Investor Call to Discuss Updated Results from SRK-181 Phase 1 DRAGON Study

June 4, 2024

ScholarRock

Forward-Looking Statements

Various statements in this presentation concerning the future expectations, plans and prospects of Scholar Rock Holding Corporation and Scholar Rock, Inc. (collectively, “Scholar Rock”), 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 preclinical studies and clinical trials for SRK-439, apitegromab, SRK-181, and other product candidates and indication selection and development timing, its cash runway, the ability of any product candidate to perform in humans in a manner consistent with earlier nonclinical, preclinical or clinical trial data, and the potential of its product candidates and proprietary platform. The use of words such as “may,” “could,” “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 for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, without limitation, that preclinical and clinical data, including the results from the Phase 2 trial of apitegromab or Part A or Part B of the Phase 1 trial of SRK-181, are not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trials of the same product candidate, including the Phase 3 clinical trial of apitegromab in SMA and Part B of the Phase 1 clinical trial of SRK-181, respectively, Scholar Rock’s ability to provide the financial support, resources and expertise necessary to identify and develop product candidates on the expected timeline, the data generated from Scholar Rock’s nonclinical and preclinical studies and clinical trials, information provided or decisions made by regulatory authorities, competition from third parties that are developing products for similar uses, Scholar Rock’s ability to obtain, maintain and protect its intellectual property, the success of Scholar Rock’s current and potential future collaborations, Scholar Rock’s dependence on third parties for development and manufacture of product candidates including, without limitation, to supply any clinical trials, 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 Scholar Rock’s Form 10-K for the year ended December 31, 2023, and Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, 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. All information in this press release is as of the date of the release, and Scholar Rock undertakes no duty to update this information unless required by law.

This presentation may also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we compete are necessarily subject to a high degree of uncertainty and risk.

Apitegromab and SRK-181 are investigational drug candidates under evaluation. Apitegromab, SRK-181, and SRK-439 have not been approved for any use by the FDA or any other regulatory agency and the safety and efficacy of apitegromab, SRK-181 and SRK-439 have not been established.

Welcome

Jay Backstrom, M.D., MPH
President and Chief Executive Officer

Company Speakers

Jay Backstrom, M.D., MPH
President & Chief
Executive Officer

Jing Marantz, M.D., Ph.D.
Chief Medical Officer

Expert Speaker

Toni Choueiri, M.D.
Director of the Lank Center for Genitourinary (GU) Oncology at Dana-Farber Cancer Institute (DFCI)

Today's Agenda

Topic	Speaker
▶ **Welcome**	**Jay Backstrom**, President & Chief Executive Officer
▶ **SRK-181 Data Update**	**Jing Marantz**, Chief Medical Officer
▶ **Discussion of SRK-181 Data with Toni Choueiri, M.D.**	**Jay Backstrom**, President & Chief Executive Officer **Toni Choueiri**, M.D., Dana-Farber Cancer Institute
▶ **Q&A**	**Jay Backstrom**, President & Chief Executive Officer **Ted Myles, Chief Operating Officer and Chief Financial Officer** **Jing Marantz**, Chief Medical Officer **Toni Choueiri**, M.D., Dana-Farber Cancer Institute
▶ **Closing Remarks**	**Jay Backstrom**, President & Chief Executive Officer
	Q&A

SRK-181 Data Update

Jing Marantz, M.D., Ph.D.
Chief Medical Officer

Phase 1 study (DRAGON) of SRK-181 (linavonkibart), a latent TGFβ1 inhibitor, combined with pembrolizumab in anti-PD1 resistant patients with advanced solid tumors: Updated results of expansion phase

Ulka Vaishampayan[1], Randy F. Sweis[2], Deepak Kilari[3], Ahmad Tarhini[4], Justin F. Gainor[5], Minal Barve[6], Guru Sonpavde[7], Meredith Mckean[8], David Park[9], Sunil Babu[10], Yawen Ju[11], Lan Liu[11], Susan Henry[11], Lu Gan[11], Timothy A. Yap[12]

[1]University of Michigan, Ann Arbor, MI; [2]University of Chicago, Chicago, IL; [3]Medical College of Wisconsin, Milwaukee, WI; [4]Moffitt Cancer Center Magnolia Campus, Tampa, FL; [5]Massachusetts General Hospital Harvard Medical School, Boston, MA; [6]Mary Crowley Cancer Research, Dallas, TX; [7]AdventHealth Medical Group, Orlando, FL; [8]Sarah Cannon Research Institute, Nashville, TN; [9]St Jude Crosson Cancer Institute/Providence Medical Foundation, Fullerton, CA; [10]Fort Wayne Medical Oncology and Hematology, Fort Wayne, IN; [11]Scholar Rock, Inc., Cambridge, MA; [12]The University of Texas MD Anderson Cancer Center, Houston, TX

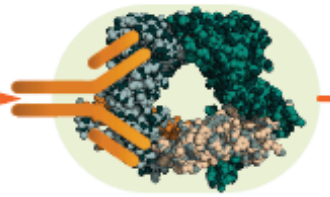
Mechanism of Action

SRK-181, a Selective Anti-TGFβ1 Antibody, Overcomes CPIs Resistance

TGFβ1 → Drives tumor immune escape that enables tumor survival[1] → Key driver of tumor resistance to CPIs[1] → Present in multiple compartments of the tumor microenvironment[1]

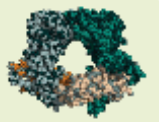
SRK-181 overcomes immune suppression and enhances tumor cell killing

Fully human IgG4 monoclonal antibody



Complete inhibition of TGFβ1

Inhibits activation of latent TGFβ-1 across ALL tumor compartments



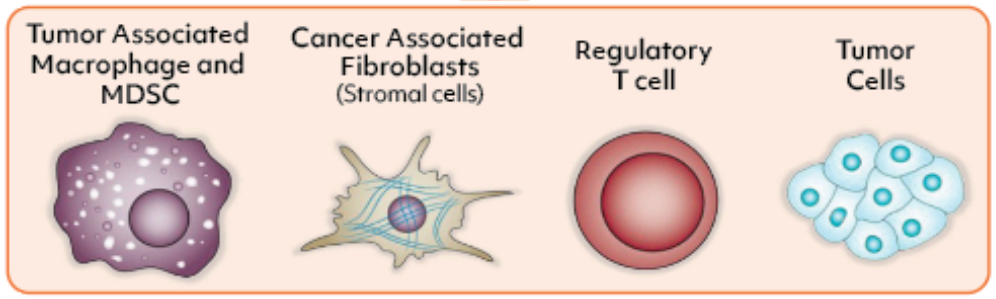
Latent TGFβ1

Mature TGFβ1

SRK-181 Targets latent TGFβ1 inhibiting growth factor before it gets activated

High selectivity to TGFβ1 vs TGFβ2/3

Increases therapeutic window and demonstrates an improved safety profile in GLP nonclinical toxicology studies, with no cardiotoxicities



Overcome immune suppression and enhance tumor cell killing

1.Batlle E, et al. *Immunity.* 2019; 50(4):924-940.

CPI, checkpoint inhibitor; GLP, good laboratory practice; MDSC, myeloid derived suppressor cells; TGFβ1, transforming growth factor beta-1.

Phase 1 Clinical Trial Overview

Dose Escalation (3+3)

Part A1: SRK-181 Single Agent
(80-3000 mg q3w/2000 mg q2w)

All advanced solid tumor
n=19

Part A2: SRK-181 + anti-PD-(L)1
(SRK-181: 240-2400mg q3w)

Advanced solid tumor non-responders to prior anti-PD-(L)1
n= 15

Dose Expansion

Part B: SRK-181 (1500mg q3w) + Pembrolizumab
n=up to 40/cohort

Key Eligibility Criteria

- ≥18-year-old and ECOG 0-1
- Measurable disease per RECIST v1.1
- At least 1 prior line of anti-PD-1 antibody
- Part B Cohort **ccRCC** and **HNSCC**:
  - Must have had PD on the most recent prior anti-PD-1
- Part B Cohorts **NSCLC**, **UC** and **MEL**:
  - Non-responders to all prior anti-PD-1

Cohort ccRCC

Cohort HNSCC

Cohort MEL

Cohort UC

Cohort NSCLC

Cohort Any Other*

Study Endpoints

Primary:
- Safety and tolerability

Secondary:
- Anti-tumor activity (BOR, ORR, DoR, and DCR)
- PK and ADA

Exploratory:
- Biomarker
- PFS, OS, etc.

*Cohort Any Other was terminated early and HNSCC was added.

ADA, anti drug antibody; BOR, best overall response; ccRCC, clear cell renal cell carcinoma; DCR, disease control rate; DoR, duration of response; ECOG, eastern cooperative oncology group; HNSCC, head and neck squamous cell carcinoma; MEL, melanoma; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PD-(L)1, PD-1/PD-L1; PFS, progression-free survival; PK, Pharmacokinetic; q2w, every 2 weeks; q3w, every 3 weeks; RECIST, response evaluation criteria in solid tumors; UC, urothelial carcinoma.

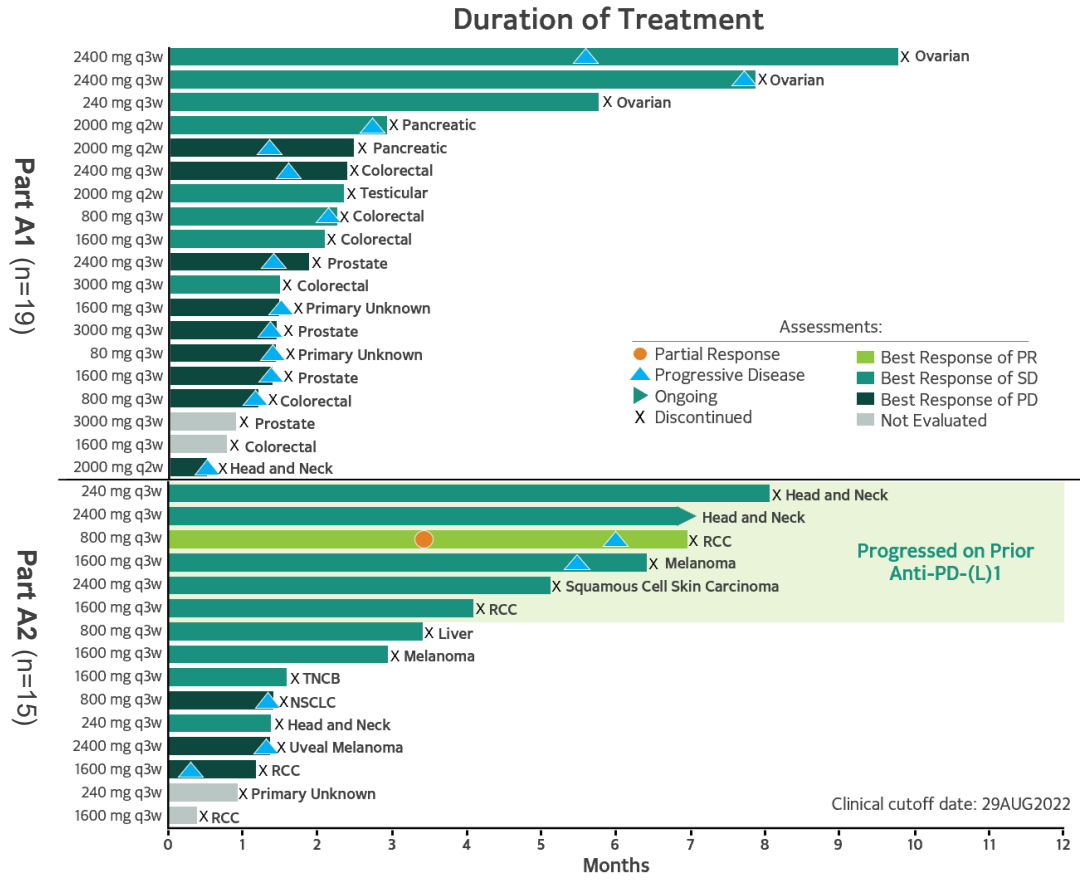
Preliminary Safety and Efficacy
Phase 1 *Dose Escalation Phase*

Safety
- **SRK-181 was well tolerated:** No DLTs observed; no Grade 4 or 5 treatment-related AEs

MAD/MTD
- **MAD:** 3000mg q3w and 2000mg q2w for single SRK-181 and 2400mg q3w for SRK-181 in combination with anti-PD-1
- **MTD not reached; recommended Part B dose** at 1500 mg q3w or 1000 mg q2w

PK
- Exposure was similar between monotherapy and combination
- Approximately dose proportional exposure over 240 mg q3w
- Minimal to no accumulation was observed after multiple doses

Efficacy
- **Part A1, Single-Agent Dose Escalation**
  - All 3 ovarian cancer patients were stable beyond ~ 6-month cutoff
- **Part A2, Combination Treatment Dose Escalation**
  - 1 PR in anti-PD-1 resistant ccRCC patient
  - 5 (33%) patients had SD for 4+ months
    - 1 HNSCC patient had a 29.4% tumor reduction



Martin CJ, et al. *Sci Transl Med.* 2020;12:eaay8456.
Yap T, et al. *J ImmunoTherapy of Cancer* 2022;10:doi: 10.1136/jitc-2022-SITC2022.0780.

AE, adverse event; ccRCC, clear cell renal cell carcinoma; DLT, dose-limiting toxicity; HNSCC, head and neck squamous cell carcinoma; MAD, maximum administered dose; MTD, maximum tolerated does; PK, Pharmacokinetic; PD, progressive disease; PR, partial response; q2w, every 2 weeks; q3w, every 3 weeks; SD, stable disease.
Data cut date: Apr 10, 2024

Patient Demographics and Disposition

Phase 1 Dose Expansion Phase

Category	All[#]
N	78
Age, median (range)	65y (32-81y)
Gender, M, n (%)	56 (71.8)
Prior Lines of Therapy, median (range)	3 (1-9)
Number of Lines of Prior Anti-PD-(L)1, n (%)	
1	48 (61.5)
2	23 (29.5)
3	6 (7.7)
4	1 (1.3)
Best Response to Prior Anti-PD-(L)1, n (%)	
Partial Response	1 (1.3)^
Stable Disease	40 (51.3)
Progressive Disease	37 (47.4)
Disease Progressed from the Last Prior Anti-PD-1, n (%)	76 (97.4)*

[#]Includes patients of 30 ccRCC, 11 HNSCC, 11 MEL, 11 UC, 11 NSCLC and 4 Any Other Cohorts.
^1 HNSCC patient had best response of PR to prior anti-PD-(L)1.
*2 MEL patients discontinued the last prior anti-PD-(L)1 due to other reason instead of disease progression.

Category	All
Enrolled	78
On Study, n (%)	10 (12.8)
Stopped Treatment, n (%)	68 (87.2)
Reason for Completion/Discontinuation, n (%)	
Disease Progression Based on RECIST 1.1	40 (51.3)
Clinical Progression	6 (7.7)
Adverse Event[&]	17 (21.8)
Investigator Decision	1 (1.3)
Withdrawal of Consent	4 (5.1)

[&]10 patients (12.8%) discontinued from the study due to treatment-related AEs: rash maculo-popular and pneumonitis (2 patients), bullous pemphigoid, colitis, erythroderma, generalized erythematous rash, invasive squamous cell carcinoma, mucositis oral (1 patient each).

AE, adverse event; ccRCC, clear cell renal cell carcinoma; HNSCC, head and neck squamous cell carcinoma; MEL, melanoma; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PD-(L)1, PD-1/PD-L1; RECIST, response evaluation criteria in solid tumors; UC, urothelial carcinoma.
Data cut date: Apr 10, 2024

Manageable Safety Profile
Phase 1 Dose Expansion Phase

Treatment-Emergent AEs Related to SRK-181 or Anti-PD(L)1

Adverse Event	All Grades (>5%) N=78	≥Grade 3 N= 78
Rash#	25 (32.1%)*	10 (12.8%)*
Pruritus	20 (25.6%)*	1 (1.3%)*
Fatigue	16 (20.5%)	1 (1.3%)
Diarrhoea	11 (14.1%)	0 (0%)
Nausea	5 (6.4%)	1 (1.3%)
ALT increased	4 (5.1%)	2 (2.6%)
AST increased	4 (5.1%)	1 (1.3%)
Arthralgia	4 (5.1%)	0 (0%)
Vomiting	4 (5.1%)	0 (0%)

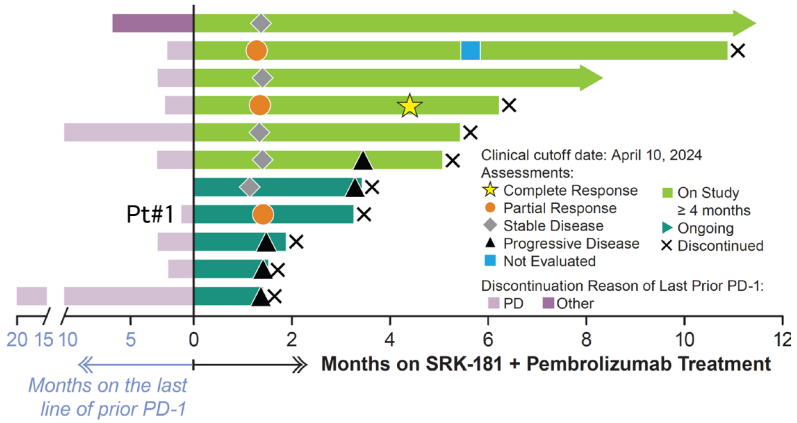
#Rash includes rash, rash macular, rash maculo-papular, rash erythematous, and rash pruritic.
*Treatment-related irAE.

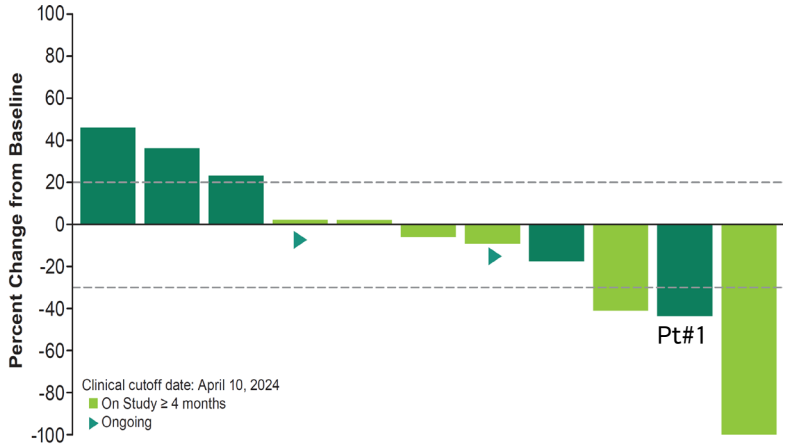
- There was 1 treatment-related Grade 4 AE (Dermatitis exfoliative generalised)
- There was no treatment-related Grade 5 AE
- Treatment-related SAE >2% (2 patients) were Pemphigoid (irAE)

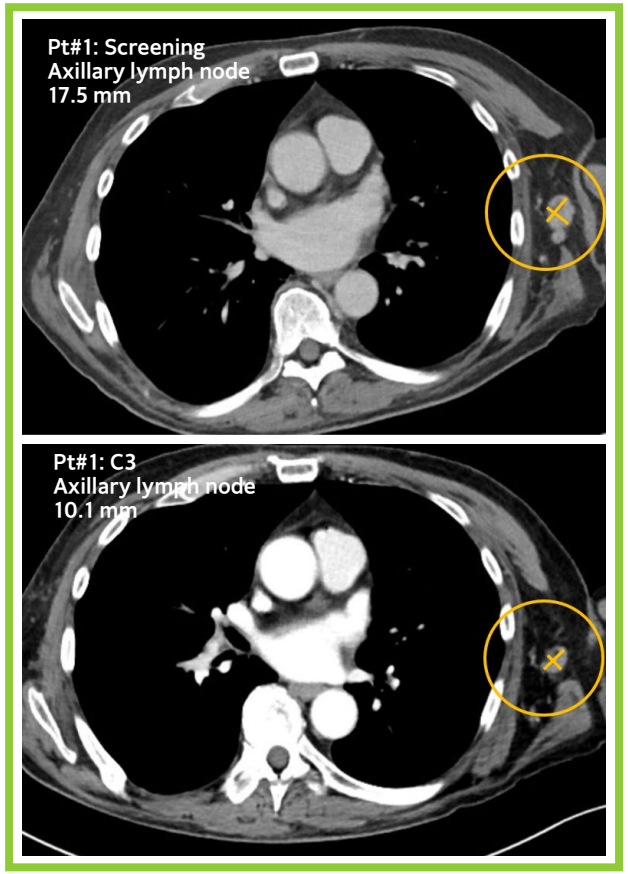
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; irAE, immune-related adverse event; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PD-(L)1, PD-1/PD-L1; SAE, serious adverse event
Data cut date: Apr 10, 2024

Efficacy in Cohort MEL

Clinical Responses in Anti-PD-1 Non-responders







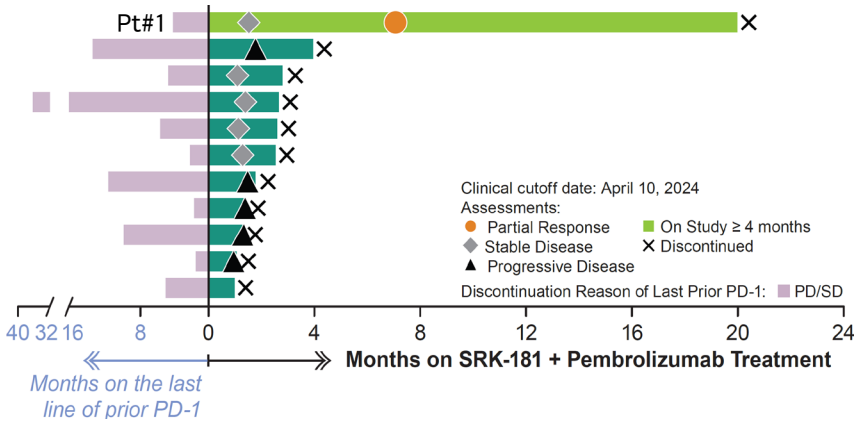
Efficacy	Intent To Treat N=11
ORR	3 (27.3%)
Confirmed CR	1 (9.1%)
Confirmed PR	1 (9.1%)
mDoR (Months)	4.9 (1.8, 7.1)
DCR	8 (72.7%)

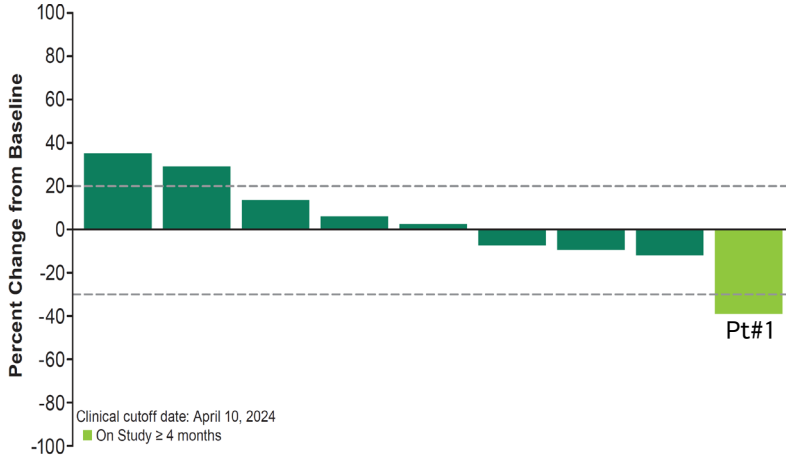
- **Median lines of prior cancer therapy: 3 (range 1 – 7)**
  - All have SD or PD as BOR to the last prior anti-PD-1
  - 9 (82%) had PD from the last prior anti-PD-1

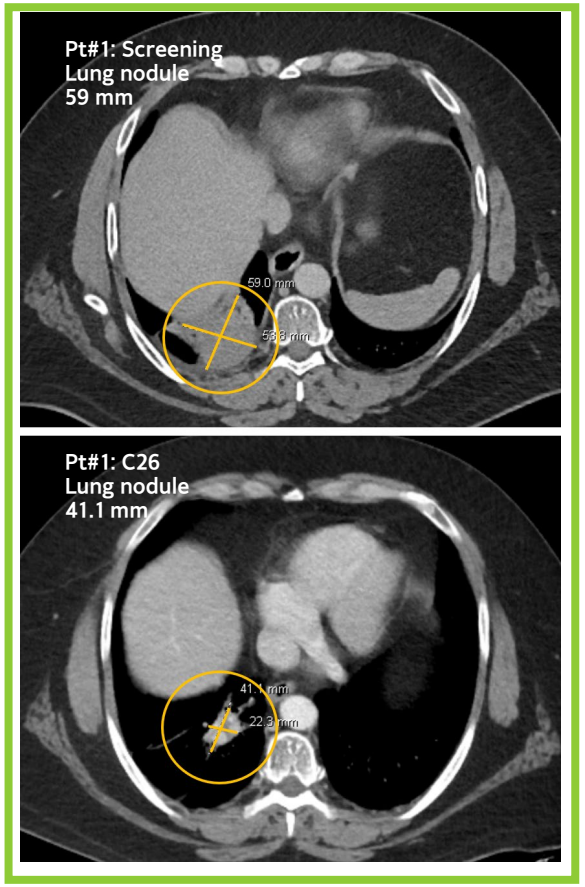
BOR, best overall response; CR, complete response; DCR, disease control rate; mDoR, median duration of response; MEL, melanoma; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response.
Data cut date: Apr 10, 2024

Efficacy in Cohort UC

Clinical Responses in Anti-PD-1 Non-responders







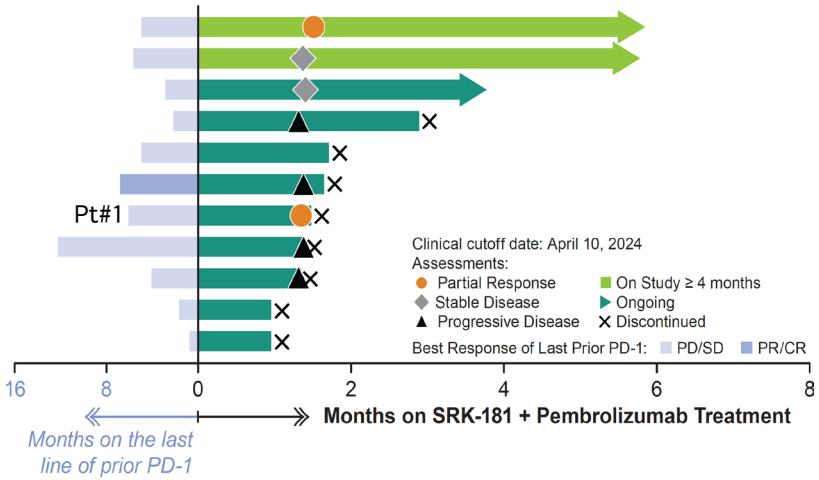
Efficacy	Intent To Treat N=11
ORR	1 (9.1%)
Confirmed PR	1 (9.1%)
mDoR (Months)	12.9 (12.9, 12.9)
DCR	5 (45.5%)

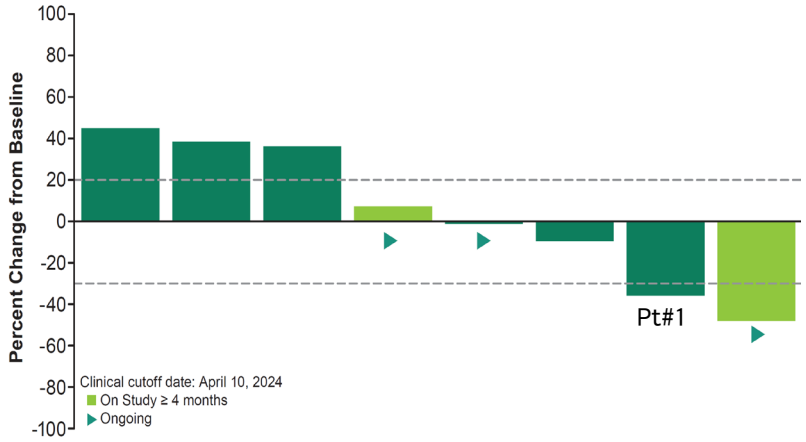
- **Median lines of prior cancer therapy: 4 (range 2 – 5)**
  - All have SD or PD as BOR to the last prior anti-PD-1
  - All had PD from the last prior anti-PD-1

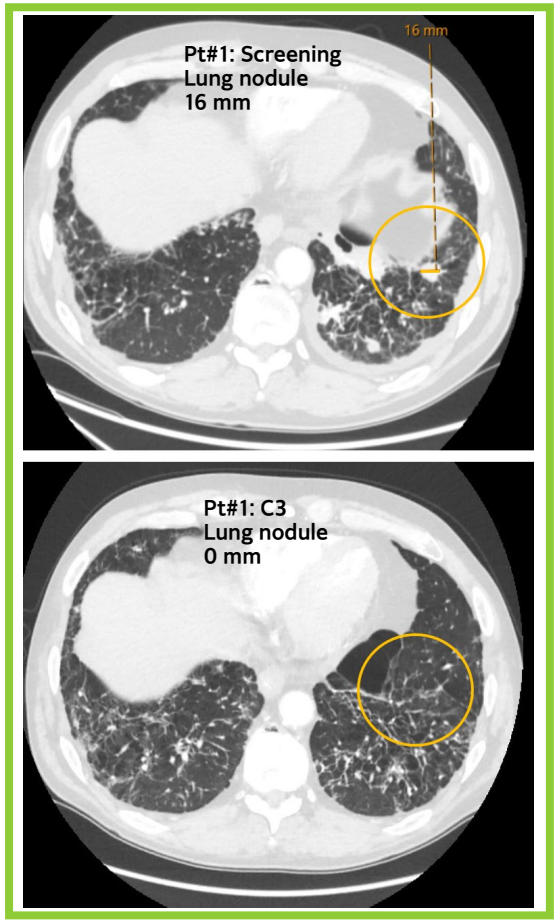
BOR, best overall response; DCR, disease control rate; mDoR, median duration of response; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease; UC, urothelial carcinoma.
Data cut date: Apr 10, 2024

Efficacy in Cohort HNSCC

Clinical Responses in Heavily Pre-treated and Anti-PD-1 Resistant Patients







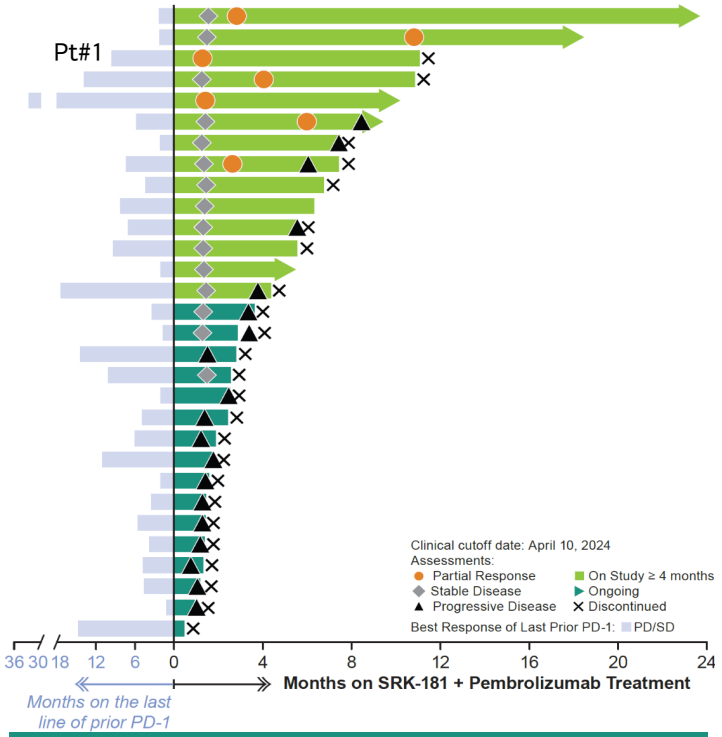
Efficacy	Intent To Treat N=11
ORR	2 (18.2%)
Confirmed PR	1 (9.1%)
mDoR (Months)	2.2+ (0.1, 4.3+)
DCR	4 (36.4%)

- **Median lines of prior cancer therapy: 3 (range 1 – 7)**
  - 10 (91%) have SD or PD as BOR to the last prior anti-PD-1
  - All had PD from the last prior anti-PD-1

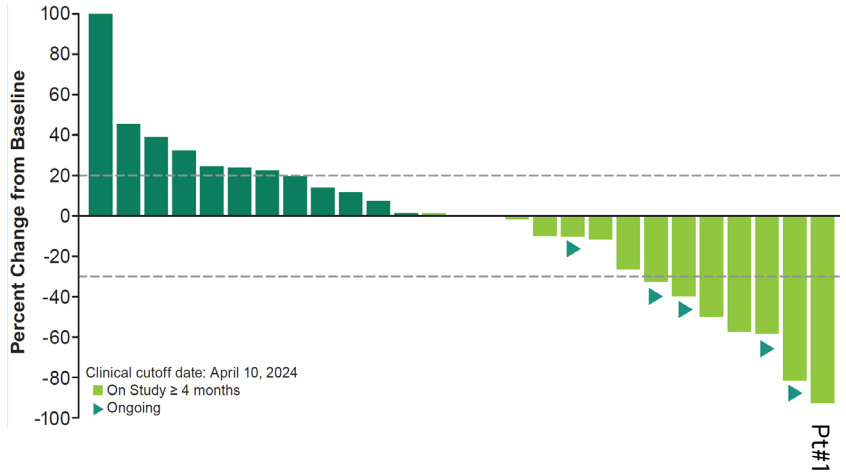
BOR, best overall response; DCR, disease control rate; HNSCC, head and neck squamous cell carcinoma; mDoR, median duration of response; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease.
Data cut date: Apr 10, 2024

Efficacy in Cohort ccRCC

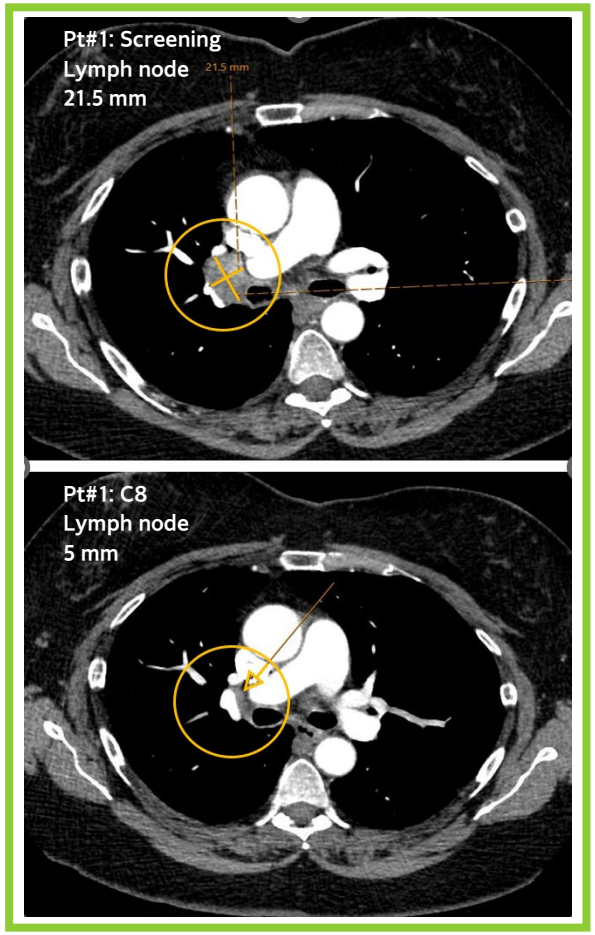
Clinical Responses in Heavily Pre-treated and Anti-PD-1 Resistant Patients



Efficacy	Intent To Treat N=30
ORR	7 (23.3%)
Confirmed PR	6 (20%)
mDoR (Months)	7.7+ (2.5+, 20.9+)
DCR	17 (56.7%)



- **IMDC score: intermediate 67%; poor 30%**
- **Median lines of prior cancer therapy: 2 (range 1 – 9)**
  - 29 (97%) received at least 1 prior anti-PD-1 and TKI
  - All had SD or PD as BOR to the last prior anti-PD-1
  - All had PD from the last prior anti-PD-1



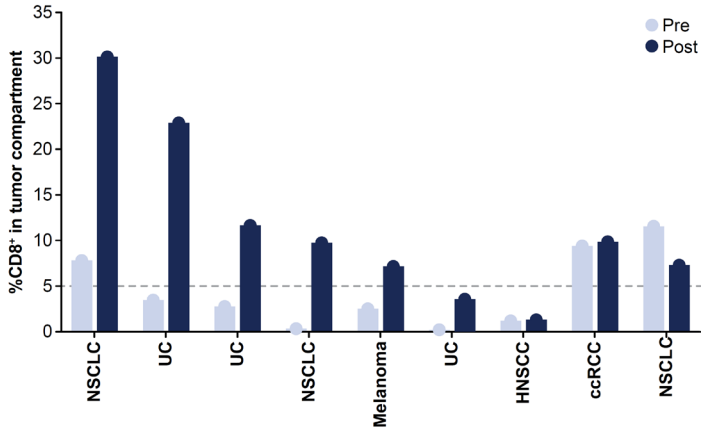
BOR, best overall response; DCR, disease control rate; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mDoR, median duration of response; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.
Data cut date: Apr 10, 2024

Proof of Mechanism

SRK-181 and Pembrolizumab Treatment Creates a Proinflammatory Microenvironment

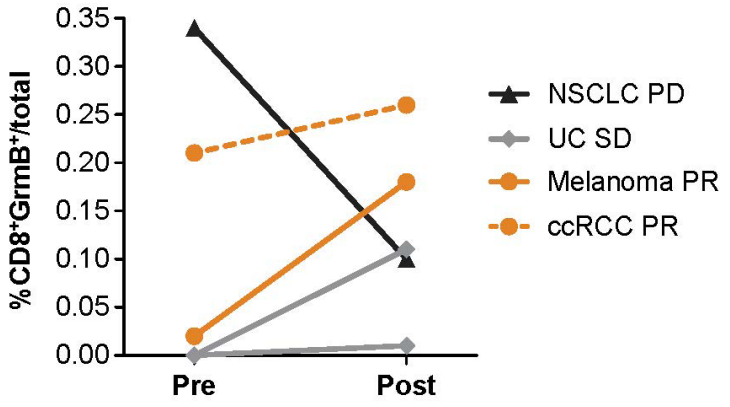
- SRK-181 and pembrolizumab increase CD8+ T-cells infiltration into tumors across multiple tumor types
- CD8+ T-cell were activated (CD8+GrmB+) in responding patients across multiple cohorts
- The number of CD8+GrmB+ cells correlates with tumor shrinkage

SRK-181 and Pembrolizumab Increased CD8+ Infiltration

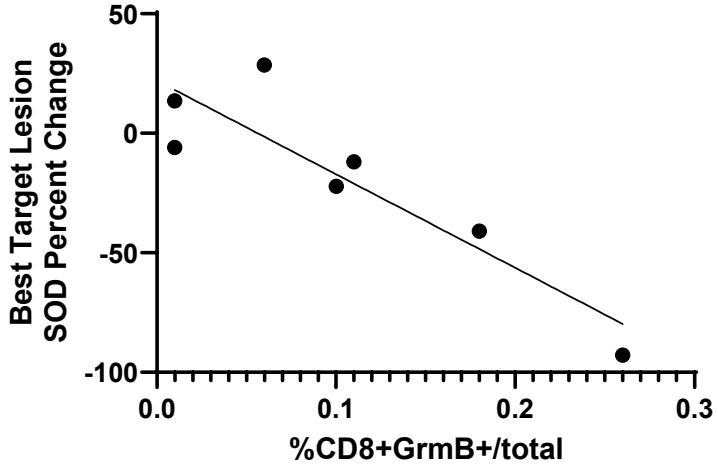


Line indicates cutoff that defines infiltrated status.
Data generated from available paired biopsies that were evaluated using a chromogenic assay.

CD8+ Cytotoxic T-cells were Activated in Responding Patients



Data generated from available paired biopsies that were evaluated using a multiplex fluorescent assay.



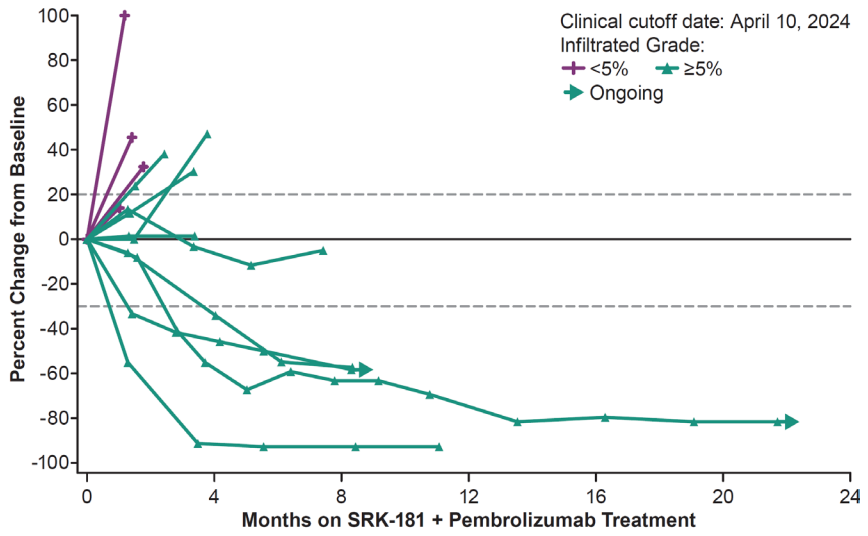
Data generated from available post treatment biopsies that were evaluated using a multiplex fluorescent assay.

ccRCC, clear cell renal cell carcinoma; CD, cluster of differentiation; GrmB, Granzyme B; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; SD, stable disease; UC, urothelial carcinoma.
Data cut date: Apr 10, 2024

Biomarker Data May Inform Patient Selection Strategy

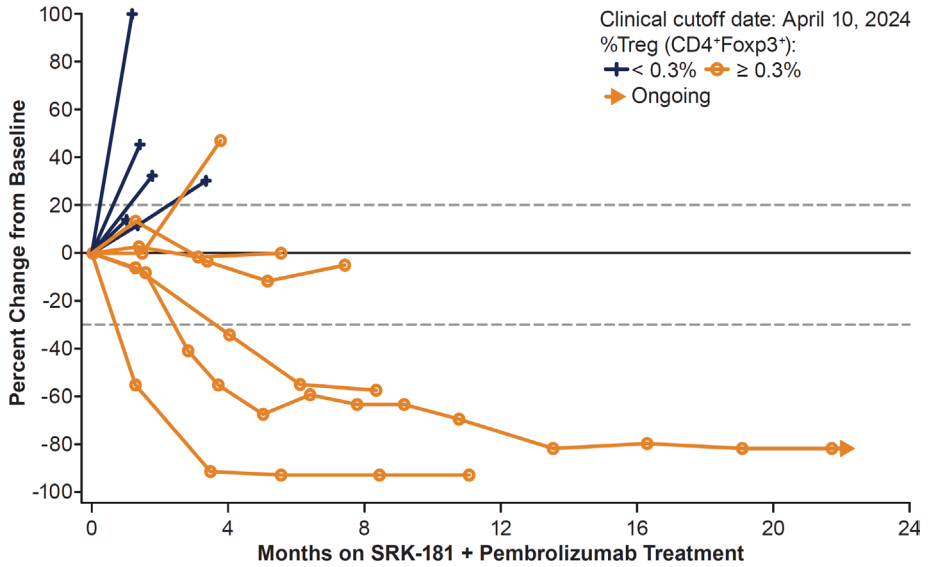
Baseline CD8+ T-cell Infiltration Status and Baseline Treg Levels Suggest a Higher Chance of Clinical Response

Baseline CD8+ Infiltration Status Suggest a Higher Chance of Response in ccRCC Patients



- Baseline data was available from 14 patients and 10 were infiltrated
- If enrollment had been limited to patients who were infiltrated at baseline:
  - ORR is increased from **23.3%** (7/30) to **40%** (4/10)
  - mDoR is improved from **7.7** months to **9.3** months

Elevated Baseline Treg (CD4+Foxp3+) Levels within Tumor Compartment Suggest a Higher Chance of Response in ccRCC Patients



- Baseline data was available from 11 patients and 6 had elevated Treg levels
- If enrollment had been limited to patients with elevated Treg at baseline
  - ORR is increased from **23.3%** (7/30) to **50%** (3/6)
  - mDoR is improved from **7.7** months to **9.8** months

*1 patient progressed prior to 1st scan, so not represented on spider plot.

ccRCC, clear cell renal cell carcinoma; CD, cluster of differentiation; mDoR, median duration of response; Foxp3, forkhead box p3; ORR, objective response rate; TGFβ1, transforming growth factor beta-1; Treg, T regulatory cells
Data cut date: Apr 10, 2024

Summary

Objective evidence of anti-tumor activity across multiple cancer types with duration of response up to 20+ months

- ORR 23.3% in ccRCC, 18.2% in HNSCC, 27.3% in MEL, including 1 CR, and 9.1% in UC
- mDoR were 7.7+m in ccRCC, 2.2+m in HNSCC, 4.9m in MEL and 12.9m in UC

Biomarker findings establish proof of mechanism and inform potential patient selection strategy

- Combination was associated with enhanced proinflammatory microenvironment with activation of CD8+ T-cells in responding patients across multiple cohorts and the number of activated T-cells correlating with tumor shrinkage
- In baseline CD8+ T-cells infiltrated ccRCC patients, ORR increases from **23.3%** to **40%** with mDoR improving from **7.7 months** to **9.3 months**
- In baseline Treg elevated ccRCC patients, ORR increases from **23.3%** to **50%** with mDoR improving from **7.7 months** to **9.8 months**

Safety profile with the combination of SRK-181 and pembrolizumab was manageable

- Treatment-related AEs were primarily skin toxicities with 1 Grade 4 skin event; no Grade 5 event
- Treatment-related G3+ AEs ≥ 5% were rash only and treatment-related SAE ≥ 2% were pemphigoid only

AE, adverse event; ccRCC, clear cell renal cell carcinoma; CD, cluster of differentiation; CR, complete response; HNSCC, head and neck squamous cell carcinoma; mDoR, median duration of response; MEL, melanoma; ORR, objective response rate; PD, progressive disease; PR, partial response; SAE, serious adverse events; SD, stable disease; Treg, T regulatory cells; UC, urothelial carcinoma.

Conclusion

- Anti-tumor activity in anti-PD1 resistant patients across multiple cancer types establishes proof-of-concept for SRK-181, a selective latent TGFβ1 inhibitor
- Biomarker results establish proof of mechanism and inform potential patient selection strategy in ccRCC
- These data warrant further investigation of SRK-181

TGFβ1, transforming growth factor beta-1.

Today's Agenda

Topic	Speaker
▶ **Welcome**	**Jay Backstrom**, President & Chief Executive Officer
▶ **SRK-181 Data Update**	**Jing Marantz**, Chief Medical Officer
▶ **Discussion of SRK-181 Data with Toni Choueiri, M.D.**	**Jay Backstrom**, President & Chief Executive Officer **Toni Choueiri**, M.D., Dana-Farber Cancer Institute
▶ **Q&A**	**Jay Backstrom**, President & Chief Executive Officer **Ted Myles, Chief Operating Officer and Chief Financial Officer** **Jing Marantz**, Chief Medical Officer **Toni Choueiri**, M.D., Dana-Farber Cancer Institute
▶ **Closing Remarks**	**Jay Backstrom**, President & Chief Executive Officer
	Q&A

Discussion of SRK-181 Data with Dr. Toni Choueiri, M.D.

Jay Backstrom, M.D., MPH
President & Chief
Executive Officer

Toni Choueiri, M.D.
Director of the Lank Center for Genitourinary (GU) Oncology at Dana-Farber Cancer Institute (DFCI)

Q&A Session

Jay Backstrom, M.D., MPH
President & Chief Executive Officer

Jing Marantz, M.D., Ph.D.
Chief Medical Officer

Ted Myles, MBA
Chief Operating Officer and Chief Financial Officer

Toni Choueiri, M.D.
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