41st Annual J.P. Morgan Healthcare Conference

Saqib Islam, Chief Executive Officer January 9, 2023





Forward-Looking Statements

Note: Unless otherwise indicated, the information presented herein is as of January 2023 and made publicly available on January 9, 2023.

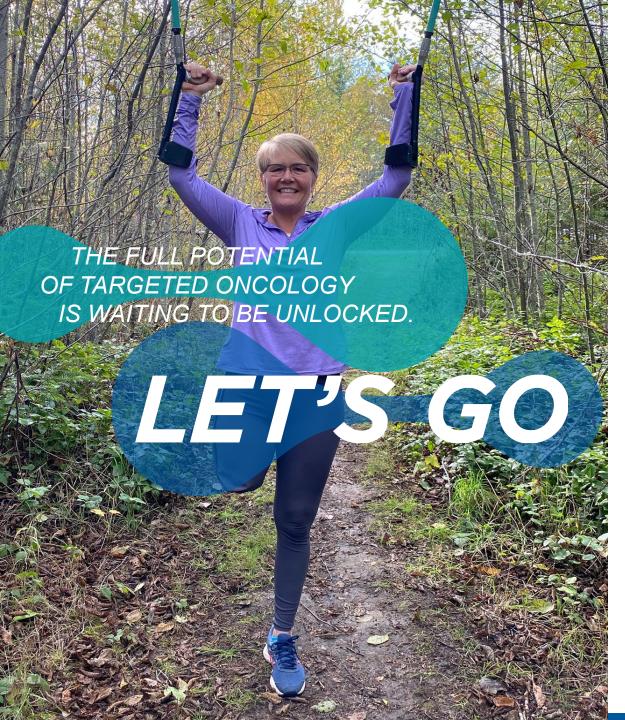
This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, relating to our business, operations, and financial conditions, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, the potential for the results of the Phase 3 DeFi clinical trial to support an NDA submission, the potential for nirogacestat to become an important new treatment for patients with desmoid tumors, our plans for seeking regulatory approval for and making nirogacestat available to desmoid tumor patients, if approved, the potential for the results of the Phase 2b ReNeu clinical trial to support an NDA submission for mirdametinib, the potential for mirdametinib to become an important new treatment for patients with NF1-PN, our plans for seeking regulatory approval for and making mirdametinib available for NF1-PN 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 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 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) the adequacy of our cash position to fund our operations through any time period indicated herein, (xi) our ability to meet any specific milestones set forth herein, and (xii) 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.





SpringWorks Therapeutics Is Transitioning into a Commercial-Stage Targeted Oncology Company in 2023

- Multiple late-stage programs with the opportunity for two approvals by 2025, starting with nirogacestat for desmoid tumors this year
- Diversified pipeline of preclinical and clinical programs focused on solid tumors and hematological malignancies
- Durable IP portfolio with U.S. patent protections extending beyond 2040
- Experienced leadership team with end-to-end expertise spanning drug development and commercialization
- Robust balance sheet with \$650M+ in cash and disciplined capital allocation approach⁽¹⁾



2022 Was a Pivotal Year for SpringWorks

Late-Stage Rare Oncology Portfolio				
Nirogacestat (Gamma Secretase Inhibitor)	 ✓ Presented highly statistically and clinically significant Phase 3 DeFi trial results at ESMO ✓ Submitted NDA for the treatment of adults with desmoid tumors ✓ Initiated Phase 2 trial evaluating nirogacestat in ovarian granulosa cell tumors ✓ Expanded IP portfolio to extend patent protection for nirogacestat into 2042 			
Mirdametinib (MEK Inhibitor)	✓ Conducted successful Type C meeting with FDA to align on the statistical analysis plan for the Phase 2b ReNeu trial and expectations for an NDA submission in NF1-PN			
Emerging Portfolio				
Nirogacestat + BCMA Therapies	 ✓ Expanded development opportunities in earlier lines of multiple myeloma treatment ✓ Clinically validated mechanism of action and synergistic activity across modalities 			
MAPK Portfolio	 ✓ Demonstrated clinical proof-of-concept for BGB-3245 and mirdametinib + lifirafenib ✓ Advanced BGB-3245 into dose expansion cohorts 			
Preclinical Programs	✓ Nominated TEAD inhibitor development candidate (SW-682)			

- ✓ Ended the year with cash runway into 2026
- ✓ Established commercial infrastructure to support first U.S. product launch for nirogacestat in desmoid tumors



2023 Marks Our Expected Transition into a Commercial-Stage Company

Late-Stage Rare Oncology	/ Portfolio
Nirogacestat (Gamma Secretase Inhibitor)	 Secure FDA approval and launch nirogacestat as first FDA-approved therapy for desmoid tumor patients Publish Phase 3 DeFi trial data in a peer-reviewed journal and present additional analyses at upcoming medical meetings Continue enrollment of Phase 2 trial in ovarian granulosa cell tumor patients
Mirdametinib (MEK Inhibitor)	☐ Present topline data from the pediatric and adult cohorts in the Phase 2b ReNeu trial
Emerging Portfolio	
Nirogacestat + BCMA Therapies	 Expand emerging data set with additional clinical data in combination with BCMA-directed therapies Support initiation of additional planned collaboration studies
Nirogacestat +	



Late-Stage Portfolio





Desmoid Tumors Are Highly Morbid Soft Tissue Tumors with No Approved Therapies, Resulting in a High Unmet Need

Disease Overview and Unmet Need

- Desmoid tumors (DT) can arise throughout the body and lead to significant, life-altering morbidities
 - Disease can be multifocal and patients oftentimes present with substantial pain, significant physical limitations,
 and diminished quality-of-life
- Severe negative outcomes from DT include lesion ulceration, organ dysfunction, amputation, longlasting pain, disfigurement and are potentially life-threatening in the event vital organs are impacted⁽¹⁾
- Clinical need is not met by available treatment options
 - No currently approved therapies; off-label systemic treatments include chemotherapy, radiation and TKIs, which
 are often poorly tolerated with inconsistent efficacy
 - Tumor recurrence can be up to 77% following surgery^(2,3)

"...the pain it causes has changed my life. It pushes on my ureters and kidneys and had wrapped itself around some of my muscles. The shooting pains sometimes leave me unable to physically move at times, much less take care of my young children."

Amy, desmoid tumor patient

"My desmoid tumor wrapped around my nerves, veins and artery behind me knee. I've had ten surgeries total, six to remove the tumor and four related to complications, and it keeps growing back."

- DeAnn, desmoid tumor patient



Nirogacestat Phase 3 DeFi Trial Delivered Potentially "Practice-Changing" Data for the Desmoid **Tumor Community**



September 10, 2022

Presidential Symposium I

DeFi: A Phase 3 Trial of Nirogacestat for Progressing Desmoid Tumors (DT)

Bernd Kasper, Ravin Ratan, Thierry Alcindor, Patrick Schöffski, Winette T. van der Graaf, Breelyn A. Wilky, Richard F. Riedel, Allison Lim, L. Mary Smith, Stephanie Moody, Steven Attia, Sant Chawla Gina D'Amato, Noah Federman, Priscilla Merriam, Brian A. Van Tine, Bruno Vincenzi, Shivaani Kummar, Mrinal Gounder, on behalf of the DeFi Study Investigators

September 10, 2022



"...could make y-secretase inhibition the standard of BioWorld care for desmoid tumors...the first randomized controlled trial to demonstrate the standard controlled trial to demonstrate clinical benefit of v-secretase in any indication..." Bernd Kasper, MD, PhD

(University of Heidelberg - Mannheim Cancer Center, Mannheim, Germany)

Medscape

"The results show benefit...with a novel treatment... in patients where treatment options are currently limited...the findings are practice changing" Jean-Yves Blay, MD, PhD (Comprehensive Cancer Centre of Lyon)

OncLive°

"...rapid, sustained, and statistically significant improvements in all primary and secondary efficacy end points..."

Bernd Kasper, MD, PhD (University of Heidelberg - Mannheim Cancer Center, Mannheim, Germany)



MEDPAGE "This improvement [in pain] is probably the most significant observation of this clinical trial..."

> Jean-Yves Blay, MD, PhD (Comprehensive Cancer Centre of Lvon)



Based on the DeFi Trial, We Expect That Nirogacestat's Novel and Differentiated Profile Will Transform the Standard-of-Care for Desmoid Tumor Patients

Progression-Free Survival

Significant PFS improvement versus placebo, with 71% reduction in risk of disease progression (hazard ratio: 0.29, p<0.001)

Tumor Shrinkage

41% ORR, with 7% CR rate and rapid time to response (5.6 months)

Quality of Life

Significant improvements in pain, physical functioning, DT-specific symptoms and overall quality-of-life

Safety

95% of adverse events reported were Grade 1 or 2 (most common: diarrhea, nausea, fatigue); 74% of all ovarian dysfunction events resolved⁽¹⁾

Durability

20.6 months of median time on treatment (ToT) at the time of primary analysis, with majority of nirogacestat patients ongoing, building on 4+ year median ToT in Phase 1 and $2^{(2)}$

Sources: Kasper et al., ESMO, 2022.

Note: CR: complete response; DT: desmoid tumor; ORR: objective response rate

Note: Summary is based on the Phase 3 DeFi trial. Unless otherwise indicated results are as of the primary data cutoff date of April 7, 2022.

⁽¹⁾ Resolution of ovarian disfunction (OD) events was defined by the investigator. Data as of July 20, 2022. 75% of women of childbearing potential who received nirogacestat reported OD. 100% resolution in patients who discontinued treatment; 64% resolution in those remaining on nirogacestat.





DeFi Trial: Primary and All Key Secondary Endpoints Met Both Statistical and Clinical Significance



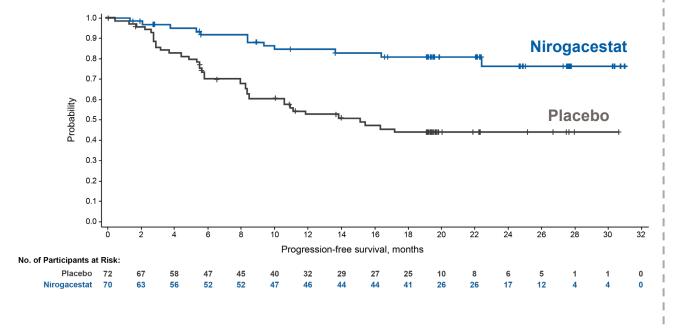
	P-Value	
Primary Endpoint	Progression-free survival	<0.001
Secondary Endpoints	Objective Response Rate	<0.001
	Brief Pain Inventory-Short Form – Average Pain Intensity	<0.001
	GODDESS Desmoid Tumor Symptom Scale – Total Symptom Score	<0.001
	GODDESS Desmoid Tumor Impact Scale – Physical Functioning Impact Score	<0.001
	EORTC QLQ-C30 Physical Functioning	<0.001
	EORTC QLQ-C30 Role Functioning	<0.001
	Global Health Status / Quality of Life	0.007

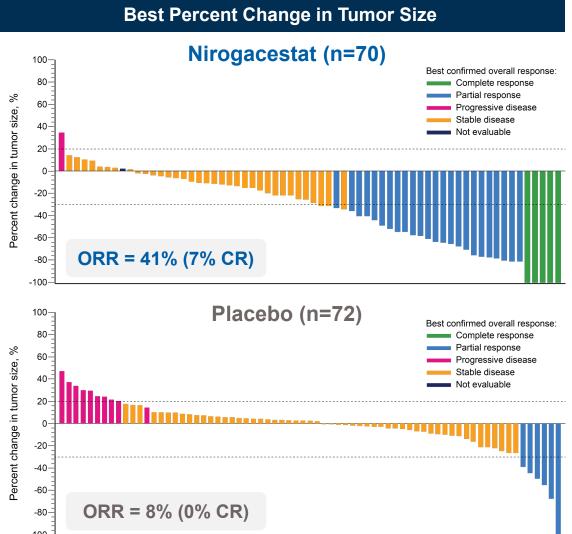


DeFi Trial: 71% Risk Reduction of Disease Progression and 41% Objective Response Rate Underscore Differentiated Efficacy Profile

Progression-Free Survival

	No. of Patients	No. of Events	Median (95% CI)	Hazard ratio (95% CI)
Nirogacestat	70	12	NE (NE, NE)	<i>P</i> <0.001
Placebo	72	37	15.1 (8.4, NE)	0.29 (0.15, 0.55)





Source: Kasper et al., ESMO, 2022. Data as of the time of primary analysis (04/07/22). Gounder at al., CTOS, 2022.

Note: Median follow-up time was 19.2 months for nirogacestat and 10.9 months for placebo.

Note: Best percent change values are averaged between 2 blinded independent reviewers unless a reader was selected for adjudication, in which case only the adjudicated value is presented.

Note: NE: not estimable. Cl: confidence interval; CR: complete response. ORR: objective response rate.



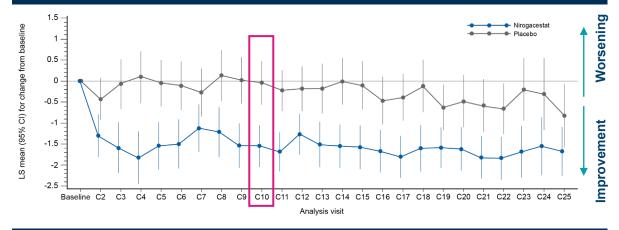
►DeFi

^{*} Patient had a complete resolution of the target lesion but still had documented non-target lesion; therefore, not a complete response.

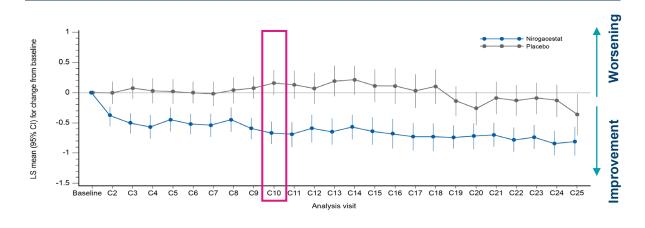
DeFi Trial: Rapid, Early and Sustained Improvements Across Quality-of-Life Measures



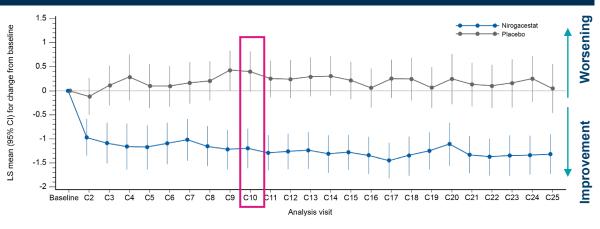
Brief Pain Inventory-Short Form – Average Pain Intensity



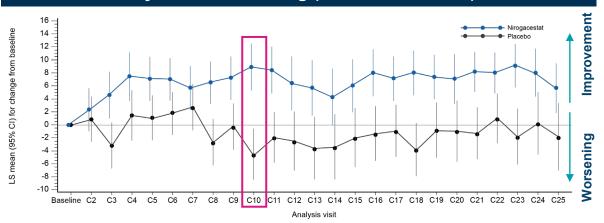
Physical Functioning Impact Score (GODDESS DTIS)



DT-Specific Symptom Severity (GODDESS DTSS)



Physical Functioning (EORTC QLQ-C30)







Significant Opportunity to Benefit Patients with Desmoid Tumors

U.S. Patient Population

~1,000-1,650
new patients
diagnosed annually

■ Incidence of 3 – 5 per million per year⁽¹⁻³⁾

~5,500-7,000 receive active treatment annually

■ ~20 – 25% of total prevalent patients are under active treatment^(3,4)

30,000+
diagnosed prevalent
patients

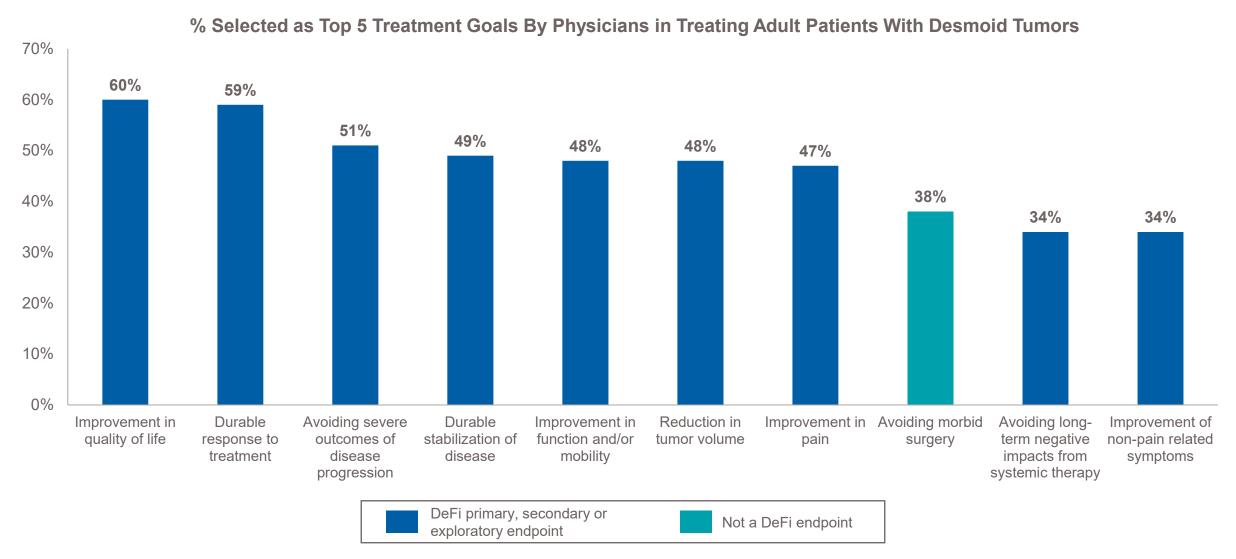
 Meaningful proportion of the diagnosed prevalent population could be addressed with a new treatment option

Key Treatment Dynamics

- Propensity to treat is high over 90% of patients receive active intervention over the course of their disease
- Continued erosion of surgery with shift away from "cut-first" mentality due to high post-surgical recurrence rates up to 77%^(5,6)
- Off-label systemic therapies are often poorly tolerated with inconsistent efficacy
- Utilization of currently available therapies is fragmented due to treatment limitations
- Increased awareness leading to more
 "inactive" patients seeking treatment

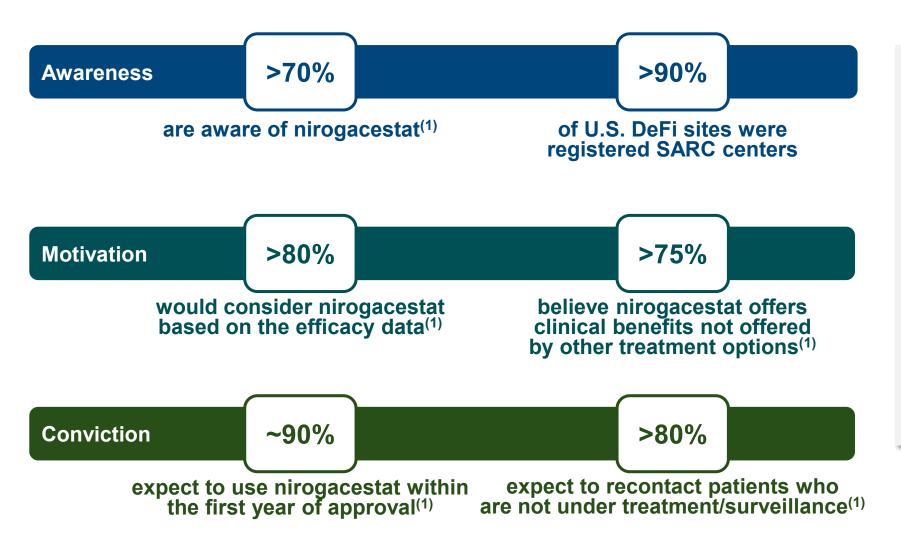


DeFi Endpoints are Well Aligned to the Most Important Desmoid Tumor Treatment Goals





Physician Feedback Supports Nirogacestat's Opportunity to Become the Standard of Care Systemic Therapy for Desmoid Tumors Following Approval



- ✓ Strong feedback from physicians and patient advocacy organizations
- ✓ High physician willingness to switch patients receiving TKIs or chemo
- ✓ Many physicians believe nirogacestat's risk/benefit profile is superior to surgery

Nirogacestat Is Well Positioned to Meaningfully Impact the Desmoid Tumor Community

Differentiated Data

Potentially **practice-changing profile** based on antitumor activity, improvements in QoL outcomes, and manageable tolerability that has been suitable for extended treatment durations

Patient Demand

Significant addressable patient population with substantial unmet need due to high recurrence rates and no approved systemic treatment options

Physician Awareness and Motivation

Awareness of nirogacestat is high and large proportion of physicians surveyed indicate that they expect to rapidly adopt nirogacestat if approved

Regulatory Path

NDA submission completed in 4Q22 under FDA's Real Time Oncology Review; potential to be **first FDA-approved therapy** in desmoid tumors

Commercial Execution

Launch activities rapidly advancing to ensure successful preparation of market, organization and brand



A Substantial Unmet Need Remains for a Best-in-Class Therapy for NF1-PN Patients



Disease Overview and Unmet Need

- NF1-associated plexiform neurofibromas (NF1-PN) patients present with significant morbidities
- NF1-PN grow along nerves and can lead to extreme pain and disfigurement

MEANINGFUL ADDRESSABLE POPULATION

- ~100,000 patients living with NF1 in the U.S.⁽¹⁾
- NF1 pts have a ~30-50% lifetime risk of developing NF1-PN⁽²⁾

TREATMENT PARADIGM

- Surgical resection is difficult due to the infiltrative tumor growth pattern along nerves and is rarely performed^(3,4)
- MEK inhibitors are a validated treatment option, but currently approved agent has uptake and compliance barriers
 - Limitations include challenging dosing requirements, administration, label restrictions and AEs^(4,5)
 - 50%+ of patients discontinued treatment within 1 year⁽⁶⁾



Mirdametinib for NF1-PN: ReNeu Trial On Track for Topline Readout in 2H 2023



Phase 2b ReNeu Trial Summary

■ Phase 2b open-label; n = 114 patients in 2 cohorts (pediatric and adults) across ~50 U.S. sites

TRIAL DESIGN

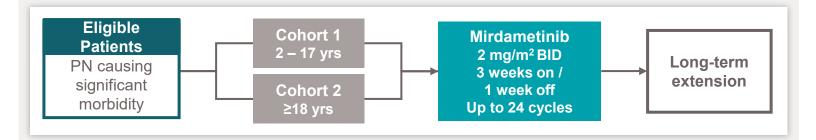
- 2 mg/m² BID dosing with intermittent course (4-week cycles of 3 weeks on, 1 week off) for up to 24 cycles; maximum dose of 4 mg BID
- Pediatric formulation (dispersible tablet) introduced in 2H 2020

PRIMARY ENDPOINT

 Objective response rate (≥20% reduction in tumor volume) determined by BICR

SECONDARY & EXPLORATORY ENDPOINTS

 Safety and tolerability, duration of response, QoL and physical functioning assessments



Opportunities for Differentiation

- With the ReNeu trial, mirdametinib has the opportunity to address the substantial unmet needs that remain for NF1-PN patients:
 - √ Therapeutic option for broader age spectrum
 - ✓ Enhanced efficacy
 - ✓ Improved safety and tolerability
 - ✓ More convenient therapy to drive compliance (lack of food effect, limited drug-drug interactions)
 - ✓ Differentiated product formulation for pediatric population



Mirdametinib for NF1-PN: ReNeu Trial On Track for Topline Readout in 2H 2023





Achieved full enrollment (2H 2021)



FDA Type C Meeting: Received agreement on proposed statistical analysis plan and guidance on NDA submission expectations (4Q 2022)



Planned disclosure of topline data (2H 2023)



Anticipated NDA submission (1H 2024)



Ovarian Granulosa Cell Tumors (OvGCT) Represent a Meaningful New Expansion Opportunity for Nirogacestat Monotherapy

Disease Overview

- OvGCT accounts for ~5% of all ovarian cancers⁽¹⁾
- >97% of OvGCT are driven by activating mutations in FOXL2, which have been shown to be sensitive to Notch inhibition^(2,3)

MEANINGFUL ADDRESSABLE POPULATION

- Median diagnosis age of 50 years
- Estimated US incidence: 1,500-2,000 per year Significant prevalent population: ~10,000-15,000^(4,5)

NO APPROVED TREATMENTS

- Early-stage disease managed with surgery; however, ~40% of patients experience post-surgical recurrence⁽¹⁾
- No currently approved therapies; limited effective treatment options in recurrent setting

Single-arm open label study, enrolling ~40 patients with recurrent OvGCT with ≥ one line of prior systemic therapy TRIAL DESIGN Dose: Nirogacestat 150mg BID PI: Panagiotis Konstantinopoulos, MD, PhD (Dana-Farber Cancer Institute) IND cleared in December 2021

PRIMARY ENDPOINT

 Objective response rate by RECIST 1.1 (response assessed every 2 months)

SECONDARY ENDPOINTS

 Progression-free survival, overall survival, duration of response, safety and tolerability, and quality of life assessments

First patient dosed in Phase 2 trial in September 2022

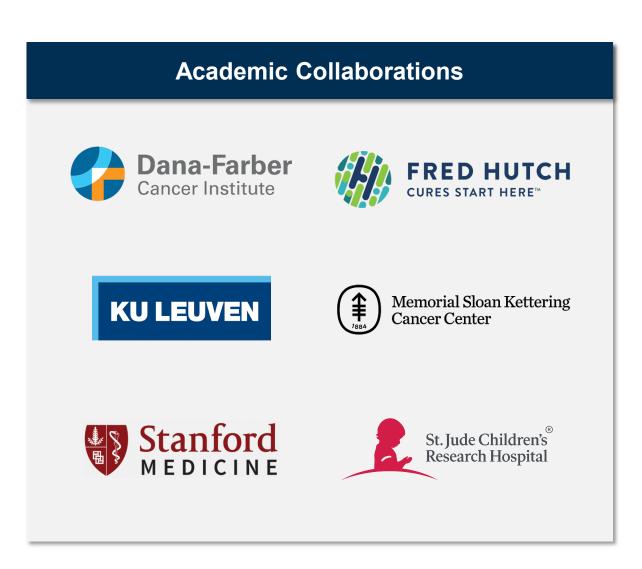


Emerging Portfolio



A Broad Network of Partnerships and Collaborations Have Expanded Our Scientific Insights and Clinical Opportunities in a Capital-Efficient Manner

Industry Collaborations abbyie **BeiGene** GSK Janssen PHARMACEUTICAL COMPANIES OF GOLUMON ASSENCES. **Pfizer** Mapkure **Seagen®** REGENERON





Broad Emerging Pipeline Continues to Advance and Offers Substantial Upside Potential

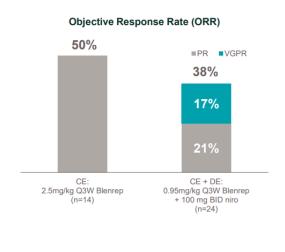
Multiple Myelema Niregeoeste	t + PCMA Directed Therepy Combinetions	2023 Milestones
+ Belantamab mafodotin (ADC) + Teclistamab (Bispecific) + Elranatamab (Bispecific) + SEA-BCMA (mAb) + ABBV-383 (Bispecific) + Linvoseltamab (Bispecific)	Phase 1 ongoing Phase 1 b/2 ongoing (Phase 1 planned (Phase 1b planned (Phase 1b planned (Phase 1b planned)	 Highlight additional clinical data and support initiation of trials across modalities
MAPK-Mutant Solid Tumors —		
Pediatric Low-Grade Gliomas MAPK Mutant Solid Tumors ER+ Metastatic Breast Cancer MEK 1/2 Mutant Solid Tumors MAPK Mutant Solid Tumors MAPK Mutant Solid Tumors	Mirda + Lifirafenib: Ph 1/2 ongoing Mirda + Fulvestrant: Ph 1b/2a ongoing Mirdametinib: Phase 1b/2a ongoing BGB-3245: Phase 1 ongoing Mirda + BGB-3245: Ph 1/2a ongoing	 Present data from BGB-3245 and mirdametinib + lifirafenib at a medical conference Dose first patient in mirdametinib + BGB-3245 study
Preclinical Programs ————		
Hippo Mutant Tumors	SW-682: IND-enabling	■ File IND for SW-682
EGFR Mutant Tumors	Discovery	



Data Releases in 2022 Support Progression of Emerging Portfolio

Nirogacestat + Belamaf Phase 1/2

- Interim data presented at ASCO
- Comparable efficacy with reduction in ocular AEs observed with nirogacestat + low-dose belamaf vs. monotherapy belamaf
- Future data presentations planned and additional studies underway



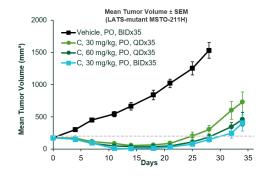
BGB-3245 Phase 1

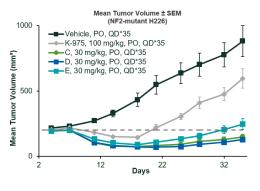
- Presented interim data cut from dose escalation at R&D Day from 25 evaluable patients
- 6 objective responses observed in patients including those who failed MEK-RAF and/or IO
- Emerging safety profile manageable and consistent with MAPK pathway inhibitors
- Advanced into Phase 1b expansion cohorts in 4Q22



SW-682 (TEAD Inhibitor)

 Development candidate nominated in 4Q22 and IND-enabling studies underway









Building Blocks for Substantial Value Creation in 2023 and Beyond



Highly clinically and statistically significant data support practice-changing, first-in-class commercial opportunity for nirogacestat in desmoid tumors



Mirdametinib topline readout in NF1-PN provides opportunity to support competitive product profile across full age spectrum



Substantial upside opportunity across wholly-owned and partnered programs, potentially yielding value-creating and thesis-validating data



Robust IP portfolio providing durable protection and preserving long-term value of lead assets



Capital efficient operating model with strong financial position that supports activities into 2026



