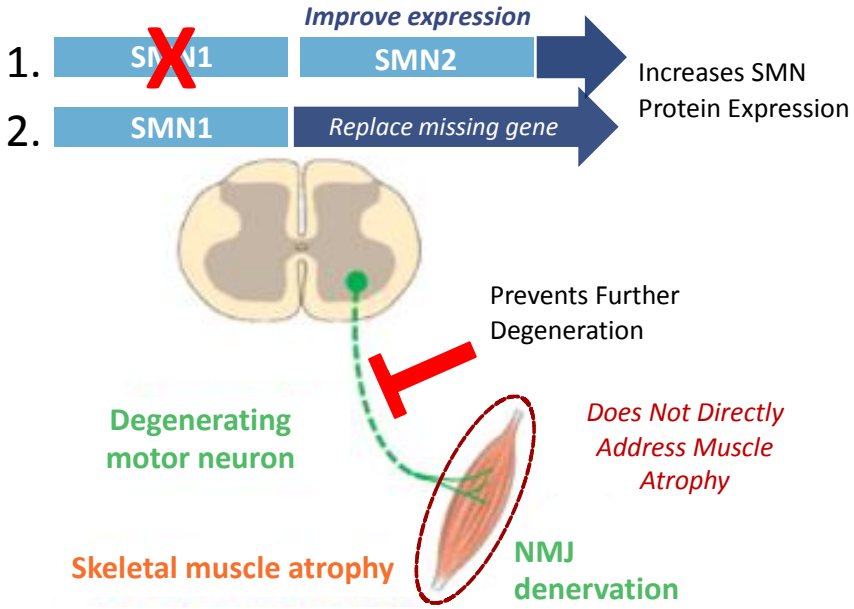
SMN Upregulators Do Not Directly Address Muscle Atrophy

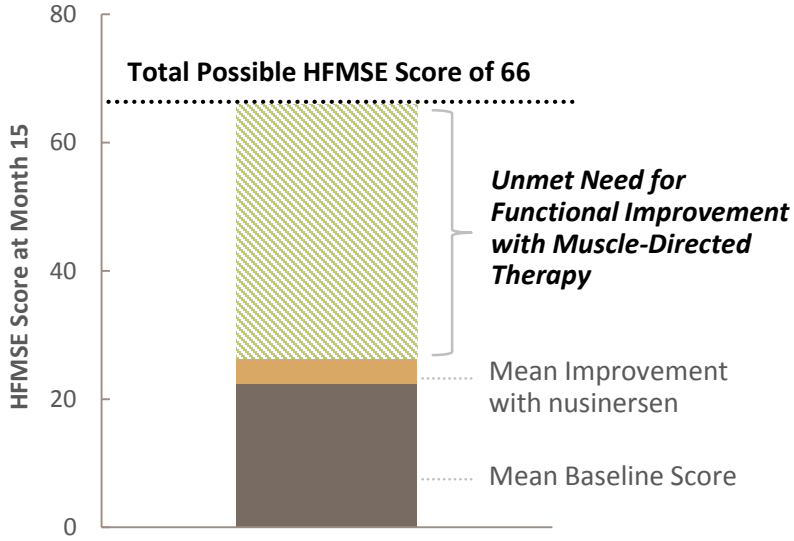
Significant Unmet Need Remains Despite Current Therapeutic Strategies



Adapted from images that were courtesy of the SMA Foundation

Muscle Function in SMA (Human)

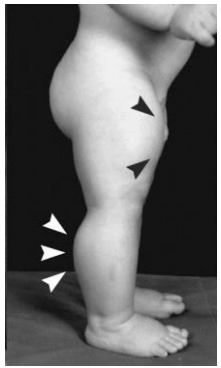
Hammersmith Functional Motor Scale Expanded (HFMSE)



Mean improvement in HFMSE score experienced by patients with later-onset SMA in the Phase 3 CHERISH clinical trial of nusinersen

SRK-015: Muscle-Directed Approach to Treating SMA

Vertebrates lacking the myostatin gene are healthy and display increased muscle mass and strength



- Myostatin is a genetically-validated, negative regulator of muscle mass expressed in skeletal muscle tissue
- There has been high interest from pharma as a potential drug target
- Clinical trial results with traditional systemic inhibitors of mature myostatin (or its receptor) have been mixed

Differentiated approach with SRK-015:

Inhibition of myostatin activation to potentially improve muscle function

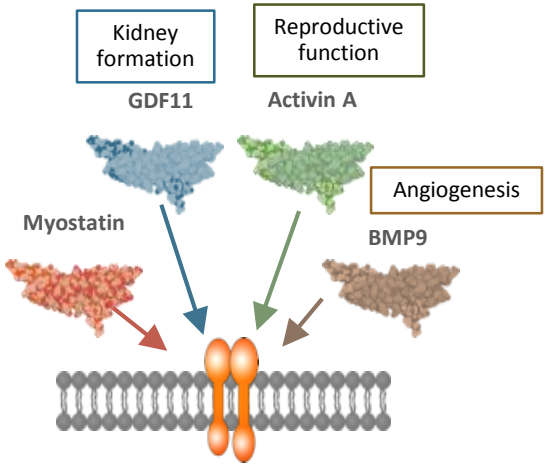
SRK-015: Aligning Therapeutic Approach with Myostatin Biology

Optimal Setting for Myostatin Inhibition		Key Characteristics of Spinal Muscular Atrophy (SMA)
Younger population	→	Genetic disorder with onset in childhood
At least partially intact innervation; no structural abnormalities	→	Incomplete loss of motor neurons; muscle capable of growth
Need for increase in fast-twitch muscle fibers	→	Substantial deficit in fast-twitch fibers
Clinical trial endpoint driven by fast-twitch fiber function	→	Fast-twitch fiber function; prominent role in SMA outcome measures

Traditional Approaches Can Raise Significant Safety Concerns

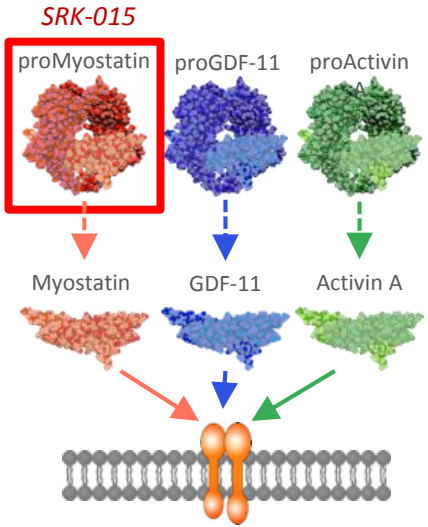
Traditional Approaches Lack Selectivity

- Most inhibitors of active myostatin also inhibit GDF11 and may inhibit other growth factors as well
- Antibodies to ActRIIb and ligand trap approaches inhibit signaling of multiple ligands



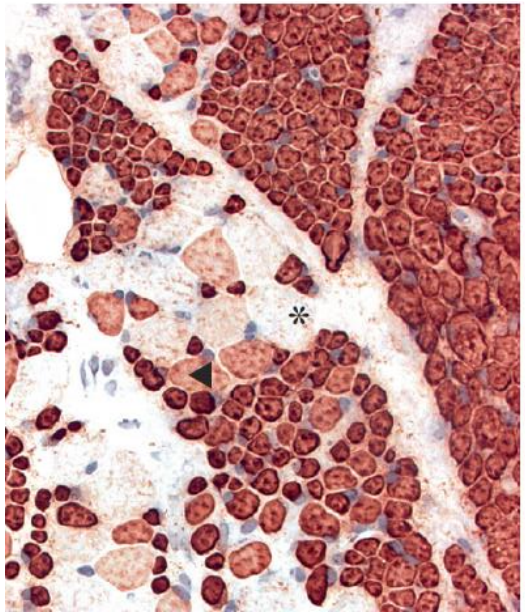
Scholar Rock Approach

Exquisite Selectivity By Targeting Precursor Form of Myostatin



Fast-Twitch Muscle Fibers May Be Preferentially Benefited by SRK-015

Muscle From 5-Year Old SMA Type II Patient

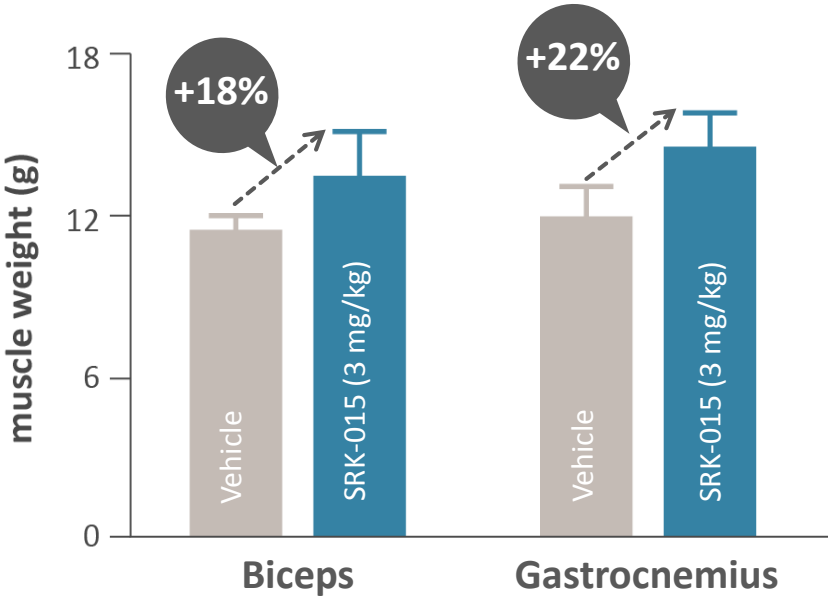


- Muscle is comprised of both slow-twitch and fast-twitch fibers
- Fast-twitch fibers significantly atrophy in patients with SMA

Dubowitz, et al., 2013. Neurogenic Disorders. Muscle Biopsy, A Practical Approach.

Healthy Non-Human Primate (Cyno)

Pronounced Effect on Fast-Twitch Muscle

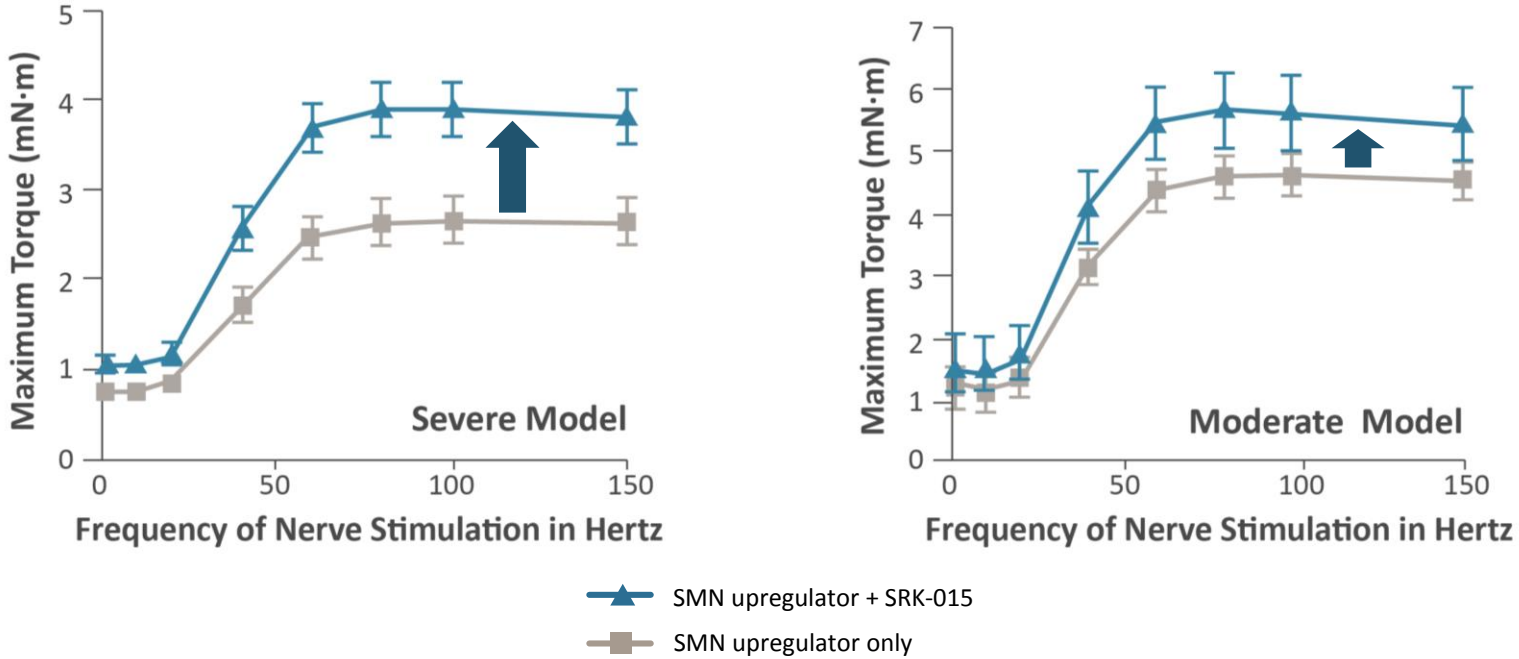


Six cynomolgus animals per group were treated once weekly with vehicle control or SRK-015 for 8 weeks and assessed after an additional 5 weeks

SRK-015 Demonstrates Potential Benefits Across SMA Severities

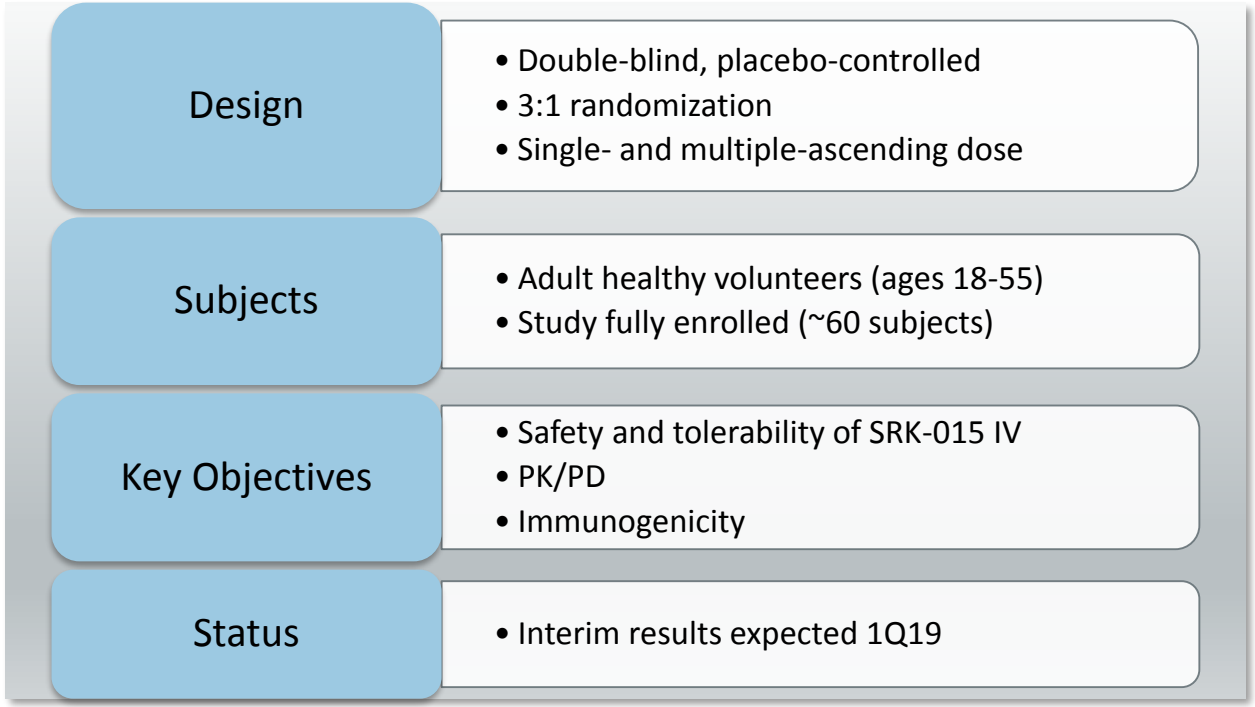
Genetic Model of SMA ("Δ7 Mouse") Demonstrate Improved *In Vivo* Muscle Force Generation

Strength of Plantarflexor Muscle Group



 Preclinical data published Nov 2018: Long, K., O'Shea, K., Khairallah, R., et al. Specific Inhibition of Myostatin Activation is Beneficial in Mouse Models of SMA Therapy. *Human Molecular Genetics,* ddy382

SRK-015 Phase 1 Trial Design

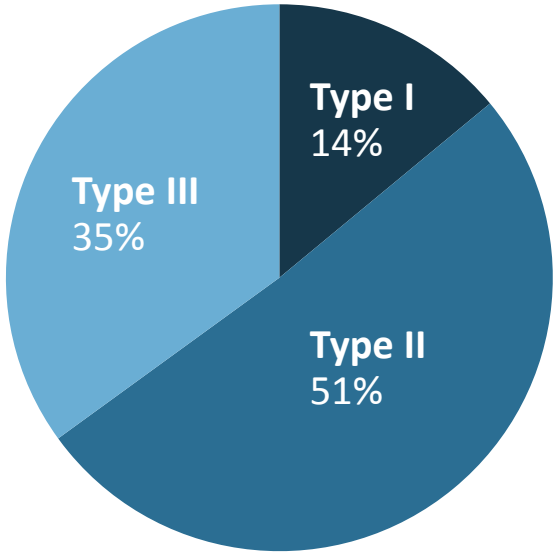


Initiate Phase 2 POC study in SMA in 1Q19

SRK-015 Opportunity in Spinal Muscular Atrophy

Overall Prevalence of 30,000-35,000 in U.S. and Europe

RELATIVE PREVALENCE AMONG PATIENTS LIVING WITH SMA



Type I:

- Infant-onset; often fatal

Type II and non-ambulatory type III:

- Later-onset but still early childhood
- Severe deficits in motor function

Potential to use SRK-015 in conjunction with current standard of care

Ambulatory type III:

- Limited mobility and substantial morbidity

Potential to use SRK-015 as monotherapy

Type IV:

- Population not well-characterized

Lally et al, Orphanet Journal of Rare Diseases, 2017

2018 Achievements

SRK-015 Clinical and Regulatory:

- ✓ IND in SMA cleared in April
- ✓ Initiated Phase 1 in healthy volunteers in May
- ✓ Completed enrollment in Phase 1 trial

Orphan Drug Designation (ODD):

- ✓ FDA granted for SMA
- ✓ EMA's COMP adopted positive opinion for SMA

Translational Science:

- ✓ Published preclinical data in *Human Molecular Genetics*[(1)] demonstrating benefits of inhibiting myostatin in mouse models of SMA
- ✓ Developed novel target engagement biomarker assay

2019 Milestones

- ❑ Announce interim results from Phase 1 trial in healthy volunteers in 1Q19
- ❑ Initiate Phase 2 proof-of-concept study in patients with SMA in 1Q19
- ❑ Present Phase 1 trial results at a medical conference
- ❑ Continue to evaluate our selective inhibitors of the activation of myostatin in various disease models
- ❑ Identify second indication for SRK-015 in 1H19

(1) Long, K., O'Shea, K., Khairallah, R., et al. Specific Inhibition of Myostatin Activation is Beneficial in Mouse Models of SMA Therapy. 2018. *Human Molecular Genetics*, ddy382

TGFβ1: Significant Opportunities in Oncology/Immuno-oncology and Fibrosis

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TGFβ1 Plays Central Role in Multiple Diseases with Unmet Need

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Oncology

- Immuno-Oncology
- Tumor-Directed Therapy
- Myeloproliferative Disorders

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Fibrosis

GILEAD

Collaboration with Gilead to Develop TGFβ Inhibitors for Fibrosis

Highly Specific Inhibitors of Local TGFβ Activation Can Offer Novel Approach to Treating Fibrotic Diseases

Fibrosis

- Fibrosis is a debilitating pathological feature of many diseases that scars tissues and vital organs and is a major cause of morbidity and mortality
- TGFβ-driven signaling has been broadly implicated as a central regulator of fibrosis
- Scholar Rock's highly specific TGFβ inhibitors act locally in the disease microenvironment
  - Shown to selectively prevent activation of growth factor in the fibrotic matrix in vitro and in preclinical models
- Aim to improve efficacy and tolerability compared to traditional approaches

Programs

- Gilead has exclusive options to license worldwide rights to product candidates from three Scholar Rock TGFβ programs:
  - Inhibitors that target activation of latent TGFβ1 with high affinity and specificity
  - Inhibitors that selectively target activation of latent TGFβ1 localized to extracellular matrix
  - Undisclosed TGFβ discovery program

Highlights of Strategic Fibrosis Collaboration with Gilead

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Responsible for antibody discovery and preclinical research thru product candidate nomination for three TGFβ programs

Retains exclusive worldwide rights to develop certain TGFβ antibodies for oncology and cancer immunotherapy

Collaborating to Develop Innovative Therapies for Fibrotic Diseases

GILEAD

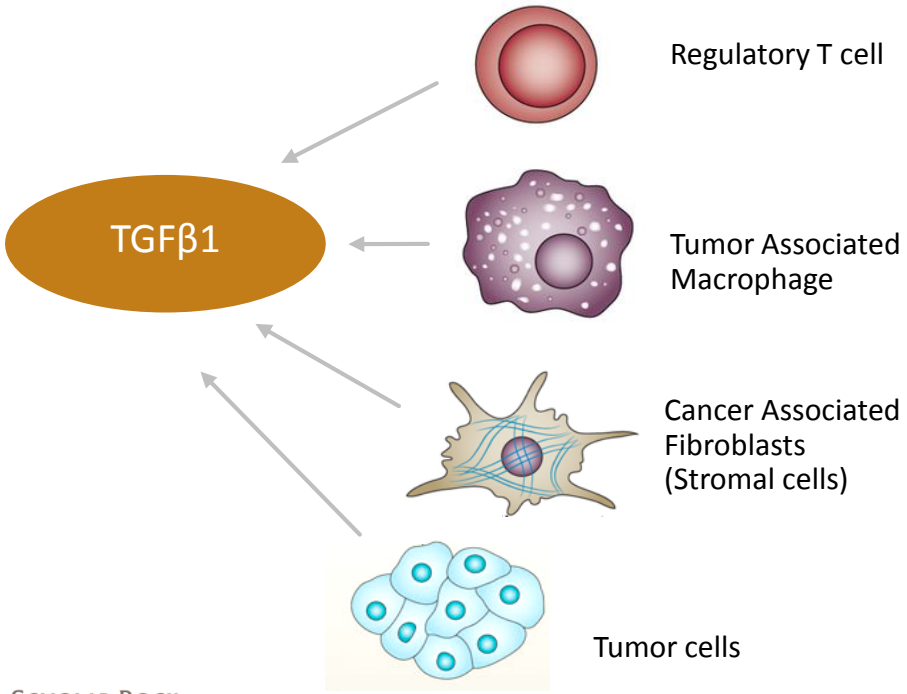
Upon option exercise, responsible for preclinical and clinical development and commercialization

Upfront cash and equity investment: **$80 million***	One-time preclinical milestone: **$25 million**	Additional development, regulatory, and commercial milestones across 3 programs: **Up to $1,425 million**	High single- to low double-digit tiered royalties on net sales

*Includes $30 million purchase of Scholar Rock common stock at price per share of $30.60

Inhibition of TGFβ1: Multipronged Approach for Immuno-Oncology

TGFβ1 is a key driver of immune system evasion by cancer cells



Nature (on-line), Feb. 14, 2018
doi:10.1038/nature25501

TGFβ attenuates tumour response to PD-L1 blockade by contributing to exclusion of T cells

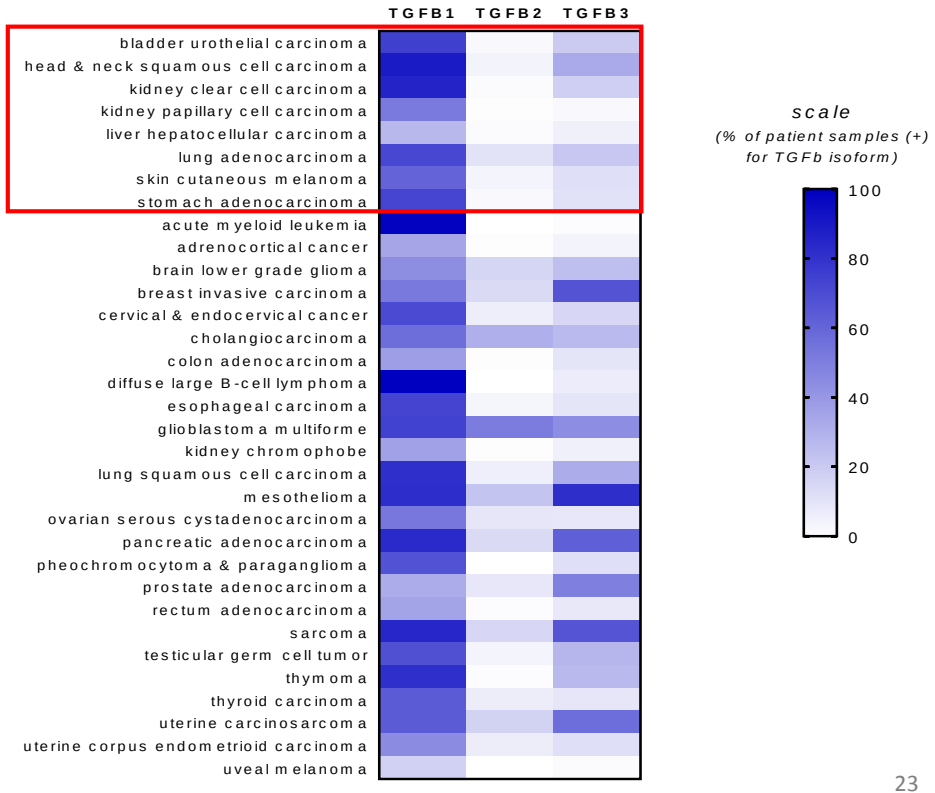
Sanjeev Mariathasan[1]*, Shannon J. Turley[1]*, Dorothee Nickles[1]*, Alessandra Castiglioni[1], Kobe Yuen[1], Yulei Wang[1], Edward E. Kadel III[1], Hartmut Koeppen[1], Jillian L. Astarita[1], Rafael Cubas[1], Suchit Jhunjhunwala[1], Romain Banchereau[1], Yagai Yang[1], Yinghui Guan[1], Cecile Chalouni[1], James Ziai[1], Yasin Şenbabaoğlu[1], Stephen Santoro[1], Daniel Sheinson[1], Jeffrey Hung[1], Jennifer M. Giltnane[1], Andrew A. Pierce[1], Kathryn Mesh[1], Steve Lianoglou[1], Johannes Riegler[1], Richard A. D. Carano[1], Pontus Eriksson[2], Mattias Höglund[2], Loan Somarriba[3], Daniel L. Halligan[3], Michiel S. van der Heijden[4], Yohann Loriot[5], Jonathan E. Rosenberg[6], Lawrence Fong[7], Ira Mellman[1], Daniel S. Chen[1], Marjorie Green[1], Christina Derleth[1], Gregg D. Fine[1], Priti S. Hegde[1], Richard Bourgon[1] & Thomas Powles[8]

- Pathway analysis points to TGFβ1 as major determinant of resistance to anti-PD-L1 (atezolizumab)
- TGFβ1 creates ‘immune excluded’ tumor microenvironment
- Anti-TGFβ antibody enhances anti-PDL1 treatment response in syngeneic EMT-6 tumor model

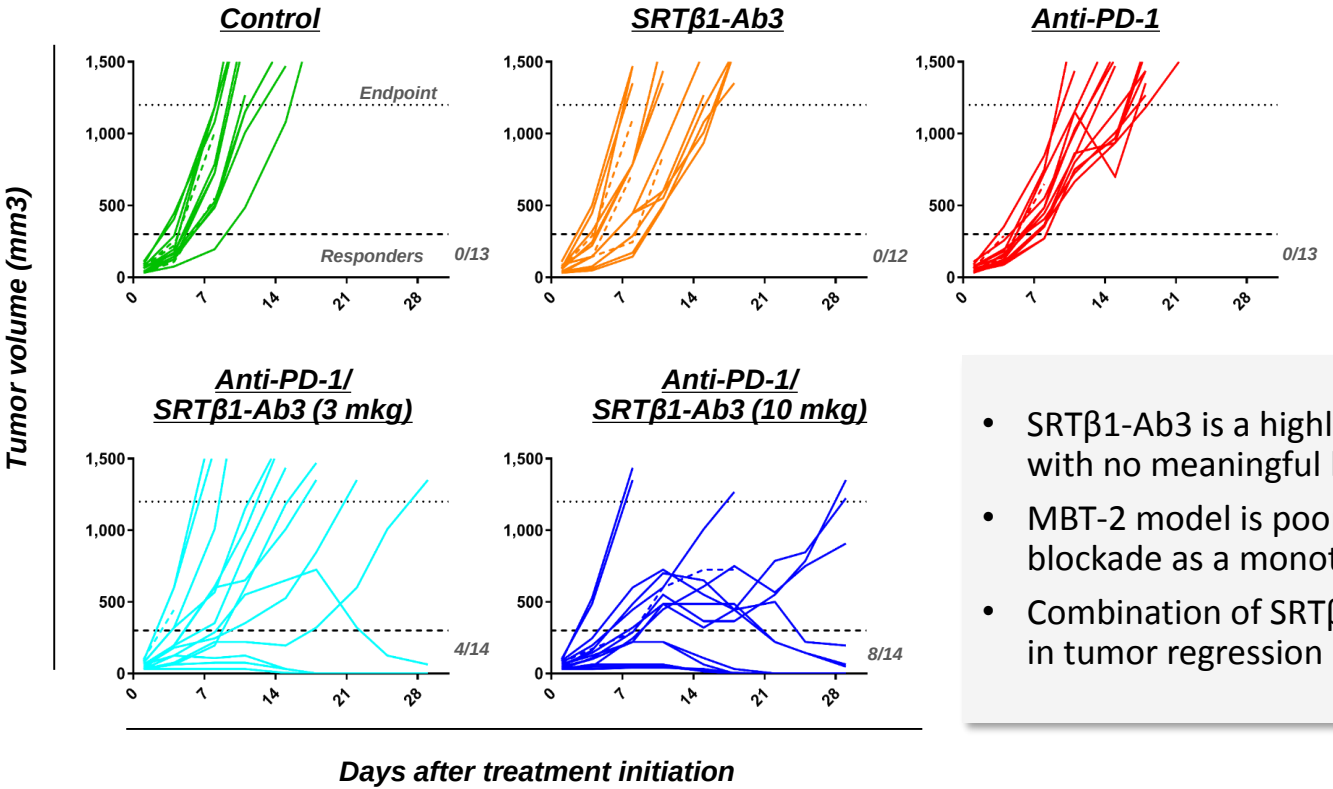
TGFβ1 is the Predominant Isoform in Most Human Tumors

The Cancer Genome Atlas RNAseq analysis: >10,000 samples spanning 33 tumor types

- TGFβ1 prevalent in human cancers for which checkpoint therapies are approved
- Expression data for most tumor types suggest that TGFβ signaling mainly driven by TGFβ1



TGFβ1 Blockade with SRTβ1-Ab3 Renders MBT-2 Tumors Susceptible to Anti-PD1 Therapy



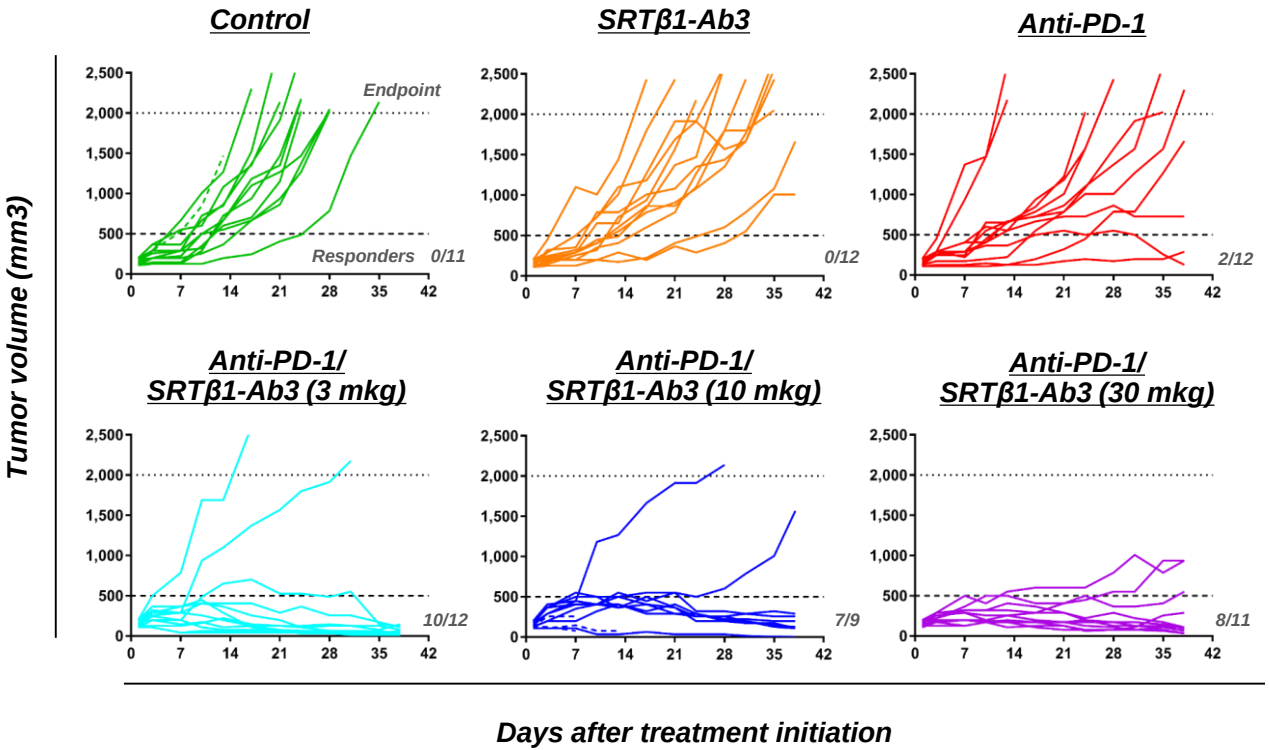
Dosing initiated when tumors reached 30-80 mm^3

Treatment with RMP1-14 anti-PD1 (5mg/kg twice weekly) and/or SRTβ1-Ab3 (once weekly at indicated dose)

- SRTβ1-Ab3 is a highly specific inhibitor of TGFβ1 with no meaningful binding to TGFβ2/TGFβ3
- MBT-2 model is poorly responsive to PD-1 blockade as a monotherapy
- Combination of SRTβ1-Ab3 and anti-PD1 resulted in tumor regression or tumor control

SCHOLAR ROCK Preclinical data shown above as presented at Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting (Nov 2018)

Anti-TGFβ1 Combination with PD-1 blockade is Effective in Cloudman S91 Melanoma Model

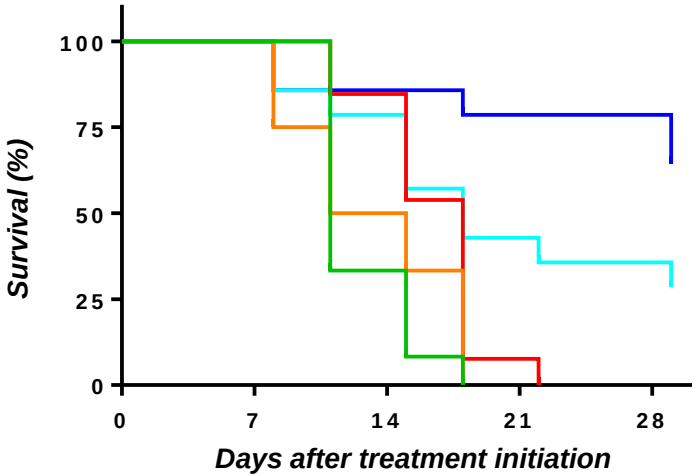


- Cloudman S91 model is poorly responsive to PD-1 blockade as a monotherapy
- Combination of SRTβ1-Ab3 and anti-PD1 resulted in tumor regression or tumor control

Interim preclinical data shown above as presented at Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting (Nov 2018)

SRTβ1-Ab3 Combined with Anti-PD1 Therapy Leads to Significant Survival Benefit

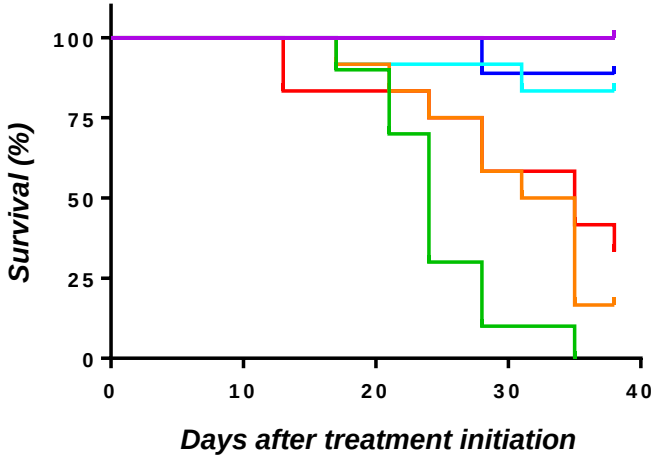
MBT-2 Bladder Cancer Tumor Model



Control (30 mkg qwk)
SRTβ1-Ab3 (10 mkg qwk)
anti-PD-1 (5 mkg twice weekly)
anti-PD-1 + SRTβ1-Ab3 (3 mkg qwk)
anti-PD-1 +SRTβ1-Ab3 (10 mkg qwk)

*** P<0.001 Log-rank (Mantel-Cox) test

Cloudman S91 Melanoma Tumor Model

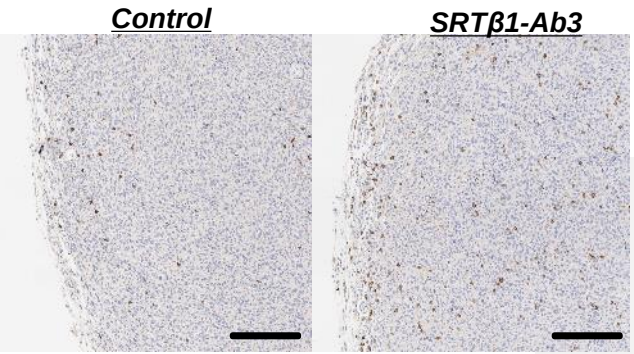


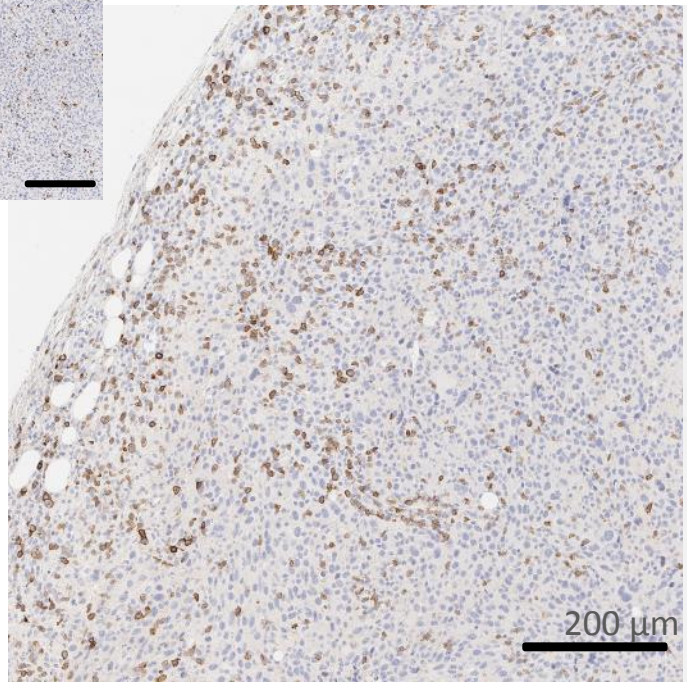
Control (30 mkg qwk)
SRTβ1-Ab3 (30 mkg qwk)
anti-PD-1 (5 mkg twice weekly)
anti-PD-1 + SRTβ1-Ab3 (3 mkg qwk)
anti-PD-1 +SRTβ1-Ab3 (10 mkg qwk)
anti-PD-1 +SRTβ1-Ab3 (30 mkg qwk)

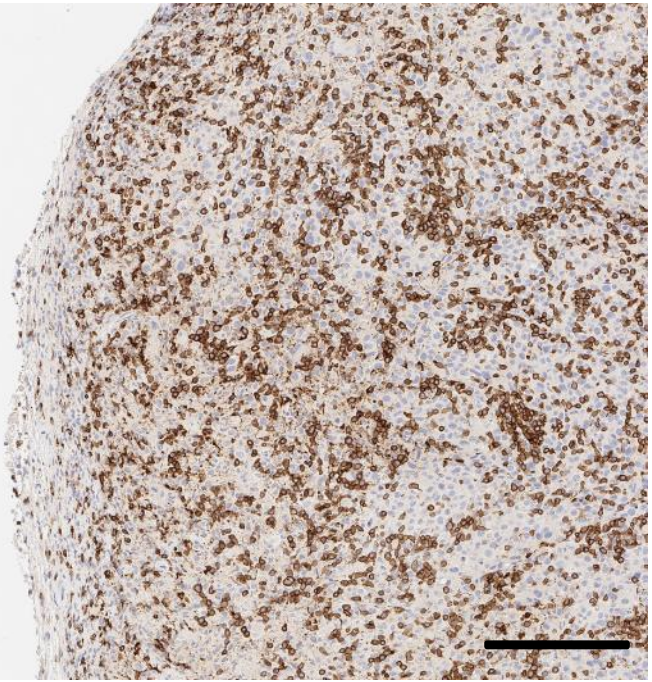
* P<0.05 Log-rank (Mantel-Cox) test
*** P<0.001

Preclinical data shown above as presented at Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting (Nov 2018)

SRTβ1-Ab3 Combination Therapy Enables Infiltration and Expansion of CD8⁺ T cells in Tumors







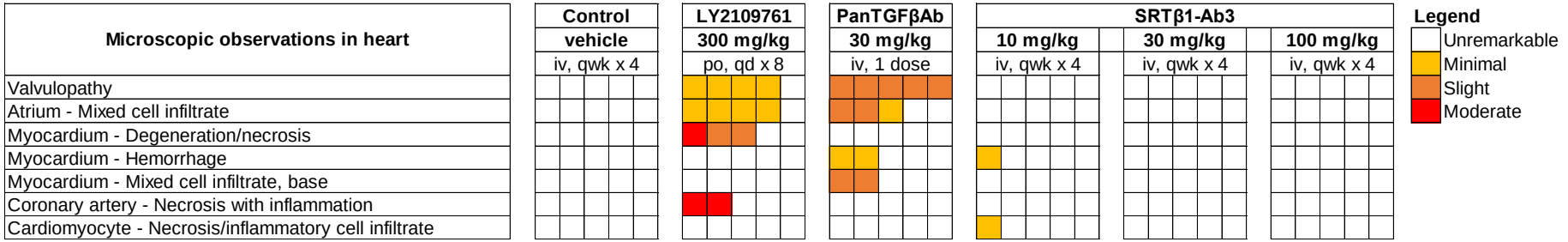
IHC of MBT-2 tumors at day 10

- Marked increase in frequency of CD8⁺ T cells within the tumor
- Consistent with flow cytometry data at day 13

 Preclinical data shown above as presented at Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting (Nov 2018)

TGFβ1 Isoform Specificity of SRTβ1-Ab3 Results in Improved Preclinical Toxicity Profile

Repeat dose pilot toxicology study in adult female Sprague Dawley rats



- Animals dosed with pan-TGFβ inhibitors, LY2109761 (inhibitor of ALK5, common TGFβ receptor kinase) or pan-TGFβ antibody, exhibited expected cardiac findings based on published data
- Exposure as assessed by SRTβ1-Ab3 serum concentration reached 2,300 µg/ml following 4 weekly doses of 100 mg/kg
- No SRTβ1-Ab3 related adverse effects were noted up to 100 mg/kg per week
- No cardiotoxicities (valvulopathy) were noted with SRTβ1-Ab3
- No observed adverse effect level (NOAEL) for SRTβ1-Ab3 was the highest dose evaluated (100 mg/kg per week), suggesting that the maximally tolerated dose (MTD) could be >100 mg/kg per week

2018 Achievements

TGFβ1 Inhibitor Discovery:

- ✓ Demonstrated immunomodulatory and anti-fibrotic activity in multiple animal models
- ✓ Achieved proof-of-concept combining TGFβ1 inhibitor and anti-PD1 treatment in mouse models of primary checkpoint resistance
  - Demonstrated tumor regression/control
  - Showed significant survival benefit
  - Presented data at the Society for Immunotherapy of Cancer (SITC) meeting
- ✓ Completed 28-day rat pilot toxicology study
  - No observed drug-related toxicity up to 100 mg/kg

2019 Milestones

- ❑ Continue to evaluate selective inhibitors of the activation of TGFβ1 in cancer immunotherapy models
- ❑ Nominate product candidate by the end of 1H19
- ❑ Continue to advance active discovery programs for context-dependent inhibition of TGFβ1
- ❑ Conduct discovery and preclinical studies as part of Gilead collaboration to discover and develop highly specific TGFβ inhibitors for fibrotic diseases

2018 Achievements

Capitalization and Collaboration:

- ✓ Raised $86M in gross proceeds from IPO in May
- ✓ Entered into strategic fibrosis collaboration with Gilead
  - $80M upfront and up to $1.45B in potential milestones

SRK-015 Clinical and Regulatory:

- ✓ Initiated Phase 1 trial of SRK-015 in May
- ✓ FDA granted and EMA adopted positive opinion on Orphan Drug Designation for SMA
- ✓ Published data showing benefits of inhibiting myostatin in mouse models of SMA in *Human Molecular Genetics*

TGFβ1 Inhibitor Discovery:

- ✓ Completed 28-day rat pilot toxicology study
- ✓ Achieved proof-of-concept with TGFβ1 inhibitor and anti-PD1 in mouse models of primary checkpoint resistance

2019 Milestones

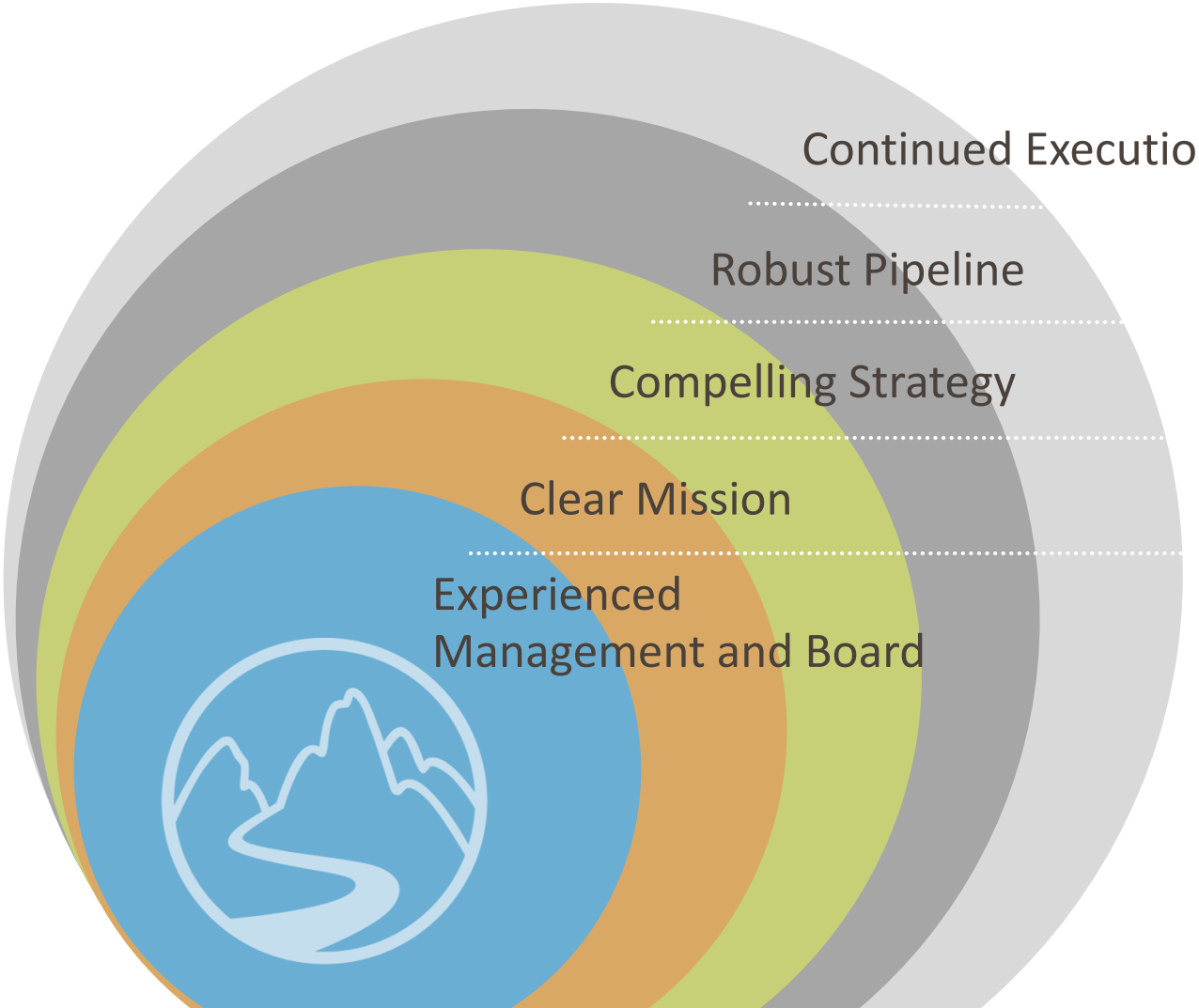
Clinical Advancements for SRK-015:

- ❑ Announce interim results from Phase 1 in 1Q19
- ❑ Initiate Phase 2 POC study in patients with SMA in 1Q19
- ❑ Present Phase 1 results at a medical conference
- ❑ Continue to evaluate our selective inhibitors of the activation of myostatin in various disease models
- ❑ Identify next indication in 1H19

Preclinical Development of TGFβ1 Inhibitors:

- ❑ Continue to evaluate selective inhibitors of the activation of TGFβ1 in cancer immunotherapy models
- ❑ Nominate product candidate in TGFβ1 program by the end of 1H19
- ❑ Continue to advance active discovery programs for context-dependent inhibition of TGFβ1
- ❑ Conduct discovery and preclinical studies as part of Gilead collaboration

Building for Success

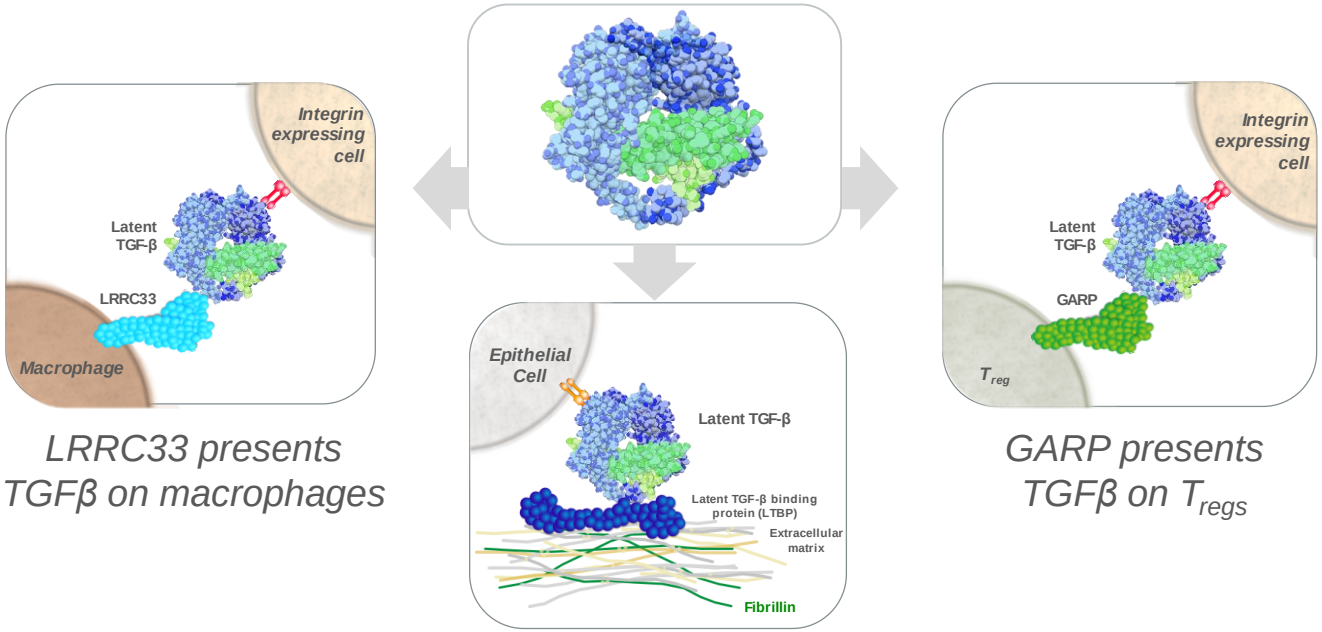


Backup

SCHOLAR ROCK

Targeting Latent TGFβs Creates Multiple “Handles” For Selectivity

Context-Dependent Inhibition of TGFβ1



LRRC33 presents TGFβ on macrophages

LTBP1 & 3 present TGFβ in connective tissue

GARP presents TGFβ on T_{regs}