

Update on Clinical Programs and R&D Pipeline

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Agenda





01 Strategic Overview

Anil Raghavan



02 Clinical Programs

Siu-Long Yao



03 SCD-153

Vikram Ramanathan



04 SBO-154

Nitin Damle



05 Financial Update Chetan Rajpara



Maturing portfolio & operating model



Cost competitive translation with global access to science



- In-house competencies and infrastructure to prosecute an idea from 'bench to bedside' with an ability to scale across modalities
- 3 NDAs approved by the USFDA and commercialized by partners, contributing significant 'non dilutive' cash to support the portfolio and operating model build-up
- Robust pipeline with 3 NCEs under clinical development in 6 indications including two 'first-in-class' opportunities

Year 2024 promises several value inflection points

High-yield assets set to read out clinical PoCs and proceed to pivotal programs

• Key catalytic events coming up every quarter during next year



Vodobatinib PD

PROSEEK Interim analysis readout



SCD-153

Phase 1 SAD study results

Vibozilimod*

Atopic dermatitis

Phase 2 study enrollment completion



Vodobatinib PD PROSEEK full data readout



SB0-154 IND submission

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Vibozilimod*

Atopic dermatitis Interim analysis and topline results

SCD-153

Phase 1 MAD study initiation



Vodobatinib reached Phase 2 enrollment target



PROSEEK read out to provide definitive PoC for the cAbl hypothesis and oxidative stress response modulation as an approach for neuroprotection



- One of the largest Phase 2 study ongoing for early PD patients (pre L-Dopa)
 - Study met enrollment target, 504 evaluable patients
 - Treatment duration of 40 weeks followed by 40 weeks' extension study
 - Data from interim analysis expected in March 2024
- Geared up for post PROSEEK outcome
 - · State of readiness for initiation of Phase 3 study
 - Engaging partners for potential collaboration



Oxidative stress in PD and related a-synucleinopathies¹



PROSEEK opens up a broad opportunity set

Unlocks significant value for SPARC with potential use across PD progression and in disorders driven by α -synuclein

- Potential to combine with symptomatic therapies in PD
- Potential for early interventions in precursor conditions
- PROSEEK offers a powerful PoC for the pathway in diseases driven by α-synuclein
- Key disorders having α-synuclein aggregation as a pivotal process include PD, MSA & DLB



Vodobatinib can emerge as the protective backbone across the continuum of care for synucleopathies and other neurodegenerative disorders resulting from misfolded proteins

Chart adapted from Is insulin-like growth factor-1 involved in Parkinson's disease development? Castilla-Cortázar et al. J Transl Med (2020) 18:70 MSA: Multiple System Atrophy I DLB: Dementia with Lewy Bodies I OCD: Obsessive Compulsive Disorder



Optionality beyond PROSEEK



SPARC pipeline includes multiple high value assets with platform potential

- SPARC's immunology program will provide additional efficacy and safety data points in 2024
- Oncology offers a potential hedge and anchor for future portfolio build across modalities
- Additional bets to understand underlying mechanisms in neurodegenerative diseases UK DRI collaboration

Immunology

- Led by 3rd generation S1PR1 agonist, Vibozilimod with potential to be best-in-class asset in Dermatology – Clinical PoC in 2024
- SCD-153 program to explore a novel pathway with a topical agent for Alopecia Areata – Safety PoC in 2024
- Potential additional indications

Oncology

- Vodobatinib in CML Recalibrating to a changing regulatory and market landscape
- MUC-1 program A differentiated targeting approach which can become a pipeline in itself beyond the first ADC
- UCSF collaboration for Small Molecule Drug Conjugates in mPC
- Strong preclinical interest in antibody mediated delivery, RNA targeted therapeutics, & collateral lethality

Additional shots on goal & enabling competencies differentiate SPARC's risk profile



Immunology program focused on autoimmune disorders in dermatology



Opportunity to become safer oral alternative to the current SoC; offers a path to build an immunology franchise

Vibozilimod

- Two Phase 2b studies recruiting patients in Psoriasis and Atopic Dermatitis; lead indication Atopic Dermatitis
- Provides an alternate mechanism to IL-4/IL-13 antibodies and JAK inhibitors
- Studies being expanded to Europe and Canada

SCD-153

- Topical application may potentially provide a safer alternative to currently approved JAK inhibitors for treatment of AA
- Phase 1 study initiated for AA
- Preclinical evaluation ongoing in other autoimmune diseases of epidermis



Oncology pipeline with multiple near-term clinical options...



...backed up by an active preclinical effort involving multiple targets and modalities

Vodobatinib for CML (SCO-088) writes down the PROSEEK risk

- Validated target; efficacy established in patients
- 5 Being developed under Frontrunner program of the USFDA; potential to move in earlier lines of treatment

Cell-targeting by ADC¹



- Antibody and small molecule ligands targeted delivery of payloads across modalities is a key focus for SPARC oncology
 - MUC-1 antibody provides a differentiated platform to build pipeline of assets targeting a defined subset of patients across multiple tumors
 - Key elements of the MUC-1 α/β hypothesis validated.
 First program on track; expected to enter clinic in 2024
 - Additional constructs with other payloads and augmented targeting are being evaluated in preclinical setting
 - Preclinical PoC established for Small Molecule Drug Conjugate
- Emerging preclinical interest in novel synthetic lethality pairings and RNA therapeutics



Rigorous translational focus



Focused on patient needs, developability considerations & asset appropriateness



- Rigorous portfolio review process Kill early, kill cheap, kill completely
- Large proportion of programs focusing on novel biology (potential first-in-class). Continued development of best-in-class assets for validated targets to balance the risk

SPARC expects additional non-dilutive cash flows from its commercial/partnered assets



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Pipeline overview



| Asset / Program | МоА | Indication | Discovery | Preclinical | Phase 1 | Phase 2 | Phase 3/ Registration Study |
|--------------------------|----------------------------|--|------------|-----------------|--------------|---------------|--------------------------------|
| | | Parkinson's Disease | 8 | | | | |
| Vodobatinib (SCC-138) | c-ABL Inhibitor | Lewy Body Dementia ¹ Alzheimer's Disease | | | | | |
| Vodobatinib (SCO-088) | BCR-ABL Inhibitor | Refracto <mark>ry</mark> CML | 1 | | | | |
| SB0-154 | Anti-MUC-1 ADC | Solid Tumors | U | - | | | |
| Vibozilimod (SCD-044) | Selective S1PR1 agonist | Psoriasis | | | | | |
| | | Atopic Dermatitis | 0 | | | | |
| SCD-153 | ltaconate derivative | Alopecia Areata | A | | | | |
| Preclinical Assets | 10+ preclinic | al assets under | developmen | t to ensure a r | obust pipeli | ne for future | growth |
| | | Neurology | Oncole | ogy 📕 Ir | nmunology | | |

Bexirestrant deprioritized based on commercial assessment and change in treatment landscape



Key priorities for next year

Execution focus is the objective



Clinical studies

- PROSEEK completion and data readout
- Vodobatinib Phase 3 study initiation for PD
- SCD-153 Phase 2 study initiation
- Vibozilimod enrollment completion for Atopic Dermatitis study

Regulatory filing

- Elepsia site transfer
- PDP-716 re-filing
- EoP2 meeting with USFDA for Vodobatinib in neurodegenerative disorders
- SBO-154 IND filing

Strategic priorities

Resourcing to ensure smooth operations

- In-licensing of potential opportunities
- Capabilities and resource building





Vodobatinib (SCC-138) for neurodegenerative diseases

Siu-Long Yao

Parkinson's disease epidemiology



PD affects ~7 mn people globally; expected to grow above 14 mn by 2040

• PD population outgrowing overall population (2-4% growth in PD vs. 1% global population growth)

• DMTs can make significant impact to the lives of PD patients by changing the trajectory of disease





Enrollment target met



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Part 1

• Data from interim analysis expected to be available by March 2024

Part 2

- Study initiated in Q4 2021
- ~87% of eligible patients enrolled in Part 2
- Continuing treatment for additional 9 months
- Continues to evaluate patients until May 2025

(19)





No significant cardiac events reported in the patients recruited



- Over 40% patients enrolled from the US
- Grade 3/4 events reported in 6.1% patients
- GI and rash were the most common AEs reported
- No changes in study protocol recommended by DSMB throughout the conduct of the study
 - 6 DSMB reviews conducted







Biomarkers under evaluation

- Target biomarker cohort enrolment 150 total (random assignment)
- Further randomization to placebo, low dose, or high dose Vodobatinib 50 assigned to each arm
- Exploratory samples (CSF, plasma, serum) at baseline, 8 & 40 weeks (EOT)



CSF: Cerebrospinal Fluid IEOT: End of Treatment| DaT-SPECT: Doparnine Transporter Single-photon Emission Computed Tomography | CRKL: CT10 Regulator of Kinase Like | NFkB: Nuclear Factor kappa B NLRP3: Nucleotide-binding domain, Leucine-Fich-containing family, Pyrin domain-containing-3 | MAPK: Mitogen-Activated Protein Kinases | PARIS: Parkin Interacting Substrate | AIMP2: Aminoacyl TRNA Synthetase Complex Interacting Multifunctional Protein 2



Vodobatinib development



Activities running in parallel before EoP2 meeting with FDA



EoP2 meeting with FDA planned in Nov 2024



Opportunities beyond Parkinson's disease

Vodobatinib reduces the intracellular load of potentially toxic proteins in iPSC - induced neurons





Vodobatinib downregulates key proteins associated with development of synucleopathies and tauopathies*

The concept of a-Synuclein strains and how different conformations may explain distinct neurodegenerative disorders. Katja M et.al. Frontiers in Neurology. 2021 *Study conducted at Brigham and Women's Hospital Boston iPSC: induced Pluripotent Stem Cells | PD: Parkinson's Disease | DLB: Dementia with Lewy Bodies | MSA: Multiple System Atrophy | iRBD: idiopathic Rapid eye movement Behavior Disorder |

BC: Pure Autonemic Failure I DMSC: Dimethyl Suffordie I ABL: cellular Abelson kinnese Lamp 1: Lysosoriated membrane protein 1

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Vodobatinib (SC0-088) for chronic myeloid leukemia

Siu-Long Yao

Chronic myeloid leukemia



Use of 2nd and 3rd generation agents increasing



• The prevalence of CML is estimated to grow primarily attributed to prolonged survival and access to TKIs

• The current value market is over US\$ 3.5 bn

Vodobatinib (SCO-088) Phase 1/2 study results sparc

Patients continue to benefit over a long period of time



• Over 1/3rd patients on study drug beyond 3 years

• Median duration on study drug being 32.3 months (range: 0.3 – 73.4 months)



Preclinical data confirms superiority of Vodobatinib over 2nd generation TKI





- Vodobatinib demonstrated better growth inhibition (GI50) over nilotinib in Ba/F3 BCR::ABL1 wildtype (WT) and its resistant mutants *in-vitro*
- Vodobatinib has better antitumor activity over nilotinib in-vivo

Nilotinib administered in mice at doses that give exposures similar to that of clinically approved dose. GI: Growth Inhibition | p.o.: per oral | o.d.: once daily

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Vodobatinib (SCO-088) registration plan alignment with FDA



Vodobatinib being developed under project Frontrunner

- Frontrunner is a program launched to make newer disease modifying therapies in earlier lines of treatment instead of late line setting
- Registration path
 - RP3D determination: Evaluate 2 investigational doses for randomized dose finding (RP3D selection) 174 mg, the proposed RP2D and lower dose of 87 mg acceptable for evaluation for RP3D selection
 - Randomized control study in earlier line of treatment: Phase 3 study in patients failing >1 TKI may be acceptable for approval
 - Clinical spend expected to increase; due to cost of comparator drug





Vibozilimod for autoimmune disorders

Siu-Long Yao

Vibozilimod (SCD-044)



Targeting fragmented dermatology market

- Highly selective S1PR1 agonist
- Leading agent in the class under development for Psoriasis and Atopic Dermatitis

| Psoriasis | Atopic Dermatitie | | | | |
|--|---|--|--|--|--|
| US Prevalence ~ 8 mn | O US prevalence ~ 18 mn | | | | |
| Dominated by biologics (injectables), limited oral agents being developed for moderate to severe disease | Systemic therapy primarily for moderate to severe disease | | | | |
| Biosimilars yet to take majority share of patients | Usage of JAK inhibitors limited primarily due to black box warning and AE profile | | | | |

Vibozilimod (SCD-044) for Psoriasis



Phase 2 Study design





Vibozilimod (SCD-044) for Atopic Dermatitis



Phase 2 Study design



- Study open in the US, Latin America and Europe
- 18 sites in the US
- 15 sites in Europe
- Primary endpoint Proportion of patients with EASI75 response at week 16



Next steps









SCD-153 for Alopecia Areata

Vikram Ramanathan

Alopecia Areata: Autoimmune disease that causes hair loss



Current treatment approaches are limited



- Estimated 6.7 mn people in the US and 160 mn people worldwide have AA²
- ~ 50% can experience spontaneous hair regrowth within one year, the majority often relapse

- O Current treatments are inadequate
 - Approved JAK1 inhibitors carry black box warning
 - Steroids cause serious AEs: systemic immuno-suppression, muscle wasting, growth retardation in pediatric population



SCD-153



Novel topical drug for treatment of Alopecia Areata



- SCD-153 inhibits inflammatory chemokines, cytokines and decreases pathogenic CD8+ T cells at base of hair follicle; restores immune privilege at hair follicle
- Being topical treatment should reduce systemic exposure thereby reducing systemic side effects



SCD-153 has demonstrated promising preclinical data



Hair growth in mouse Alopecia Areata model



n=7; 85-100% alopecia; >45 weeks age Spontaneous severe C3H/HsJ AA mouse model Data are represented as mean ± SD; two-way ANOVA, followed by Bonterroni's multiple comparisons test (° p < 0.05 vs Vehicle)



- It also showed suppression of inflammatory markers in skin.
- Potential to use in combination with other agents



#n=1 from each group has completed Week 14

ned

SCD-153 inhibited IFN signature gene expression in skin of AA diseased mice





- Significant reduction in IFN signature genes in treated skin at different administered doses was observed.
- Suppressed Inflammatory markers in skin



SCD-153 Phase 1 study



A Randomized, Double-Blind, Vehicle-Controlled, Study to Evaluate the Safety, Tolerability and Pharmacokinetics of topically applied SCD-153 in Healthy Volunteers



- Phase 1 SAD study initiated in India
- 5 dose levels
- Cohorts administered active drug and placebo

Primary Objective:

• To evaluate the safety and local tolerability

Secondary Objective:

 To evaluate the plasma pharmacokinetics of SCD-153 and its metabolite





SCD-153: potential to expand in other epidermal diseases



- IFNγ induces CXCL9, CXCL10 & CXCL11 in vitiligous skin. These chemokines recruit pathogenic CD8+ T cells to the pigment-containing melanocyte in the epidermis
- CD8+ T cells release cytokines that destroy the melanocytes causing depigmentation
- In-vitro studies have shown that SCD-153 inhibits:
 - Expression of CXCL9, 10 and 11 in stimulated human keratinocytes
 - IFNγ secretion from stimulated murine CD8+ T cells





SBO-154 for multiple cancer indications

Nitin Damle

Antibody drug conjugates

Large market expected to reach ~ 25 bn by 2038







US\$ 25.34 Bn Projected ADC market by 2028



Approved ADCs







SBO-154 (Anti-MUC-1 ADC)



Novel antigen & approach to target MUC1-SEA domain, with an opportunity to therapeutically address multiple cancer indications

- Tumor agnostic opportunity in-licensed from Biomodifying LLC
- SEA targeting hypothesis validated
- Preclinical PoC of anti-tumor efficacy of anti-MUC-1-SEA targeted ADC established
- So far, no directly competing agents targeting MUC1-SEA in clinical development





SBO-154: Efficacy demonstrated in large established tumors





SBO-154 causes regression of large established tumors with high MUC-1 SEA expression

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SBO-154 development update



INTERACT meeting granted by FDA

 INTERACT Meeting (Initial Targeted Engagement for Regulatory Advice on CBER CDER Products) Request

 Meeting to seek early advice from the FDA to validate preclinical developmental strategy for the IND-enablement of the product and serve as a prelude to Pre-IND meeting prior to IND filing

• FDA response anticipated in November 2023





Financial summary



| Year | FY19 | FY20 | FY21 | FY22 | FY23 | Q1FY24 |
|-------------------------|-------|-------|-------|-------|-------|--------|
| USD INR | 69.95 | 70.91 | 74.23 | 74.49 | 80.37 | 82.17 |
| INR Cr | | | | | | |
| Total Income | 196 | 87 | 258 | 144 | 250 | 34 |
| Total Expenses | 342 | 399 | 410 | 347 | 472 | 129 |
| Profit/(Loss) after Tax | -145 | -312 | -151 | -203 | -223 | -95 |
| USD Mn | | | | | | |
| Total Income | 28.1 | 12.2 | 34.8 | 19.3 | 31.1 | 4.2 |
| Total Expenses | 48.9 | 56.3 | 55.2 | 46.6 | 58.8 | 15.8 |
| Profit/(Loss) after Tax | -20.8 | -44.1 | -20.4 | -27.3 | -27.7 | -11.6 |



Cash and liquidity



- Out-licensed SEZABY to SPI Inc. in Q4 2022 and received an upfront sum of US\$ 10mn. In addition, SPARC is eligible to receive regulatory and sales linked milestone payments and tiered royalties on sales
- Received ₹703 Cr (US\$ 93mn) in Jan-2023 against the conversion of warrants. With this, the entire proceed of the Preferential Issue (i.e. ₹1,112 Cr) stands received
- Cash and cash equivalent as of September 30, 2023 was ₹363 Cr (US\$ 44mn)
- The Company has
 - (a) Sanctioned bank facilities for ₹175 Cr (US\$ 21mn)
 - (b) Line of credit from the parent company for ₹250 Cr (US\$ 30mn) in place. Utilization of limits as of September 30, 2023 is NIL
- Obtained shareholders' approval in Aug-2023 AGM for raising a sum up to ₹1,800 Cr (US\$ 220mn) by way of fresh issuance





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