Phase 3 DeFi Trial Topline Results Conference Call

May 24, 2022

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Forward-Looking Statements

Note: Unless otherwise indicated, the information presented herein is as of May 2022 and made publicly available on May 24, 2022.

This presentation may contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, relating to our business, operations, and financial conditions, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, our plans to report additional data from the Phase 3 DeFi clinical trial at an upcoming medical conference, the potential for the results of the Phase 3 DeFi clinical trial to support an NDA submission, the timing of our planned NDA submission for nirogacestat, and our plans for seeking regulatory approval for and making nirogacestat available to desmoid tumor patients, if approved, as well as relating to other future conditions. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should” and “could,” and similar expressions or words, identify forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Any forward-looking statements in this presentation are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) the success and timing of our product development activities, including the initiation and completion of SpringWorks’ clinical trials, (ii) the fact that topline or interim data from the Phase 3 DeFi trial or other clinical studies may not be predictive of the final or more detailed results of such study or the results of other ongoing or future studies, (iii) the success and timing of our collaboration partners’ ongoing and planned clinical trials, (iv) the timing of our planned regulatory submissions and interactions, including the NDA for nirogacestat planned for the second half of 2022 and the timing and outcome of decisions made by the U.S. Food and Drug Administration (FDA) and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; (v) whether FDA or other regulatory authorities will require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including nirogacestat and mirdametinib, (vi) our ability to obtain and maintain regulatory approval of any of our product candidates, (vii) our plans to research, discover and develop additional product candidates, (viii) our ability to enter into collaborations for the development of new product candidates, (ix) our ability to establish manufacturing capabilities, and our and our collaboration partners’ abilities to manufacture our product candidates and scale production, (x) our ability to meet any specific milestones set forth herein, and (xi) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks’ business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines.

Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

For further information regarding the risks, uncertainties and other factors that may cause differences between SpringWorks’ expectations and actual results, you should review the “Risk Factors” section(s) of our filings with the Securities and Exchange Commission.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While SpringWorks believes these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Opening Remarks

Saqib Islam

Chief Executive Officer

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THE FULL POTENTIAL
OF TARGETED ONCOLOGY
IS WAITING TO BE UNLOCKED.

LET'S GO

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for patients with devastating cancers.

- Multiple late-stage opportunities with **first approval expected in 2023** and **two marketed products expected by 2025**
- **Deep pipeline of 18 R&D programs** with steady cadence of near-term and long-term value-creating milestones
- **End-to-end resident expertise** spanning therapeutic identification, clinical development, manufacturing and commercialization
- Expanding portfolio with several **pipeline-in-a-product molecules** and **collaborative relationships** to continually unlock new opportunities
- **Durable intellectual property portfolio** and **robust balance sheet** with disciplined approach to capital allocation

Multiple Opportunities for Value Creation Across Three Distinct Oncology Segments

1 Rare Oncology

Two registrational trials with best-in-class potential in areas of high unmet need

- **Nirogacestat**
  Desmoid Tumors
- **Nirogacestat**
  Pediatric Desmoid Tumors
- **Mirdametinib**
  NF1 Plexiform Neurofibromas
- **Mirdametinib**
  Pediatric Low-Grade Gliomas

2 BCMA Combinations in Multiple Myeloma

Advancing nirogacestat as a cornerstone of BCMA combination therapy across four modalities

- **Nirogacestat + BLENREP**
  BCMA ADC
- **Nirogacestat + ALLO-715**
  BCMA Allogeneic CAR-T
- **Nirogacestat + Teclistamab**
  BCMA-CD3 Bispecific
- **Nirogacestat + PBCAR269A**
  BCMA Allogeneic CAR-T
- **Nirogacestat + Elranatamab**
  BCMA-CD3 Bispecific
- **Nirogacestat + SEA-BCMA**
  BCMA Monoclonal Antibody
- **Nirogacestat + ABBV-383**
  BCMA-CD3 Bispecific
- **Nirogacestat + REGN5458**
  BCMA-CD3 Bispecific

3 Biomarker-Defined Metastatic Solid Tumors

Precision oncology approach to highly prevalent cancers with near-term clinical POC readouts

- **Mirdametinib + Lifirafenib**
  RAS/RAF Mutant Solid Tumors
- **Mirdametinib + Fulvestrant**
  ER+ Metastatic Breast Cancer
- **Mirdametinib**
  MEK 1/2 Mutant Solid Tumors
- **BGB-3245**
  RAF Mutant Solid Tumors
- **TEAD Inhibitor**
  Hippo Mutant Tumors
- **EGFR Inhibitor**
  EGFR Mutant Tumors

Nirogacestat: First-in-Class Gamma Secretase Inhibitor Being Evaluated Across Multiple Indications

- Nirogacestat is an investigational oral, selective gamma secretase inhibitor with over 10 years of clinical experience
- Fast Track and Breakthrough Therapy Designations received from FDA and Orphan Drug Designation received from both FDA and European Commission[1]
- Achieved statistical significance on primary and all key secondary endpoints in Phase 3 DeFi trial in adult patients with progressing desmoid tumors
- Potential to become cornerstone of BCMA combination therapy in multiple myeloma with eight current collaborations representing all major modalities

Anticipated NDA Filing in Desmoid Tumors:	**2H 2022**
Clinical Trials Ongoing or On Track for 2022 Initiation:	**11**
BCMA Collaborations:	**8**
US Composition of Matter and Method of Use patent protection:	**2039**

(1) Orphan Drug, Fast Track and Breakthrough Therapy Designations received from FDA for desmoid tumors and Orphan Drug Designation received from European Commission for soft tissue sarcoma.

Phase 3 DeFi Trial Topline Results

L. Mary Smith, Ph.D.

Chief Development Officer

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Dana
Desmoid tumor patient

Desmoid Tumors Are Highly Morbid Soft Tissue Tumors That Are Often Poorly Responsive to Surgical Interventions and Off-Label Therapies

Disease Characteristics

- Desmoid tumors can lead to significant morbidities and manifest throughout the body including in the extremities, the head and neck region, intra-abdominally and the thoracic region; the disease can be multifocal with patients potentially having multiple lesions
- Desmoid tumors can lead to severe negative outcomes including lesion ulceration, organ dysfunction, amputation, long-lasting pain due to nerve compression or tumor pressure, disfigurement and in rare cases when vital organs are impacted, they can be life-threatening[1]
- Recurrence can be up to 70% post-surgery, making the approach much less favored in clinical practice today[1,2]; follow-on treatments include chemo, radiation and off-label TKIs

- 1,000-1,650 newly incident patients per year in US[3]
- 5,500-7,000 patients actively receiving treatment in the US in any given year[3]

- No currently approved therapies and limited treatment options
- Off-label systemic therapies are often poorly tolerated with inconsistent efficacy

Sources: (1) Penel et al., *European Journal of Cancer*, 2017; (2) Tsagozis et al., *Annals of Medicine & Surgery*, 2017; (3) Van Broekhoven et al., *Annals of Surgical Oncology,* 2015; Reitamo et al., *J Clin Path,* 1982; SpringWorks market research.

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Phase 3 DeFi Trial Design

PHASE 1 | PHASE 2 | **PHASE 3**

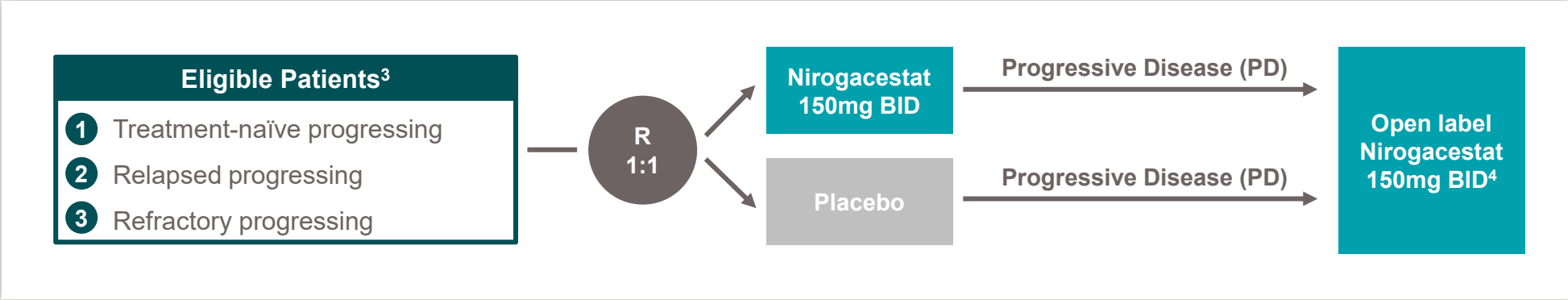
DeFi

Trial Summary

- Global (North America and Europe), randomized (1:1), double-blind, placebo-controlled study
- 142 patients randomized with open label extension available upon radiographic disease progression
- 90% powered to show ~12-month median PFS difference between nirogacestat and placebo[1]

Summary of Endpoints

- Primary Endpoint: Progression-free survival[2]
- Secondary and Exploratory Endpoints: Safety and tolerability, objective response rate (ORR), duration of response, volumetric tumor change assessed by MRI, patient-reported outcomes (PROs)



(1) A total of 51 events will provide 90% power and a 1-sided type 1 error rate of 0.025 (1-side hypothesis) to detect a difference between nirogacestat and placebo, assuming the median PFS is 20 months in the nirogacestat group and 8 months in the placebo group.
(2) PFS is defined as the time from randomization until the date of assessment of radiographic progression as determined using RECIST v1.1, the date of assessment of clinical progression or death by any cause. Radiographic or clinical progression determined by blinded independent central review.
(3) Progression defined ≥20% increase over past 12 months by RECIST v1.1.
(4) Once the end of double-blind phase notification had been issued and the primary PFS analysis had been completed, patients remaining on study that had not achieved a radiographic progression could enroll in the OLE.

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Nirogacestat Achieved Primary and All Key Secondary Endpoints in Phase 3 DeFi Trial

	Hazard Ratio (HR)	P-value
Progression-Free Survival (PFS)	0.29 (95% CI: 0.15, 0.55)	< 0.001

- Results demonstrated a statistically significant improvement for nirogacestat over placebo, with a 71% reduction in risk of disease progression as assed by blinded independent central review (hazard ratio (HR) = 0.29; P < 0.001)
- Statistical significance was achieved on all key secondary endpoints, including objective response rate (ORR) and patient-reported outcomes (PROs)
- Nirogacestat was generally well tolerated with a manageable safety profile
  - The majority of women of child-bearing potential had adverse events consistent with ovarian dysfunction
  - Other adverse events were generally consistent with previously reported data
- Additional data are expected to be presented at an upcoming medical conference in 2H 2022

NDA filing for nirogacestat in desmoid tumors expected 2H 2022

Closing Remarks

Saqib Islam

Chief Executive Officer

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Summary of Today's Announcement

Statistically significant results demonstrated on primary and all key secondary endpoints

Generally well tolerated with a manageable safety profile

Additional data expected to be presented at an upcoming medical conference in 2H 2022

NDA submission expected in 2H 2022

Beyond DeFi, Multiple Value-Driving Data Readouts and Program Updates Anticipated in 2022

Milestone	Expected Timing
Nirogacestat	
Phase 3 DeFi topline readout in desmoid tumors	✓
Long-term data from NCI-Sponsored Phase 2 study in desmoid tumors	ASCO 2022
Announce new monotherapy indication opportunity	R&D Day
Additional DeFi data at medical conference	2H 2022
Planned NDA filing in desmoid tumors	2H 2022
Nirogacestat + BCMA therapies	
Initial clinical data from combo trial with GSK (BLENREP)	ASCO 2022
Additional combo trial initiations and data presentations	2H 2022
Mirdametinib	
Phase 1b/2 initial data readout in pediatric low-grade glioma (pLGG)	2Q 2022
Mirdametinib + Lifirafenib	
Phase 1b/2 initial data readout in RAS/RAF-mutant solid tumors	R&D Day
BGB-3245	
Phase 1 initial data readout in RAF-mutant solid tumors	R&D Day
TEAD inhibitor program	
Preclinical data at AACR	✓
DC nomination	2H 2022
Potential for additional data readouts and updates from other programs ▪ ReNeu trial for mirdametinib in NF1 plexiform neurofibroma (NF1-PN) ▪ Preclinical EGFR inhibitor program	Full year

Thank You

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Q&A

Saqib Islam, Chief Executive Officer
L. Mary Smith, Ph.D., Chief Development Officer
Badreddin Edris, Ph.D., Chief Operating Officer

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