UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 10, 2022

SPRINGWORKS THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39044**	**83-4066827**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

100 Washington Blvd
Stamford, CT 06902
(Address of principal executive offices, including zip code)

(203) 883-9490
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	SWTX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On June 10, 2022, SpringWorks Therapeutics, Inc. ("SpringWorks" or the "Company") hosted a virtual research and development day (the "R&D Day"). The program included presentations by members of the SpringWorks' executive leadership team as well as external thought leaders in SpringWorks' core development areas. A copy of the Company's presentation materials for the R&D Day is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	R&D Day Presentation by SpringWorks Therapeutics, Inc. on June 10, 2022.
104	Cover page interactive data file (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SpringWorks Therapeutics, Inc.

Date: June 10, 2022

By: /s/ Francis I. Perier, Jr.
Francis I. Perier, Jr.
Chief Financial Officer

Exhibit 99.1

SpringWorks R&D Day

June 10, 2022

SpringWorks THERAPEUTICS

Forward-Looking Statements

Note: Unless otherwise indicated, the information presented herein is as of June 2022 and made publicly available on June 10, 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.

SpringWorks Leadership Team and External Speakers Participating Today

SpringWorks Participants

Saqib Islam
Chief Executive Officer

Badreddin Edris, PhD
Chief Operating Officer

L. Mary Smith, PhD
Chief Development Officer

Bhavesh Ashar
Chief Commercial Officer

Mike Burgess, MBChB, PhD
Head of R&D

Jim Cassidy, MD, PhD
Chief Medical Officer

External Key Opinion Leaders

Breelyn Wilky, MD
Director of Sarcoma Medical Oncology, Deputy Associate Director for Clinical Research
University of Colorado, Denver

Neal Rosen, MD, PhD
Director, Center for Mechanism-Based Therapy, Enid A. Haupt Chair in Medical Oncology
Memorial Sloan Kettering Cancer Center, New York

Agenda

Program	Session	Presenter
	Introduction and Business Overview	Saqib Islam Badreddin Edris, PhD
Nirogacestat	KOL Presentation: Unmet Need in Desmoid Tumors	Bree Wilky, MD (CU Denver)
	Clinical Experience in Desmoid Tumors	Mary Smith, PhD
	Desmoid Tumor Commercial Opportunity	Bhavesh Ashar
	Additional Expansion Opportunity	Badreddin Edris, PhD
	BCMA Therapy Combination Development	Mike Burgess, MBChB, PhD
	Program Break	
MAPK Pathway	Mirdametinib: NF1-PN	Mary Smith, PhD
	Mirdametinib: Additional Expansion Opportunities	Jim Cassidy, MD, PhD
	Mirdametinib + Lifirafenib: Combination Development	Jim Cassidy, MD, PhD
	KOL Presentation: Introduction to BGB-3245	Neal Rosen, MD, PhD (MSKCC)
	BGB-3245: Initial Clinical Data and Program Update	Jim Cassidy, MD, PhD
Preclinical Pipeline	TEAD and EGFR Inhibitor Program Overview	Mike Burgess, MBChB, PhD
	Closing Remarks Q&A	Saqib Islam

Introduction

Saqib Islam, *Chief Executive Officer*
Badreddin Edris, PhD, *Chief Operating Officer*

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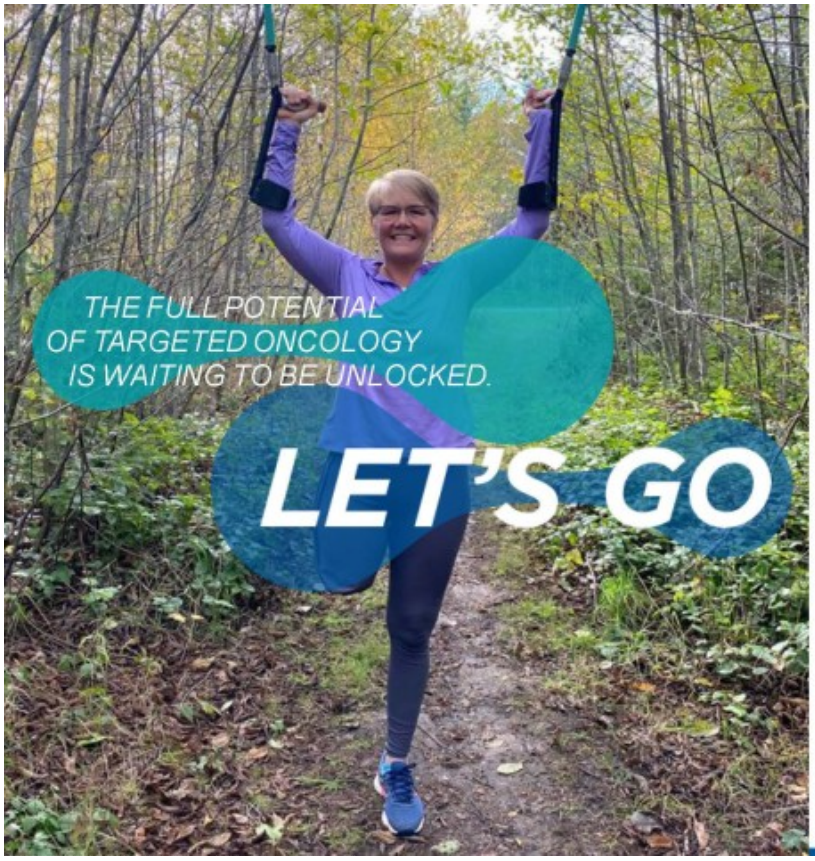

SpringWorks' Efforts Over the Past 5 Years Have Led To…

2022	First NDA filing on track for later this year
2	Marketed products by 2025 with potential to serve patients across 4 indications
$381M	Runway into 2024[1]

…with the singular goal of making a profound impact on the lives of people living with devastating cancers

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(1) Cash, cash equivalents and investments as of March 31, 2022.

Executive Leadership Team: Demonstrated Track Record of Advancing and Commercializing Transformative Oncology Therapies

Saqib Islam
Chief Executive Officer

Badreddin Edris, PhD
Chief Operating Officer

Mike Burgess, MBChB, PhD
Head of R&D

Jim Cassidy, MD, PhD
Chief Medical Officer

L. Mary Smith, PhD
Chief Development Officer

Frank Perier, Jr.
Chief Financial Officer

Bhavesh Ashar
Chief Commercial Officer

Daniel Pichl
Chief People Officer

Herschel Weinstein, JD
General Counsel

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Repeatable and Sustainable Business Model Has Driven Rapid Portfolio Expansion in Areas of Significant Unmet Need

1 IDENTIFY

- Partner of choice for leading academic and industry asset originators
- Versatile and validated molecules with pipeline-in-a-product potential
- Fit-for-purpose business development

2 DEVELOP

- Patient-centric clinical development
- Translational insights guiding biomarker-driven development pathways
- Strong execution on clinical development and regulatory strategy

3 EXPAND

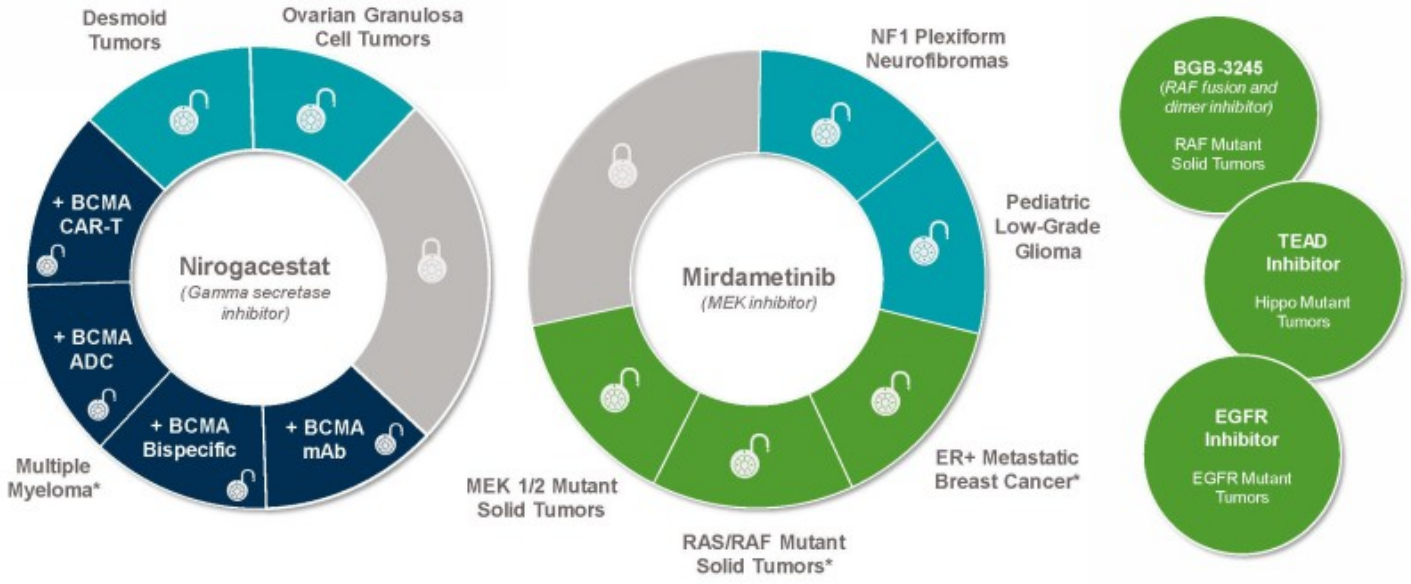
- Opportunity expansion via monotherapy and combination approaches
- Ideation and execution via academic and industry collaborators

4 DELIVER

- Fully-integrated commercial organization
- High-touch relationships with providers and payers
- Emphasis on patient support

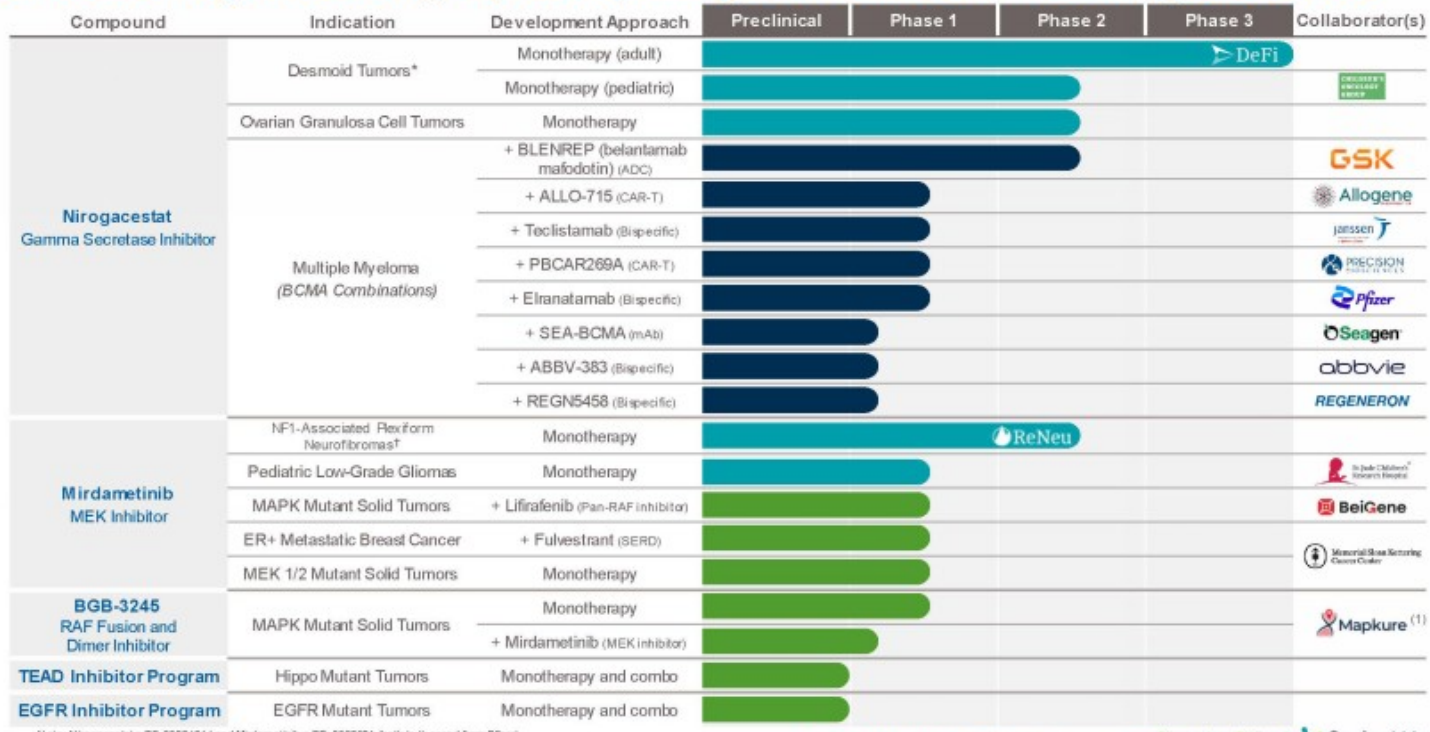
Continued emphasis on strategic capital allocation, operating efficiency, and fit-for-purpose partnerships has grown portfolio from 2 to 19 active R&D programs in under 5 years

Unlocking the Full Potential of Every Molecule



Note: * Being developed as a combination therapy.

Diversified Targeted Oncology Pipeline Spanning Solid Tumors and Hematological Cancers



Note: Nirogacestat = PF-03084014 and Mirdametinib = PD-0325901 (both in-licensed from Pfizer).
* Received Orphan Drug, Fast Track and Breakthrough Therapy Designations. † Received Orphan Drug and Fast Track Designations.
(1) Being developed by MapKure, LLC, jointly owned by SpringWorks and BeiGene.

On the Path to Multiple Revenue Generating Opportunities by 2025

2019

- First patients dosed in DeFi and ReNeu trials
- First BCMA collaboration signed with GSK
- 5 total programs in development
- Nasdaq IPO

2022

- Positive topline results from DeFi trial in desmoid tumors
- First NDA submission expected
- Clinical PoC demonstrated in BCMA combinations
- 8 BCMA industry collaborations
- 19 total programs in development

2025 Plan

- Establish nirogacestat as the standard of care in desmoid tumors
- Serve patients with 2 approved products in up to 4 different indications
- Advance mature portfolio of late-stage clinical programs
- Continue disciplined capital allocation across earlier-stage programs and business development opportunities

Today's Highlights

Clinical Data Across Our Three Oncology Segments	**Nirogacestat:** ▪ Phase 3 DeFi topline results in desmoid tumors **Nirogacestat + BCMA therapies:** ▪ Initial clinical data from combo trial with GSK (low-dose BLENREP) **Biomarker-defined solid tumors:** ▪ Phase 1b/2 initial data readout from MEK/RAF combo trial in RAS/RAF-mutant solid tumors ▪ Phase 1 initial data readout from BGB-3245 program in RAS/RAF-mutant solid tumors
Strategic Priorities to Drive Our Growth	▪ **Launch** preparation to serve patients with desmoid tumors in the U.S. beginning in 2023 ▪ **Expand** opportunity for nirogacestat into additional indication ▪ **Continue** development of mirdametinib both as a monotherapy and combination therapy ▪ **Advance** early-stage pipeline ▪ **Continue** disciplined capital allocation across R&D and BD

OUR COMMITMENT

IS TO MAKE A PROFOUND IMPACT FOR PEOPLE SUFFERING FROM RARE DISEASES AND CANCER

Nirogacestat

SpringWorks THERAPEUTICS

Nirogacestat: A Potentially Best-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.

Nirogacestat: Clinical Experience in Desmoid Tumors

L. Mary Smith, PhD, *Chief Development Officer*

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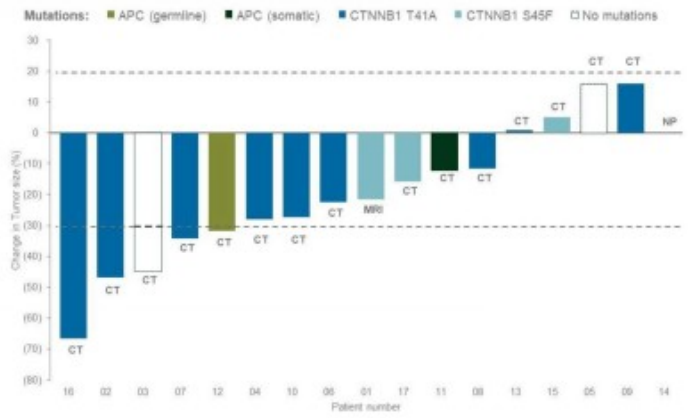
Encouraging Phase 2 Data in Progressing Desmoid Tumors Demonstrated at the Time of 2017 Publication

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

Clinical Responses by RECIST v1.1



- mPFS: Not reached by the time of publication in 2017 due to lack of tumor progression events
  - At time of enrollment, all patients had progressing tumors
  - Patients failed a median of 4 prior lines (1-9) of systemic therapy(1)
  - Objective response rate (ORR) = 29.4% (5/17) with no progressive disease

Note: Per RECIST 1.1, 17 patients were evaluable. One treatment cycle = 150 mg BID continuously for 21 days. Patient #1 had a missing baseline measurement (but had MRI). Patient #14 was not evaluable per protocol, withdrew from study after cycle 1 due to travel requirements.

Source: Kummar et al., *Journal of Clinical Oncology*, 2017.

(1) 71% had received chemotherapy, 65% NSAIDs, and 59% TKIs; 4/5 partial responses had previously failed imatinib or sorafenib.

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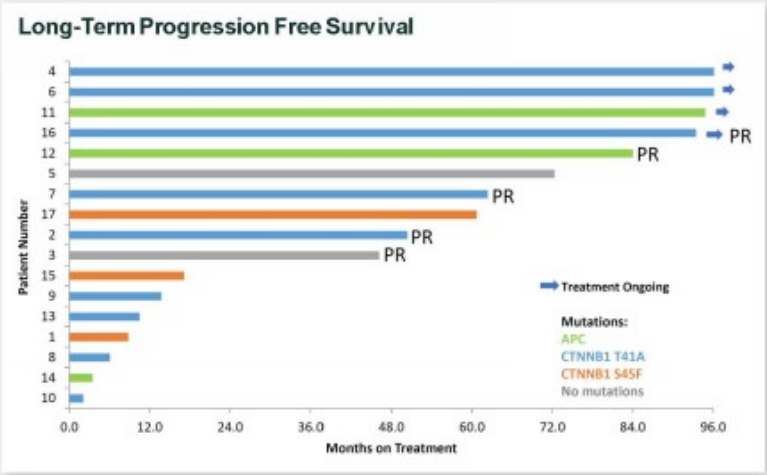
With Maturation of Trial, 2022 Data Cut Demonstrated 4.4 Years of Median Time on Treatment

PHASE 1 | PHASE 2 | PHASE 3



- Among 17 treated patients, median time on treatment 4.4 years (range: 0.17 – 7.99 years)
- 4 patients remain on study after >7 years
- ORR = 29% (5/17) with no progressive disease maintained with long-term follow-up
- Nirogacestat was well tolerated
  - Most commonly (>50%) reported treatment-related AEs included diarrhea, fatigue, nausea, AST increase, lymphocyte decrease, hypophosphatemia, and rash (maculopapular)

Source: O'Sullivan Coyne et al., ASCO, 2022.

Phase 3 DeFi Trial Was Designed to Robustly Demonstrate Clinical Benefit of Nirogacestat

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

DeFi

	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

Note: Topline data from Phase 3 DeFi trial were announced 05/24/22.

Putting Ovarian Dysfunction Into Context

What is ovarian dysfunction?

- Ovarian dysfunction is a constellation of MedDRA preferred terms and includes:
  - Premature menopause[1]
  - Menopause
  - Ovarian failure
  - Amenorrhea

How is ovarian dysfunction being evaluated in the DeFi trial?

- DeFi data analysis for the affected participants will include (but is not limited to):
  - Baseline demographics
  - Prior therapies
  - Potential for resolution
  - Time to onset and duration of events
  - Concomitant medications
  - Dose modifications
  - Hormone levels

Is reproductive toxicity a concern for other desmoid tumor treatments?

- Other therapeutic options for the treatment of desmoid tumors have the potential to impact ovarian function and/or embryo-fetal health, including:
  - Chemotherapy
  - Tyrosine kinase inhibitors
  - Radiation
  - Hormone blockers

Note: MedDRA = Medical Dictionary for Regulatory Activities.
(1) A disorder characterized by premature ovarian failure. Symptoms may include hot flashes, night sweats, mood swings, and a decrease in sex drive. Laboratory findings include elevated luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

Next Steps for the DeFi Program

Detailed study results expected to be presented at a medical conference and published in a peer-reviewed journal in 2H 2022

FDA NDA filing is projected for 2H 2022

- Nirogacestat currently has Orphan Drug, Fast Track, and Breakthrough Therapy Designations
- FDA acknowledged that the nirogacestat NDA can be submitted under the Real-Time Oncology Review (RTOR) program
  - RTOR is an initiative of the FDA's Oncology Center of Excellence that aims to provide a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible
  - Under the RTOR program, the FDA has access to clinical trial data before the information is formally submitted to the agency

Nirogacestat: Desmoid Tumor Commercial Opportunity

Bhavesh Ashar, *Chief Commercial Officer*

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We Are Eager to Serve the Desmoid Tumor Community

Real-World Perspectives Highlight the Significant Unmet Need

"I do these surgeries but I worry, 'Did I get it all?' There are all kinds of risks with surgeries. There is loss of function, loss of mobility, and there can be potential amputation."
– Surgical oncologist (sarcoma specialist)

"I have done 3 amputations in the last 2 years. I would argue that these are not benign tumors!"
– Surgical oncologist (sarcoma specialist)

"The most challenging aspect of my journey is not being able to fix it. There is no solution or resolution to this, and the possible treatments are all worse than the actual symptoms for now. I just have to live with it; It's a weakness in my body that I cannot strengthen, control or overcome. That is, by far, the hardest thing to accept." What if it returns?"
– Desmoid tumor patient

"I shouldn't have agreed to surgery – I should have asked [my physician] to educate himself a bit more or to please refer me to someone that understood desmoid tumors better."
– Desmoid tumor patient

"This is a slow, long-term process. These patients are frustrated because there is no end; no well-defined treatment options. There is no resolution of any kind and they do not know what the future holds."
– Medical oncologist (community)

"This tumor is aggressive. I have seen these start in the toes and then recur in the ankle. After some time, it recurred in the calf and later in the knee. The next recurrence was in the upper thigh and finally, it showed up in the groin area."
– Radiation oncologist

"My doctor suggested we start with a targeted chemo first. There were so many side effects from this drug. I got so overwhelmed I told my oncologist I needed to stop, that my body was falling apart."
– Desmoid tumor patient

"I am not able to physically move in my core area. Because of the scar tissue I am having issues with my bowel and food digestion. It has caused a few painful trips to the ER and hospital stays. The surgical area and scars are not nice to look at. The fear of 'what if?' lingers in the back of my mind. What if more problems happen? What if it returns?"
– Desmoid tumor patient

Desmoid tumors are anything but benign – their morbidities are "malignant"

Source: SWTX Qualitative Research with HCPs and patients.

Building Blocks to Support a Substantial Market Opportunity

Large prevalent population due to high recurrence rates

1,000 to 1,650 incident patients annually

Up to 77% post-surgical recurrence
reported in the literature and confirmed in real-world data sets[1]

Estimated prevalence 3-7x incidence[2]
in a nationwide Danish epidemiology study

5,500 to 7,000 US patients treated annually

High degree of physician awareness and engagement

>70% of oncologists are aware of nirogacestat[3]
in a survey of 100 US oncologists treating patients with desmoid tumors

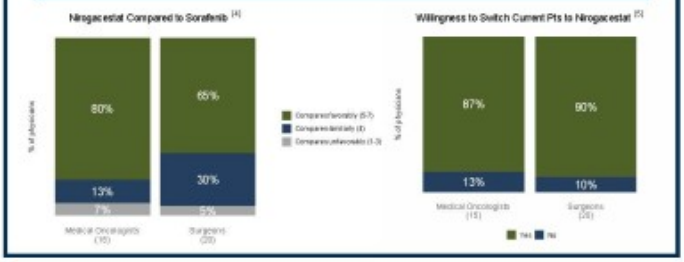
More than 90% of U.S. DeFi sites were registered SARC centers

~65% were NCCN centers

Potential to be first and best in category

- ✓ Rigorously designed Phase 3 (progressing population, BICR)
- ✓ Statistically significant improvement in PFS (HR = 0.29; P < 0.001)
- ✓ Statistical significance on all key secondary endpoints, including ORR and PROs
- ✓ Generally well-tolerated with a manageable safety profile
- ✓ Evidence of long treatment durations in Phase 1 and Phase 2 trials with maturing Phase 3 data

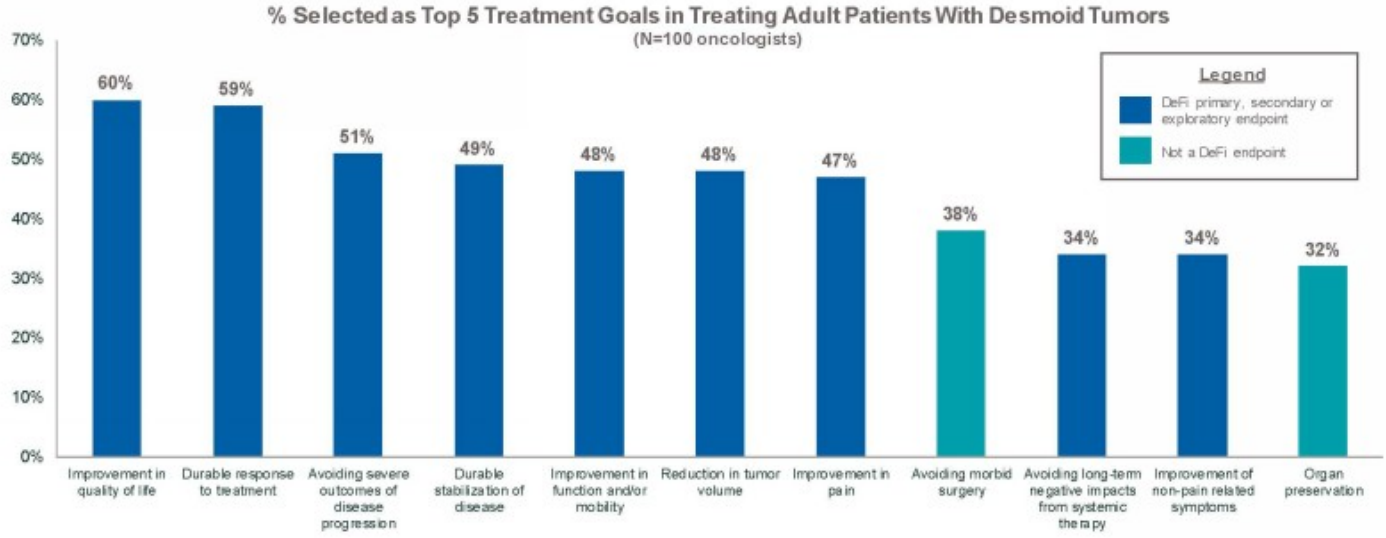
Substantial enthusiasm for nirogacestat profile



(1) Skubitz et al., *Mayo Clin Proc*, 2017; Easter DW, Halasz NA, *Ann Surg*, 1989.
(2) White et al., *DTRF Research Workshop*, 2021. Given that desmoid tumor patients are predominantly an otherwise young and healthy population, annual prevalence was estimated as the number of newly incident desmoid tumor patients plus desmoid tumor patients from the Danish Sarcoma Database who had contact at a hospital in each calendar year divided by total population size of Denmark as of the end of that same calendar year. Prevalence-to-incidence ratio range from 2013 to 2016.
(3) SWTX Primary Research, 2Q22; aided awareness.
(4) Physicians were shown blinded profiles, including one commensurate with the efficacy and tolerability achieved in DeFi. Physicians were also shown sorafenib results from Gounder et al., *NEJM*, 2018, and asked how the Drug A profile compared.
(5) "If drug A were currently available, how many of the [X] desmoid patients you currently treat or monitor would you recommend transitioning from their therapies or monitoring regimen to drug A?" "Yes" includes all physicians with >0 patients.

SpringWorks Therapeutics

Desmoid Tumor Physician Treatment Goals are Driven by Efficacy, Durability and Patient QoL



DeFi endpoints are well aligned to the most important desmoid tumor treatment goals

Source: SWTX Primary Research, 2Q22, N=100 Oncologists.

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Existing Off-label Systemic Therapy Options Have Significant Limitations

Therapy	FDA Approval Status for DT	Phase 3 Evidence	Statistically Significant Improvement in PFS (Primary Endpoint)	Statistically Significant Improvement in ORR (Secondary Endpoint)	Statistically Significant Improvement in PROs/QoL (Secondary Endpoint)	Female Reproductive Toxicity considerations
Nirogacestat (completed Phase 3)	NDA filing planned 2H22 Accepted under RTOR	✓ Company-sponsored (N=142) 100% of patients progressing at enrollment per inclusion criteria, response and progression assessed by BICR	✓	✓	✓	Yes
Sorafenib[1]	✗	✓ Investigator-sponsored (N=87) 38% of patients entering the study had a progressing desmoid tumor(s)	✓	✗	✗	Yes
Imatinib[2]	✗	✗	NA	NA	NA	Yes
Pazopanib[3]	✗	✗	NA	NA	NA	Yes
Sunitinib[4]	✗	✗	NA	NA	NA	Yes
Chemotherapy[5]	✗	✗	NA	NA	NA	Yes

Lack of systemic therapy with strong efficacy, improved quality of life and manageable safety profile has led to a fragmented treatment landscape; nirogacestat profile supports potential to become standard of care, if approved

Sources: (1) Gounder et al., *N Engl J Med*, 2018; Nieavar U SPI; Yildiz et al., *Reprod Sci*, 2015; (2) Christopoulos et al., *N Engl J Med*, 2008; Palassini et al., *Cancer J*, 2017; Salem et al., *J Assist Reprod Genet*, 2020; Salem et al., *Sci Rep*, 2019; (3) De Sanctis et al., *Medicine*, 2019; Toulmonde et al., *Lancet Oncol*, 2019; (4) Bernard et al., *Plos One*, 2018; (5) Palassini et al., *Cancer J*, 2017.

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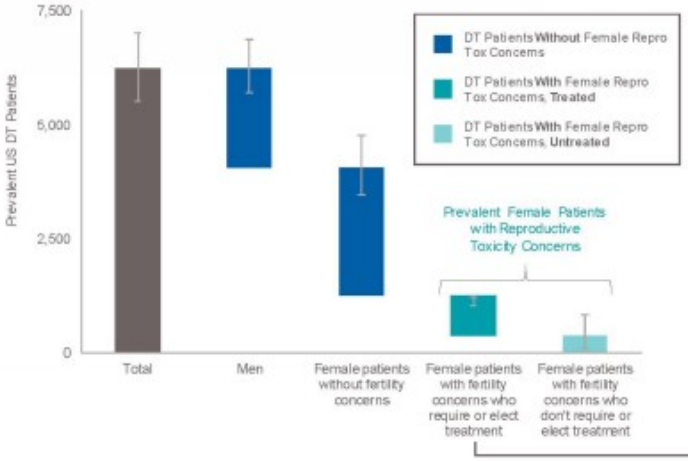
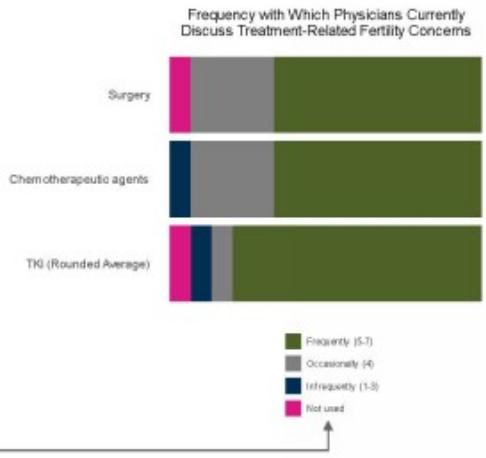
Female Reproductive Toxicity Concerns Are Expected to Impact Treatment Decisions for a Minority of Patients and Apply to All Current DT Treatments

<10%[1] of Addressable DT Patients Are Expected to Forgo Treatment Due to Female Reproductive Toxicity Concerns



All Current Therapies Pose Fertility Concerns That Physicians Routinely Discuss with DT Patients[2]



Note: DT: desmoid tumors; repro tox: reproductive toxicity.

(1) Active desmoid tumor prevalent patients 5,500-7,000 (Mean = 6,250). Male DT patients represent 30-40% of prevalent patients. Per market research and KOL interviews, an estimated 20% of total patients are expected to have female reproductive toxicity concerns. On average, an estimated 70% of these patients will eventually require active treatment.

(2) Medical oncologists (n=15) were asked, "On a scale from 1-7 where 1 is 'never,' 4 is 'sometimes,' and 7 is 'always,' how frequently do you currently discuss treatment-related fertility concerns with your female patients of child-bearing potential who are receiving the following treatment?" Physicians were asked about sorafenib, pazopanib, and imatinib separately and the responses were aggregated to create a rounded TKI average.

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Launch Activities Rapidly Advancing to Ensure Successful Preparation of Market, Organization and Brand

Preparing the Market

Establishing deep understanding of the unmet needs and identifying opportunities to generate awareness, educate, and improve the journey of patients with desmoid tumors

Preparing the Organization

Hiring teams and developing cross-functional strategic, operational, and tactical plans; building scalable infrastructure

Preparing the Brand

Generating evidence, building the brand, and preparing to bring differentiated value to patients, HCPs, and payers

Medical Affairs	Marketing	Market Access	Sales
✓ KOL engagement	✓ Go-to-market strategy	✓ Payer engagement	✓ Customer segmentation
✓ Medical Education activities	✓ KOL engagement	✓ Value story / dossier	✓ Sales force sizing
✓ Publication and Congresses	✓ Disease State Education	✓ Distribution model	✓ Recruitment strategy
✓ Advocacy group engagement	✓ Brand building	✓ Patient Support Strategy	

Systems and commercial infrastructure build on track and commercial supply secured

Summary of the Desmoid Tumor Opportunity

- ~1,000–1,650 incident/new cases, and **large prevalent pool** with ~5,500–7,000 patients actively receiving treatment annually in the U.S.
- **Propensity to treat is high** with over 90% of US DT patients receiving an active intervention; utilization of currently available therapies is **fragmented due to treatment limitations**
- DT experts and guidelines **moving away from surgery first** due to invasive nature and **high recurrence rates up to 77%**
- **Nirogacestat differentiated** based on evidence of efficacy, manageable tolerability, QoL improvement and oral convenience, which supports potential for extended duration of treatment
- **Awareness of nirogacestat is high** and significant clinical experience at SARC and NCCN centers; **potential to be first FDA-approved therapy** with IP protection through 2039

Nirogacestat: Additional Expansion Opportunity

Badreddin Edris, PhD, *Chief Operating Officer*

SpringWorks THERAPEUTICS

Nirogacestat has the potential to be the first targeted therapy for OvGCT patients

Nirogacestat in Ovarian Granulosa Cell Tumors: Monotherapy Expansion Opportunity in Rare Ovarian Cancer with Significant Unmet Need

Disease Characteristics

- Ovarian granulosa cell tumors (OvGCT) are a rare ovarian cancer subtype that are usually slow-growing and have limited impact on mortality, resulting in a large prevalent patient population
- OvGCT are most commonly diagnosed in women during the perimenopausal / early postmenopausal period (median diagnosis age of 50 years)
- Patients typically present with abdominal pain and abnormal or postmenopausal bleeding alongside a large pelvic or abdominal mass
- Recurrences can occur late, thereby requiring long-term surveillance and intervention to avoid bulky disease that is resistant to therapy

- OvGCT accounts for ~5% of all ovarian cancers
- Estimated US incidence of 1,500-2,000 per year with a significant pool of prevalent patients of ~10,000-15,000

- No currently approved therapies and limited treatment options
- Surgery is mainstay of treatment, but ~40% of patients experience recurrence
- Systemic therapies (e.g., chemo, bevacizumab, paclitaxel and carboplatin) have shown limited benefit and tolerability

Source: Dridi et al., *Int J Surg Oncol*, 2016; SEER.

SpringWorks THERAPEUTICS

Gamma Secretase Inhibitors Could Address Need for Targeted Therapy Options in OvGCT

OvGCT are potentially susceptible to gamma secretase inhibition due to mutations in *FOXL2*

>97% of OvGCT are driven by C124W mutation in *FOXL2*, a transcription factor required for development and function of granulosa cells

Mutant *FOXL2* alters multiple signaling pathways and gene expression of granulosa cells related to proliferation and apoptosis

Notch signaling has been shown to **block apoptosis and increase proliferation** of OvGCT cells

Preclinically, GSIs have been able to address the fundamental driver mutation in this tumor type

Threshold for inclusion in NCCN guidelines likely to be low given precedents and limited therapeutic options

- Modest activity in clinical studies has been observed for single agents and combination regimens to date
- Single arm trials with published data have been sufficient to support inclusion of regimens in NCCN Guidelines
- Select benchmark data from completed OvGCT trials:

	Single agent bevacizumab	Single agent paclitaxel vs. Paclitaxel + bevacizumab	
Study	Ph 2 single arm study N = 36	Ph 2 ALIENOR/ENGOT-ov7 randomized trial (n = 60)	
		Paclitaxel N = 32	Bev + paclitaxel N = 28
ORR	17%	23%	44%
mPFS	9.3 mo	14.9 mo	14.7 mo

Note: GSI: gamma secretase inhibitor; NCCN: National Comprehensive Cancer Network; OvGCT: ovarian granulosa cell tumor; ORR: objective response rate; PFS: progression-free survival.
Sources: Li et al., *Journal of Ovarian Research*, 2018; Irusta et al., *Biol Reprod*, 2013; Ray-Coquard et al., *JAMA Oncol*, 2020; Brown et al., *Cancer*, 2014.

Emerging Insights From OvGCT Physician Market Research

- Preliminary market research survey conducted to assess practice demographics and current treatment practices and to gather feedback on physician need for new treatments for OvGCT
  - Responses were collected from 31 physicians, including OB-GYNs, gynecologic oncologists, gynecologic surgeons and medical oncologists, with practices covering the academic and community settings
  - On average, each of these physicians currently treats ~5 OvGCT patients, with ~15 patients treated per physician in the last 5 years
- Key insights relating to perceived unmet need and current limitations of existing treatments noted by physicians include:
  - Need for options in the post-surgical recurrent setting, placing emphasis on long-term control after first recurrence and reducing recurrence rate
  - Need for late-line options that do not involve surgery
  - Improvements in screening with better diagnosis, predictive testing for stage and risk of recurrence as well as non-invasive screening options

"There are no good options for patients after relapsed disease. Surgical and radiation options are quite poor. Systemic therapy is very much needed."

– Gynecological Medical Oncologist

"An oral option for treatment allows for greater access to care. Many patients will review an oral treatment favorably as compared to an IV."

– Gynecologic Surgeon

Note: OvGCT: ovarian granulosa cell tumor.
Source: SpringWorks market research.

Phase 2 Study of Nirogacestat in Recurrent Ovarian Granulosa Cell Tumors

PHASE 2

Trial Summary

- Single-arm open label study to determine the efficacy, tolerability, safety, and pharmacokinetics of nirogacestat for the treatment of recurrent OvGCT
- Expected enrollment of ~40 patients
  - Principal Investigator: Dr. Panagiotis Konstantinopoulos at Dana-Farber Cancer Institute
- IND cleared in December 2021

Summary of Endpoints

- Primary Endpoint: Objective response rate by RECIST 1.1
- Secondary Endpoints: Progression-free survival, overall survival, duration of response, safety and tolerability, and quality of life assessments

First site activation anticipated in June 2022

Note: BID: twice daily; IND: investigational new drug.

SpringWorks THERAPEUTICS

Nirogacestat: BCMA Combination Therapy Development

Mike Burgess, MBChB, PhD, *Head of Research and Development*

SpringWorks THERAPEUTICS

Nirogacestat is positioned to be a potential cornerstone of BCMA combination therapy

Nirogacestat in Multiple Myeloma: A Potentially Best-in-Class Combination Backbone for BCMA-Directed Therapies

Rationale and Development Strategy

- Gamma secretase directly cleaves membrane BCMA, a clinically validated multiple myeloma target across modalities (ADC, CAR T, mAb, bispecific)
- Emerging clinical data and strong preclinical synergy support combining gamma secretase inhibitors across BCMA modalities
- Pursuing broad collaboration strategy with leading BCMA therapy developers to generate a diverse dataset to position nirogacestat as the "go-to" GSI for MM

- ~40,000 multiple myeloma patients receiving 1L and 2L therapy annually in the US[1]
- ~15,000 relapsed/refractory multiple myeloma patients receiving 3L+ therapy annually in the US[1]

- Combination use being investigated across all BCMA-targeted therapy modalities
- Potential for use alongside SoC MM therapies across lines of treatment

Note: ADC: antibody-drug conjugate; CAR T: chimeric antigen receptor T-cell; BCMA: B-cell maturation antigen; GSI: gamma secretase inhibitor; mAb: monoclonal antibody; MM: multiple myeloma; SoC: standard of care.
Source: (1) Siegel et al., *Cancer Statistics*, 2022; DRG market research.

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Multiple Myeloma is a Large and Evolving Market

- Multiple myeloma represents the 3rd largest oncology revenue opportunity despite having a lower 5-year prevalence than solid tumors including breast, prostate, lung, and colorectal
  - Opportunity driven by long durations of therapy, particularly in early lines
  - First- and second-line drug sales account for ~75% of total market
- Combination regimens are utilized across lines of therapy to achieve the longest durations of PFS by addressing the polyclonal nature of the disease
- Over 70% of MM is treated in the community setting – adoption requires strong efficacy, tolerability and relative convenience
  - BCMA therapies are poised to become a new SoC, but broad uptake in community settings may be challenging due to current profiles
    - > ADCs: ocular toxicity (keratopathy)
    - > Bispecifics and CAR-Ts: cytokine release syndrome, neurotoxicity, neutropenia, conditioning regimens, extended hospitalizations
- Clinical development in myeloma typically begins with monotherapy treatment in RRMM before advancing in combination with SoC in first- and second-line settings

Nirogacestat has the potential to improve the benefit-risk profile of each type of BCMA modality and foster earlier and broader adoption

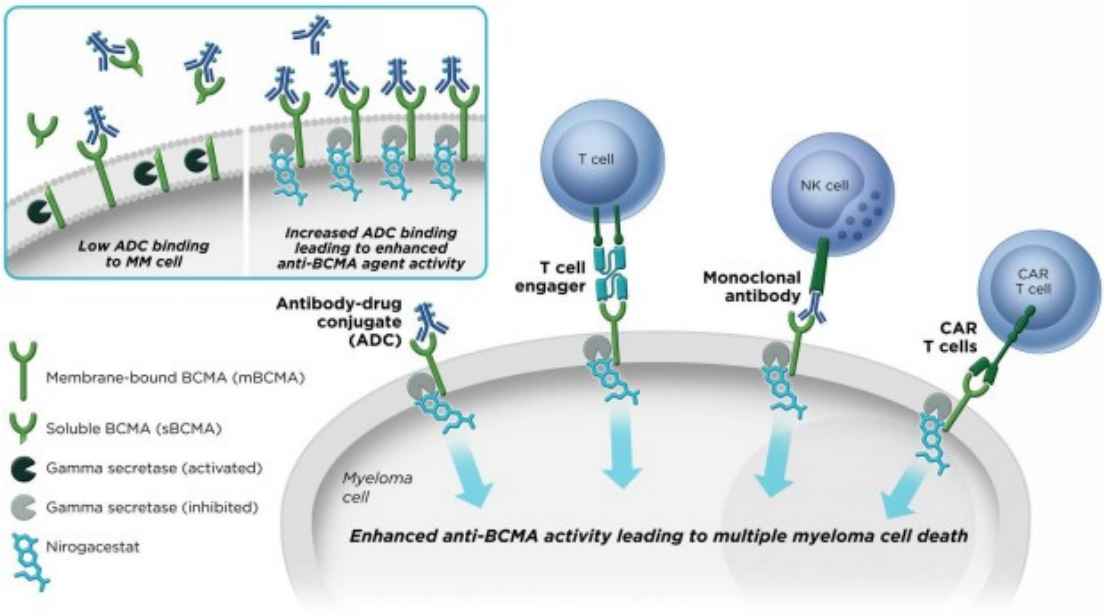
Note: MM: multiple myeloma; PFS: progression-free survival; RRMM: relapsed/refractory multiple myeloma; SoC: standard of care.
Sources: Braunlin et al., *Leukemia and Lymphoma*, 2021; Facon et al., *Lancet Oncology*, 2021; Decision Resources Market Forecast Dashboard, 2021; IQVIA.

Eight Clinical Collaborations Ongoing Covering All Key BCMA Therapeutic Modalities

Collaborator	Program	Modality				Collaboration Signed	Current Status
		ADC	Bispecific	CAR-T	mAb		
GSK	BLENREP (belantamab mafodotin)	✓				June 2019	Advanced into randomized Phase 2 trial
Allogene	ALLO-715			✓		January 2020	Phase 1 trial ongoing
janssen	Teclistamab		✓			September 2020	Phase 1 trial ongoing
PRECISION BIOSCIENCES	PBCAR269A			✓		September 2020	Phase 1 trial ongoing
Pfizer	Elranatamab		✓			October 2020	Phase 1b/2 trial ongoing
Seagen	SEA-BCMA				✓	June 2021	Phase 1 trial planned
abbvie	ABBV-383		✓			December 2021	Phase 1b trial planned
REGENERON	REGN5458		✓			April 2022	Phase 1b trial planned

Expecting additional clinical data releases for BCMA collaboration trials in 2022

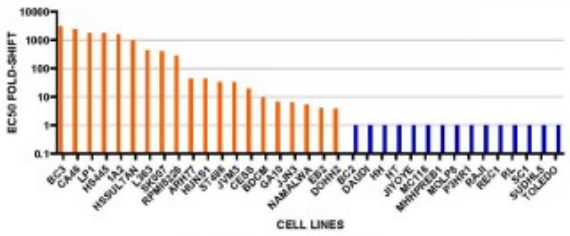
SpringWorks is Leading the Mechanistic Understanding and Clinical Development of GSI + BCMA in Multiple Myeloma



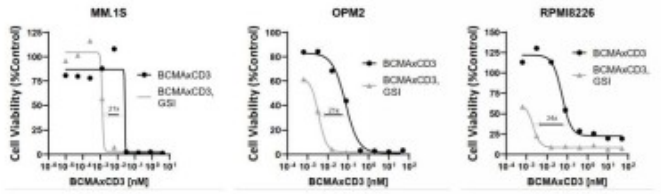
Note: GSI: gamma secretase inhibitor.

Nirogacestat Has Been Validated Preclinically in Combination with BCMA Therapies Across All Key Modalities

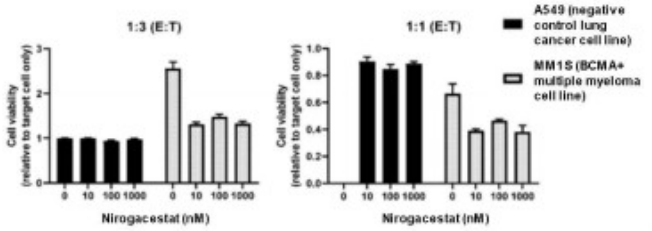
BCMA ADC[1]



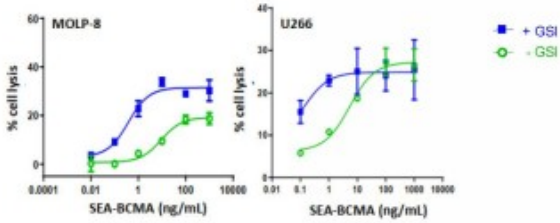
BCMA-CD3 Bispecific[2]



BCMA CAR-T[3]



BCMA mAb[4]



Sources: (1) Eastman et al., *ASH*, 2019; (2) Karwacz et al., *AACR*, 2020; (3) Balakumaran, A. et al., "Combination therapies of chimeric antigen receptors targeting B-cell maturation antigen and gamma secretase inhibitors", World patent WO2021148604A1, July 2021; (4) Yu et al., *EHA*, 2021.

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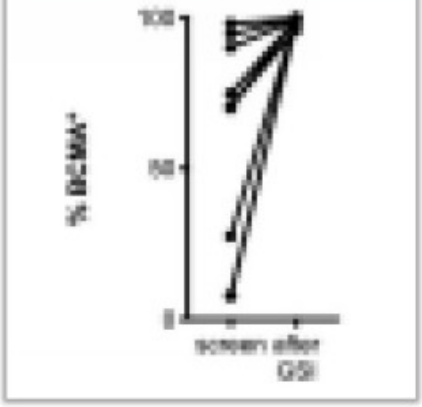
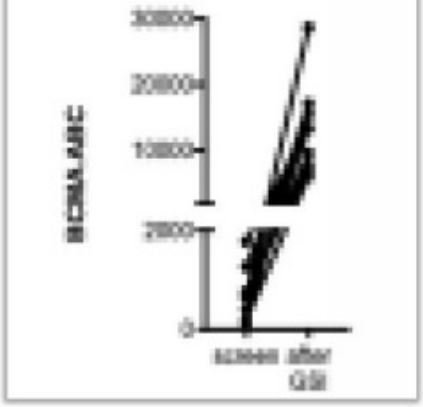
Gamma Secretase Inhibition Shown to Increase Membrane BCMA in Multiple Myeloma Patients

Median BCMA Expression Post GSI is 99% (96-100%)



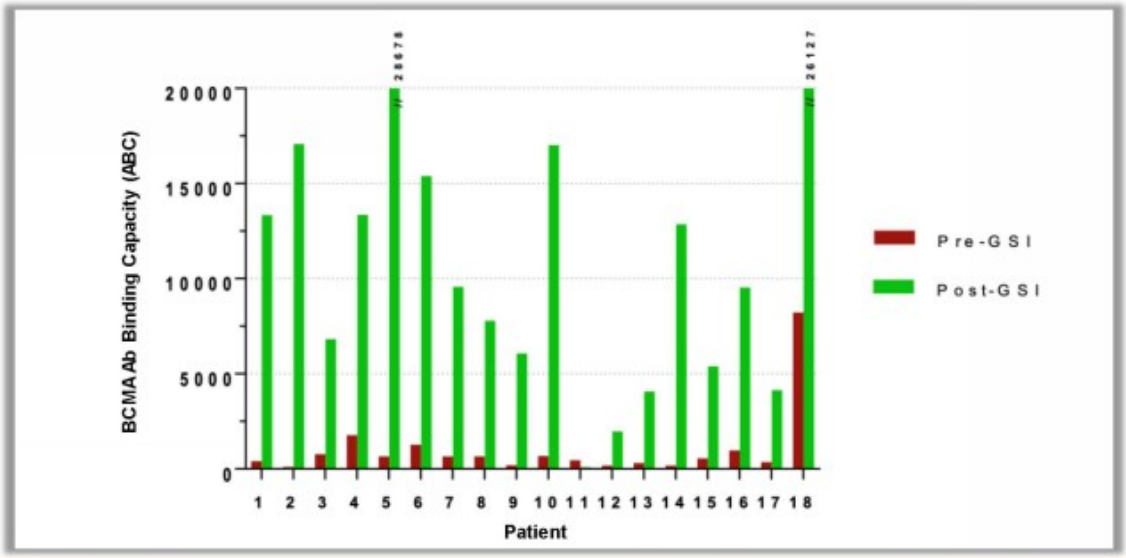
Median 20-Fold Increase in BCMA Surface Density (8-157-fold)



3 doses of GSI (JSMD194/Crenigacestat) over 1 week led to substantial increases in BCMA positive cells and BCMA cell surface density on myeloma cells from patient bone marrow aspirates

Source: Cowan et al., *ASH*, 2019.
Note: GSI (gamma secretase inhibitor) data shown from crenigacestat.

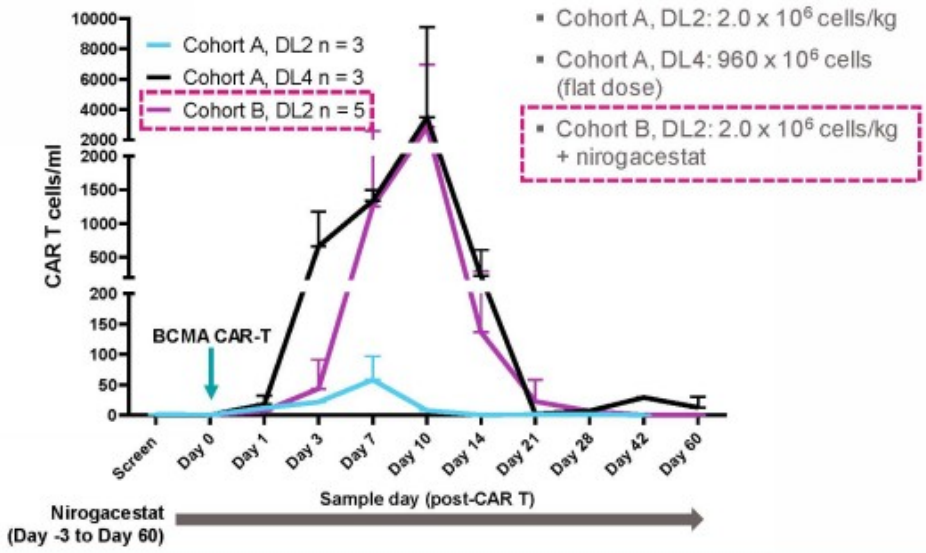
With Longer Follow-up and More Patients, GSI Demonstrated Consistent Ability to Increase BCMA Receptor Density



GSI (JSMD194/Crenigacestat) treatment shown to reproducibly increase BCMA cell surface density on myeloma cells from patient bone marrow aspirates

Source: Cowan et al., *ASH*, 2021.
Note: GSI (gamma secretase inhibitor) data shown from crenigacestat.

Preliminary Clinical Data Demonstrate That Nirogacestat Treatment Can Lead to Profound Expansion of BCMA CAR-T Cells in Relapsed/Refractory Multiple Myeloma Patients



When combined with nirogacestat, a low dose of allogeneic BCMA CAR-T cells (PBCAR269A) achieved a similar level of expansion and persistence as a 7-fold higher dose of CAR-T cells administered as a monotherapy

Note: DL: dose level.
Source: Precision BioSciences investor materials (presented 12/11/21); preliminary data from ongoing Precision-sponsored trial (NCT04171843).

Most Advanced Nirogacestat BCMA Combination Is With Low-dose BLENREP (ADC)

BLENREP was approved in relapsed/refractory multiple myeloma (RRMM) in 2020

- BLENREP RRMM approval study (DREAMM-2) utilized 2.5 mg/kg Q3W monotherapy dose and schedule, resulting in deep and durable responses in a triple-class refractory population with a **31% ORR**[1]
- In DREAMM-2, a **44.5% Grade 3/4 keratopathy rate** using KVA scale was observed – keratopathy leading to dose modification in DREAMM-2: dosage interruption (47%), dose reduction (23%) and permanent discontinuation (2.1%)[1]

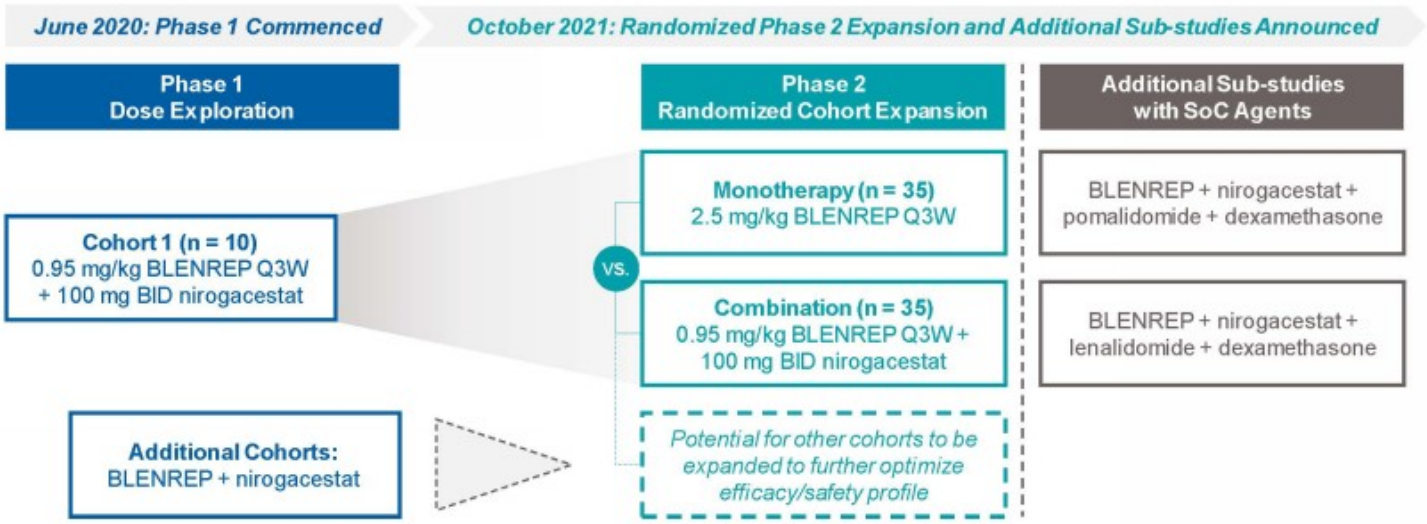
BCMA potentiation via nirogacestat may preserve efficacy of low-dose BLENREP while reducing ocular toxicity

- Low-dose BLENREP (0.95 mg/kg Q3W) not expected to be clinically active based on DREAMM-1 study (2/29 objective responses at ≤ 2.5 mg/kg Q3W BLENREP)[2]
- *"The idea of using **gamma secretase inhibition to increase expression of BCMA** on the plasma cells to **further optimize the regimen by reducing the dose**, which hopefully, will **maintain efficacy and potentially reduce ocular [toxicity]** ..."* – GSK 1Q22 Earnings Call (01/27/22)

Note: KVA Scale: Keratopathy and Visual Acuity Scale; ORR: objective response rate; Q3W: once every 3 weeks; REMS: Risk Evaluation and Mitigation Strategy; RRMM: relapsed/refractory multiple myeloma.

(1) BLENREP USPI.
(2) Trudel et al., *Lancet Oncology*, 2018.

Initial Low-dose BLENREP + Nirogacestat DREAMM-5 Cohort Has Advanced to Randomized Phase 2 Expansion Cohort



Additional sub-studies with standard-of-care agents expected to commence dosing mid-year

Note: SoC = standard of care

Interim Data from DREAMM-5 Study Evaluating Nirogacestat in Combination with Low-dose BLENREP vs. BLENREP Monotherapy Presented at ASCO 2022

Patient Characteristics			
	2.5 mg/kg BLENREP CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat DE (N = 10)
High-risk cytogenetics	6 (43)	7 (50)	8 (80)
Extramedullary Disease			
Yes	1 (7)	4 (29)	2 (20)
No	13 (93)	10 (71)	8 (80)
Autologous stem cell transplant			
Yes	9 (64)	10 (71)	9 (90)
No	5 (36)	4 (29)	1 (10)
Prior lines of therapy, median (min – max)	4.5 (3 – 7)	4.5 (3 – 10)	4.5 (3 – 10)

Note: CE: Cohort Expansion; DE: Dose Exploration; BID: twice daily.
Source: Lonial et al., *ASCO*, 2022.

No Significant Difference Noted in Grade ≥ 3 Non-Ocular AEs Between Combination and BLENREP Monotherapy at Interim Analysis

Drug-Related Grade ≥3 Adverse Events by System Organ Class and Preferred Term			
	2.5 mg/kg BLENREP CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat DE (N = 10)
Blood and Lymphatic	**2 (14)**	**4 (29)**	**3 (30)**
Thrombocytopenia	2 (14)	3 (21)	2 (20)
Febrile neutropenia	1 (7)	1 (7)	1 (10)
Gastrointestinal	**1 (7)**	**3 (21)**	**1 (10)**
Diarrhea	1 (7)	2 (14)	1 (10)
Upper abdominal pain	-	1 (7)	-
Investigations	**3 (21)**	**2 (14)**	**-**
Blood magnesium decrease	-	-	-
AST increase	1 (7)	-	-
Platelet count decrease	2 (14)	1 (7)	-
Blood urea increase	-	1 (7)	-
General and administration site conditions	**-**	**-**	**-**
Metabolism and nutrition	**-**	**1 (7)**	**1 (10)**
Hypophosphatemia	-	1 (7)	1 (10)
Injury and procedural complications	**1 (7)**	**-**	**2 (20)**
Infusion Related Reaction	1 (7)	-	2 (20)
Renal and urinary	**-**	**1 (7)**	**-**
Proteinuria	-	1 (7)	-
Respiratory, thoracic and mediastinal	**1 (7)**	**-**	**-**
Pulmonary embolism	1 (7)	-	-
Musculoskeletal and connective tissue	**-**	**-**	**-**

49 Note: Five patient deaths were also reported on study, all unrelated to study treatment.
Source: Lonial et al., ASCO, 2022

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Reduction in Ocular Adverse Events Observed with Combination Versus BLENREP Monotherapy at Interim Analysis

	2.5 mg/kg BLENREP CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat CE (N = 14)	0.95 mg/kg BLENREP + 100 mg BID Nirogacestat DE (N = 10)
Grading Methodology	**KVA**	**KVA**	**CTCAEv5**
Number of Subjects with Any Ocular Event	12 (86%)	7 (50%)	6 (60%)
Grade 1	0	4 (29%)	2 (20%)
Grade 2	5 (36%)	2 (14%)	2 (20%)
Grade 3	7 (50%)	1 (7%)	2 (20%)
Grade 4	0	0	0
Median (range) number of treatment cycles	2.0 (1-5)	4.0 (1-9)	8.5 (1-29)
Median (range) follow-up duration (weeks)	12.0 (3–22)	12.0 (3–24)	34.5 (5–88)

Note: CE: Cohort Expansion; DE: Dose Exploration; BID: twice daily; CTCAE: common terminology criteria for adverse events; KVA: keratopathy and visual acuity.
Note: BLENREP + niro combination DE cohort N=10 was fully enrolled prior to the opening of the CE cohort. CE cohorts (total N=28) were concurrently randomized.
(1) 5 of the 6 patients who experienced an ocular event of any grade by the CTCAE5 scale had a KVA event of any grade.
Source: Lonial et al., ASCO, 2022.

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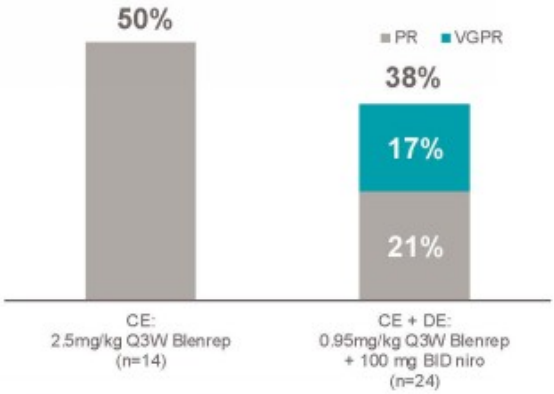
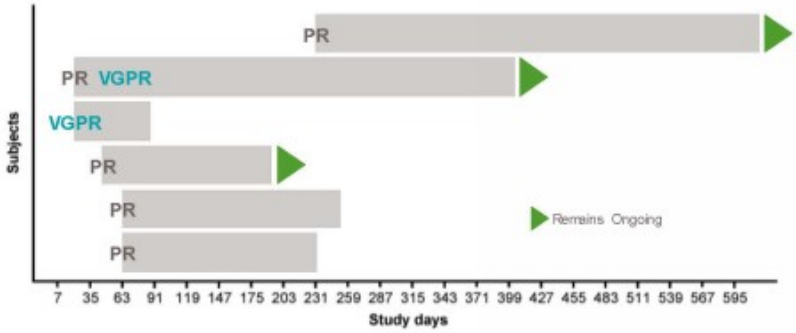
Emerging Efficacy Profile of Low-dose BLENREP in Combination with Nirogacestat

Objective Response Rate (ORR)



- Comparable efficacy with nirogacestat + low-dose BLENREP vs. monotherapy BLENREP

Onset and Duration of Response In Responders (6/10) from the DE Cohort



- More mature data on profile of response to be presented at future congress, including data on complete CE cohorts (n=70)

Nirogacestat and low-dose BLENREP combination may provide an attractive benefit-risk profile compared to BLENREP monotherapy at approved dose given a reduced incidence of Grade 3 ocular toxicity while maintaining comparable efficacy

Note: PR: partial response; VGPR: very good partial response; BID: twice daily; CE: cohort expansion; DE: dose exploration; Q3W: once every 3 weeks.
Source: Lonial et al., *ASCO*, 2022.

SpringWorks Therapeutics

Nirogacestat May Help Open the Path for BLENREP in Earlier Treatment Lines

Precedents support move from RRMM to NDMM

- Daratumumab demonstrated 29.2% single-agent ORR (12.2% VGPR or better) in the SIRIUS study[1] and subsequently significantly enhanced activity in combination with SoC (92.9% ORR with improved MRD and PFS) in the POLLUX study[2] in RRMM
- SoC improvement in RRMM preceded evaluation and ultimate approval of daratumumab in earlier-line treatment

BLENREP has demonstrated increased response rate when combined with SoC

- BLENREP evaluated in combination with bortezomib, lenalidomide, and dexamethasone (VRd) regimen in transplant-ineligible newly diagnosed MM patients at variety of doses and schedules[3]
- On interim analysis (n=36 patients), 83-100% ORR with significant VGPR rate reported, demonstrating proof of concept for additive efficacy of BLENREP in first-line patients
- Grade 3 ocular toxicity rate of 33-83% reported based on various doses and schedules evaluated

Preservation of BLENREP monotherapy efficacy with significantly improved ocular safety profile in RRMM could support broader development in combination with SoC agents across lines of therapy

Note: MRD: minimal residual disease; NDMM: newly diagnosed multiple myeloma; ORR: objective response rate; PFS: progression-free survival; POC: proof of concept; RRMM: relapsed/refractory multiple myeloma; SoC: standard of care; VGPR: very good partial response.
Sources: (1) Lonial et al., *Lancet*, 2016; (2) Dimopoulos et al., *NEJM*, 2016; (3) Usmani et al., *ASH*, 2021.

Additional Data Readouts and Trial Starts Anticipated in 2022 Across Several BCMA Collaboration Programs

Nirogacestat evaluation in combination with BLENREP alone and in combination with standard of care agents

- DREAMM-5 Randomized Cohort Expansion (Phase 2): Updated data on additional patients with longer follow-up expected in 2H22
- DREAMM-5 Sub-studies: Enrollment to be initiated mid-year in cohorts combining low-dose BLENREP and nirogacestat with lenalidomide/dexamethasone and with pomalidomide/dexamethasone to support potential development in earlier lines of therapy

Nirogacestat evaluation in combination with other BCMA-targeted therapeutic modalities

- BCMA-CD3 bispecific antibodies: 2 clinical trials ongoing, 2 planned
- BCMA allogeneic CAR T-cell therapies: 2 clinical trials ongoing
- BCMA monoclonal antibody: 1 study planned

BCMA-targeted therapies are positioned to become a cornerstone of MM treatment – nirogacestat has potential to enhance risk/benefit profile across agents and lines of therapy

Program Break: 5 Minutes

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Mirdametinib

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Mirdametinib: Potent and Selective MEK Inhibitor With Differentiated Safety Profile

- Mirdametinib is an investigational oral, allosteric MEK1/2 inhibitor with over 10 years of clinical experience
- Granted Orphan Drug Designation for NF1 by FDA and European Commission and Fast Track Designation for NF1-PN by FDA
- Ongoing Phase 2b ReNeu trial in NF1-PN is fully enrolled; NF1 is one of the largest genetic tumor predisposition syndromes with ~100k patients in the US today
- Compound potency, optimized dose/schedule, lack of food effect, limited DDI potential, and CNS exposure may allow for potentially differentiated development settings
- Monotherapy and combination studies ongoing in NF1-PN, low-grade glioma, breast cancer, RAS/RAF-mutated solid tumors and other indications

Pediatric and Adult NF1-PN Patients Enrolled on ReNeu	114
Clinical Trials Ongoing or On Track for 2022 Initiation:	5
US Composition of Matter Patent Protection:	2041

Note: NF1-PN: Neurofibromatosis type 1-associated plexiform neurofibroma; DDI: drug-drug interaction.

Biomarker-Guided Pipeline-in-a-Molecule Development Strategy for Mirdametinib

Indication	Development Approach	Preclinical	Phase 1	Phase 2	Phase 3	Collaborator(s)	Potential Annual Patient Population[1]	Biomarker(s)
NF1-PN	Monotherapy		ReNeu				~40,000[2]	NF1
MAPK Mutant Solid Tumors	+ Lifirafenib (Pan-RAF inhibitor)					Mapkure	70,000+[3]	RAS, RAF
	+ BGB-3245 (RAF dimer inhibitor)							
Pediatric Low-Grade Gliomas	Monotherapy					St. Jude Children's Research Hospital	~15,000[4]	MAPK Mutations
ER+ Metastatic Breast Cancer	+ Fulvestrant (SERD)					Memorial Sloan Kettering Cancer Center	~12,000[5]	NF1 and Other MAPK Mutations
MEK 1/2 Mutant Solid Tumors	Monotherapy						~12,500[6]	MEK1/2 Mutations

Mirdametinib has a potential total addressable population of 150,000+ patients annually and data are expected across studies in 2022

Sources: (1) Estimates are rounded and based on incidence reported by American Cancer Society Cancer Facts & Figures 2021 (U.S.) and other sources as noted. (2) Rasmussen et al., *Am J Epidemiol.*, 2000; Ferner et al., *J Med Genet.*, 2007; 2020 U.S. Census data. (3) Includes KRAS-mutant NSCLC and NRAS-mutant melanoma among other indications. Westcott et al., *Chin J Cancer*, 2013; Munoz-Couselo et al., *Onco Targets Ther*, 2017. (4) Ostrom et al., *Neuro Oncol*, 2020. Note addressable population includes prevalent population in addition to incident patients. (5) Razavi et al., *Cancer Cell*, 2018. (6) Hamrahan et al., *Cancer Research*, 2020.

SpringWorks Therapeutics

Mirdametinib: NF1-PN

L. Mary Smith, PhD, *Chief Development Officer*

SpringWorks THERAPEUTICS

Kendall
NF1 Patient

Plexiform Neurofibromas Are Painful, Disfiguring Tumors That Grow Along Peripheral Nerve Sheaths

Disease Characteristics

- NF1-associated plexiform neurofibromas (NF1-PN) patients present with significant morbidities
- NF1 mutations cause loss of neurofibromin, a key MAPK pathway repressor, leading to uncontrolled tumor growth across the body
- NF1-PN grow along nerves and can lead to extreme pain and disfigurement
- NF1 patients can experience neurocognitive deficits and developmental delays

- ~100,000 patients living with NF1 in the US
- NF1 patients have a ~30-50% lifetime risk of developing NF1-PN

- MEK inhibitors are a validated class for NF1-PN treatment
- Surgical resection is challenging due to the infiltrative tumor growth pattern along nerves and can lead to permanent nerve damage and disfigurement

Source: Kim et al., *Sarcoma*, 2017.

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Potentially Registrational Pediatric and Adult Phase 2b ReNeu Trial is Fully Enrolled

ReNeu

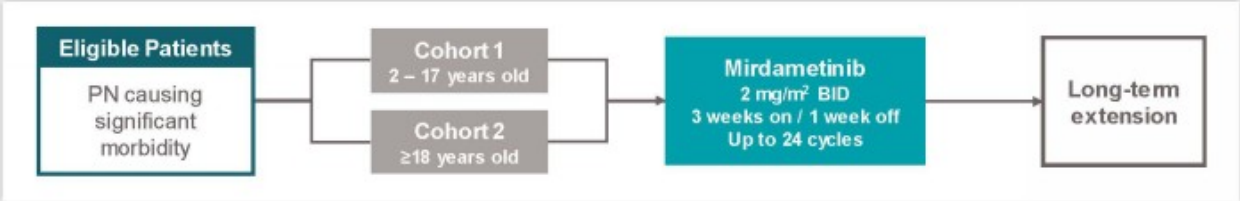
PHASE 2 | PHASE 2B

Trial Summary

- Study fully enrolled with 114 patients in 2 cohorts (pediatric, adult participants) across ~50 sites in the US
- 2 mg/m^2 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
  - Treatment duration designed to evaluate longer-term benefit of mirdametinib in NF1-PN

Study Endpoints

- Primary Endpoint: Objective response rate (≥20% reduction in tumor volume)
  - Blinded Independent Central Review (BICR) used for tumor assessments
- Secondary and Exploratory Endpoints: Safety and tolerability, duration of response, quality of life, and physical functioning assessments



Adult cohort fully enrolled in August 2021 and pediatric cohort fully enrolled in December 2021

Note: BID: twice daily; PN: plexiform neurofibroma.

SpringWorks Therapeutics

Mirdametinib NF1-PN Program Highlights

- Mirdametinib has the potential to benefit a broader set of NF1-PN patients
  - MEK inhibitors are a proven therapeutic approach for NF1-PN
  - NF1-PN is rapidly emerging as a validated commercial market
  - No currently approved treatment for the adult NF1-PN population
  - Potential for approval of a pediatric formulation as well as the potential for a label which allows for dosing of mirdametinib without regard to food/drug effect may greatly decrease patient burden and increase access to therapy
- ReNeu study fully enrolled
  - 56 participants enrolled in the pediatric cohort and 58 participants enrolled in the adult cohort
  - Participants completing 24 cycles of treatment have entered the long-term extension phase of the study
- Regulatory status
  - Planned 2022 FDA interactions to align on data expectations and path to regulatory approval

Mirdametinib: Additional Expansion Opportunities

Jim Cassidy, MD, PhD, *Chief Medical Officer*

SpringWorks THERAPEUTICS

Phase 2 Trial in Pediatric Low-Grade Glioma Provides Additional Expansion Opportunity for Mirdametinib

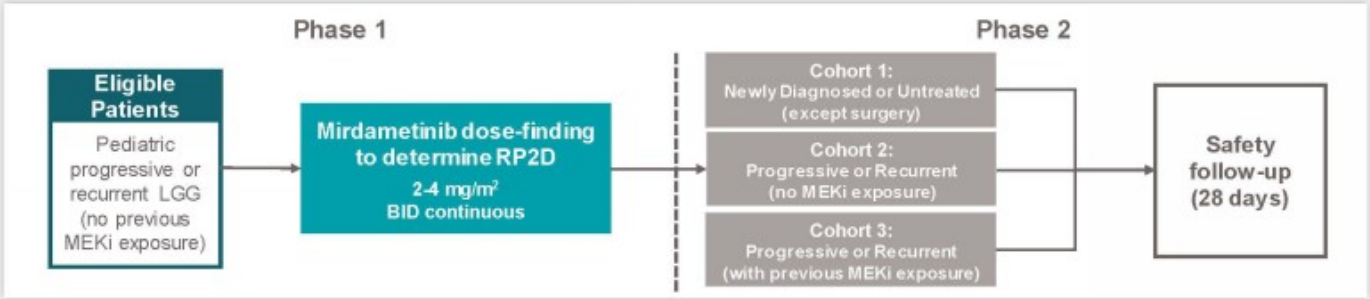
PHASE 1 | PHASE 2

Trial Summary

- Open-label, multi-center study evaluating single agent mirdametinib, a brain penetrant MEK 1/2 inhibitor, in pediatric low-grade gliomas
- Recommended dose from Phase 1 dose-finding/dose-escalation study will be used (2-4 mg/m^2, BID continuous)

Summary of Endpoints

- Primary Endpoint: Objective response rate
- Secondary Endpoints: Safety and tolerability, duration of response, and quality of life assessments



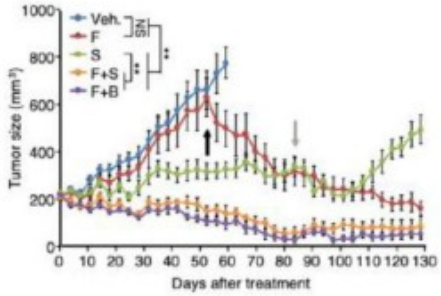
Manageable safety profile and blood-brain barrier penetration properties set the stage for a potential best-in-class profile for pediatric low-grade gliomas – initial data to be presented at ISPNO on June 13 and 14

Note: BID: twice daily; ISPNO: International Symposium on Pediatric Neuro-Oncology; LGG: low-grade glioma; RP2D: recommended Phase 2 dose.

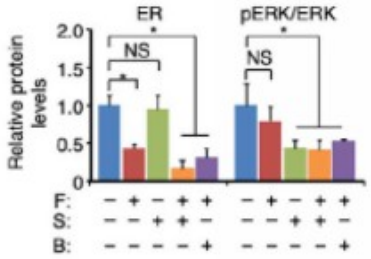
Mirdametinib: MEK Inhibitors Can Potentially Address Endocrine Therapy Resistance Due to MAPK Mutations in ER+ Breast Cancer

- MAPK mutations in ER+ mBC cells can lead to fulvestrant resistance, which can be reversed with MEK inhibition
- ~25% of ER+ mBC patients progress on endocrine therapy
- *NF1* deficiency has been shown to enhance ER transcriptional activity leading to hormone resistance
  - Up to 15% of mBC harbor MAPK pathway mutations, including *NF1* LoF

NF1-Deficient ER+ BC PDX: Durable Tumor Growth Inhibition with MEKi + Fulvestrant



MEKi + Fulvestrant Modulates ER and MAPK Signaling



Phase 1 trial ongoing for mirdametinib + fulvestrant in ER+ breast cancer patients with MAPK-mediated resistance

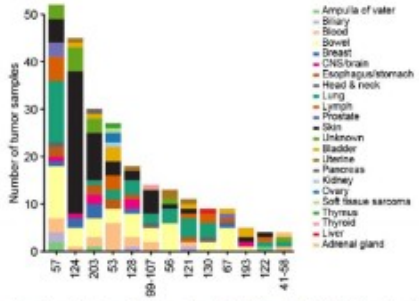
Note: B: buparlisib (PI3K inhibitor); BC: breast cancer; F: fulvestrant; LoF: loss of function; mBC: metastatic breast cancer; S: selumetinib (MEK inhibitor); SoC: standard of care; V: vehicle.
Source: Sokol et al., *ESMO*, 2019; Zheng et al., *Cancer Cell*, 2020.

SpringWorks THERAPEUTICS

Mirdametinib: Activity Demonstrated in Preclinical Models Driven by Activating Mutations in MEK1 and MEK2

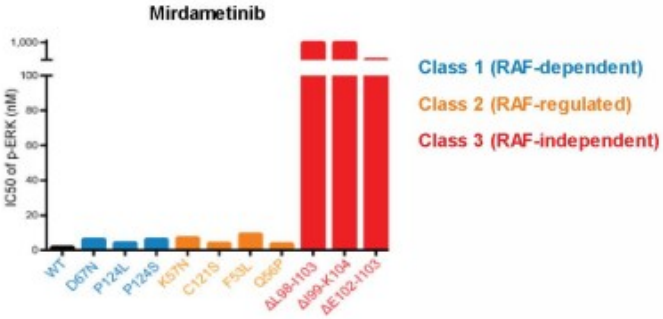
- Mirdametinib shows potent preclinical activity against Class 1 and Class 2 mutations in *MEK1* and *MEK2*
- *MEK1* and *MEK2* have been validated as oncogenic targets with mutations present in ~2% of solid tumors
- Clinical case reports with allosteric MEK inhibitors also support utility of mirdametinib in tumors driven by MEK mutations

MEK 1/2 Mutants Occur Across Tumor Types



Supplementary Figure S1. Tumor type distribution of *MAP2K1* hotspot mutations.
Tumor type incidence per hotspot *MAP2K1* missense or in-frame deletion mutant.

Class 1 and 2 MEK Mutants Are Sensitive to Mirdametinib *in vitro*



Phase 1 trial ongoing for mirdametinib in patients with MEK1/2-mutant solid tumors

Source: Gao et al., *Cancer Discovery*, 2018; Hannahan et al., *Cancer Research*, 2020.

Building on Mirdametinib's Potential Best-In-Class Profile, We Developed Our MAPK Targeted Portfolio with Complementary Combination Opportunities in Collaboration with BeiGene

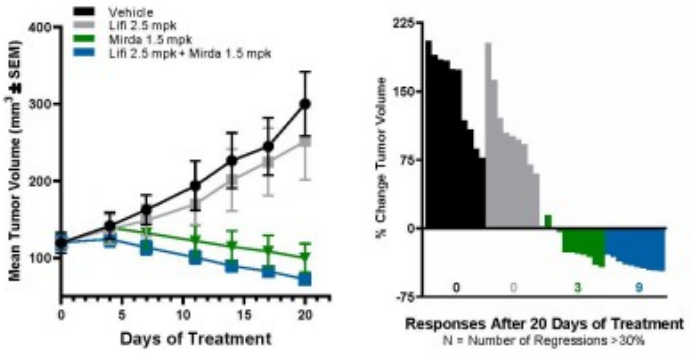
Key Accomplishments from BeiGene Collaborations:

- Demonstrated **activity and tolerability of vertical MAPK pathway inhibition** in RAS and RAF mutant solid tumors with mirdametinib + lifirafenib combination
- Commenced first-in-human study of BGB-3245 and demonstrated **tolerability and monotherapy clinical activity** in tumor types of interest
- Defined priority tumor types and mutations for **next stage of clinical development** across MAPK portfolio
- Completed additional **equity investment in MapKure** joint venture to enable expanded focus and development

Mirdametinib + Lifirafenib: Combination Synergy Demonstrated Across RAS Mutant Preclinical Models Informed Phase 1 Study Design

NSCLC Cell Line	RAS Mutation	Max EC_{50} shift with mirdametinib combo
Calu-6	K-RAS Q61K	59 fold ↓
SW1573	K-RAS G12C	97 fold ↓
NCI-H23	K-RAS G12C	22 fold ↓
NCI-H2122	K-RAS G12C	21 fold ↓
NCI-H358	K-RAS G12C	18 fold ↓
Calu-1	K-RAS G12C	No shift
Sk-Lu-1	K-RAS G12D	32 fold ↓
A549	K-RAS G12S	11 fold ↓
NCI-H1299	N-RAS Q61K	16 fold ↓

Mirdametinib + Lifirafenib *In Vivo* Activity (NCI-H358)



Preclinical synergy demonstrated with mirdametinib and lifirafenib *in vitro* across *RAS* mutations and *in vivo* at clinically relevant doses

Sources: Desai et al., *J Clin Oncol*, 2020; Tang et al., *Mol Cancer Ther*, 2015; Yuan et al., *Molecular Oncology*, 2020; Yuan et al., *AACR*, 2020.

SpringWorks THERAPEUTICS

Diverse Group of Solid Tumor Patients with MAPK Activating Mutations Enrolled in Dose Escalation Cohort of the Mirdametinib and Lifirafenib Study

As of 11/05/21

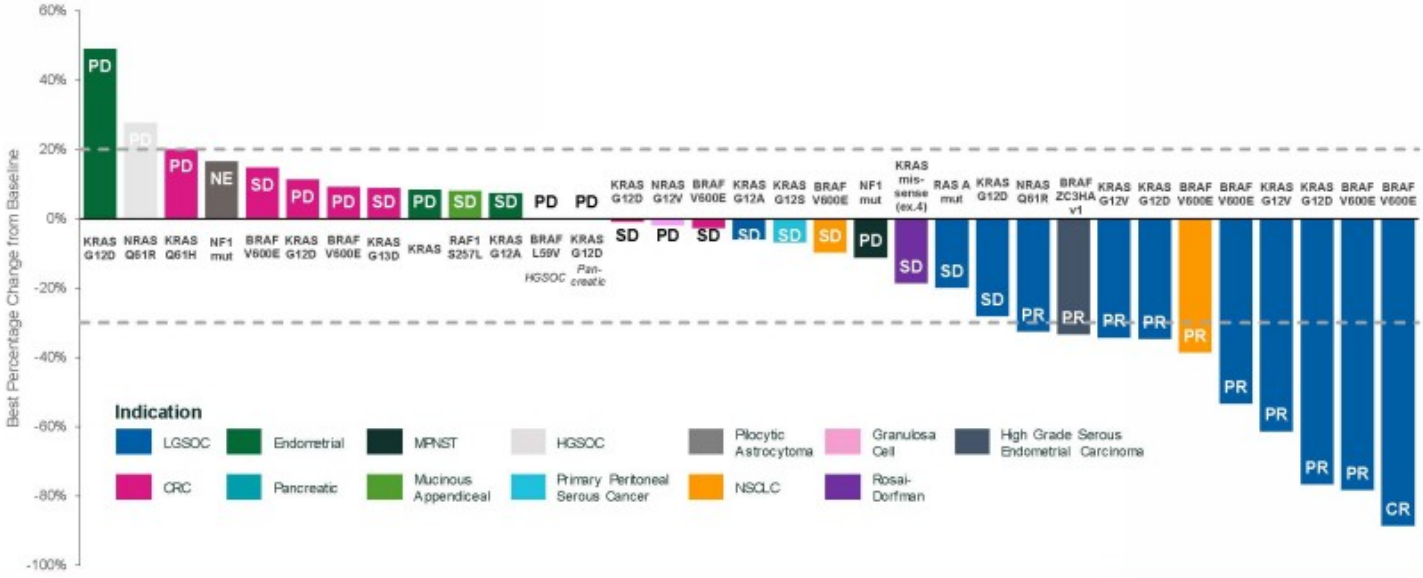
Baseline Characteristics	Overall, n (%)
Patients treated	35 (100)
Still on Treatment	13 (37.1)
Sex	
Male	9 (25.7)
Female	26 (74.3)
Age	
Mean	58.3
Median (Range)	60 (22-78)
Cancer stage at entry	
III	5 (14.3)
IV	30 (85.7)

Baseline Characteristics	Overall, n (%)
Prior systemic cancer regimens	
Median (Range)	3 (1-9)
ECOG status at entry	
0	24 (68.6)
1	11 (31.4)
Location of Tumor	
Gynecological	21 (60.0)
Gastrointestinal	9 (25.7)
Lung	2 (5.7)
Other	3 (8.6)
Mutation Status	
RAS	22 (62.9)
RAF	11 (31.4)
NF1	2 (5.7)

Note: Data are preliminary, investigator assessed, and have not been centrally reviewed; response data as of 11/05/21.

Mirdametinib + Lifirafenib: Clinical Efficacy Observed During Dose Escalation

As of 11/05/21



10 objective responses observed in 33 evaluable patients

CR: complete response; CRC: colorectal cancer; HGSOC: high-grade serous ovarian carcinoma; LGSOC: low-grade serous ovarian carcinoma; MPNST: malignant peripheral nerve sheath tumor; PD: progressive disease; PR: partial response; SD: stable disease.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed; response data as of 11/05/21.

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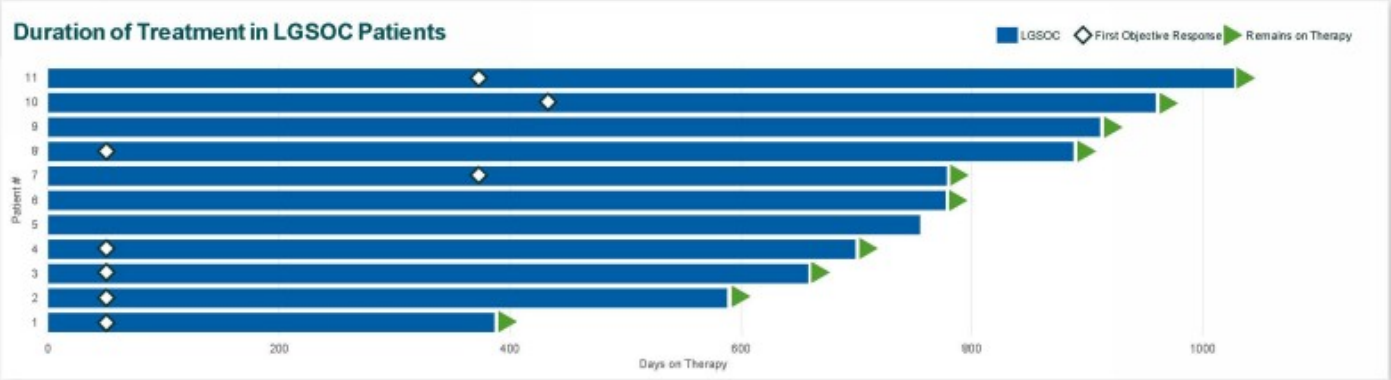
LGSOC Patients Demonstrate Potential for Long Term Responses and Tolerability

Enrollment data as of 05/11/22



- 100% Disease Control Rate (DCR) with median time on therapy of ~26 months with 10 of 11 patients remaining on therapy (13-34 months) as of May 2022
- 73% ORR in LGSOC (1 CR + 7 PRs (out of 11), 3 durable SDs ≥72 weeks) with deepening or stable responses over time
- Responses seen irrespective of underlying RAS/RAF mutation (2 KRAS G12V, 2 KRAS G12D, 1 NRAS Q61R, and 3 BRAF V600E)

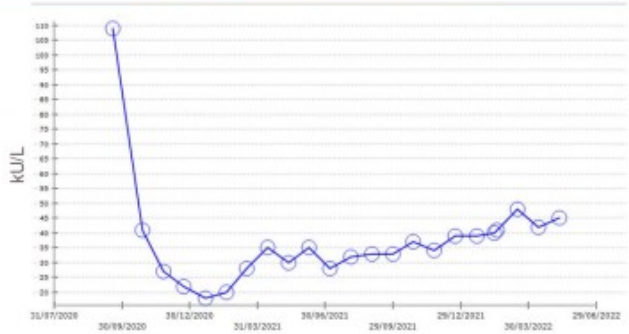
Combination clinical activity and tolerability demonstrated by durable antitumor activity (median time on therapy ~26 months in LGSOC)

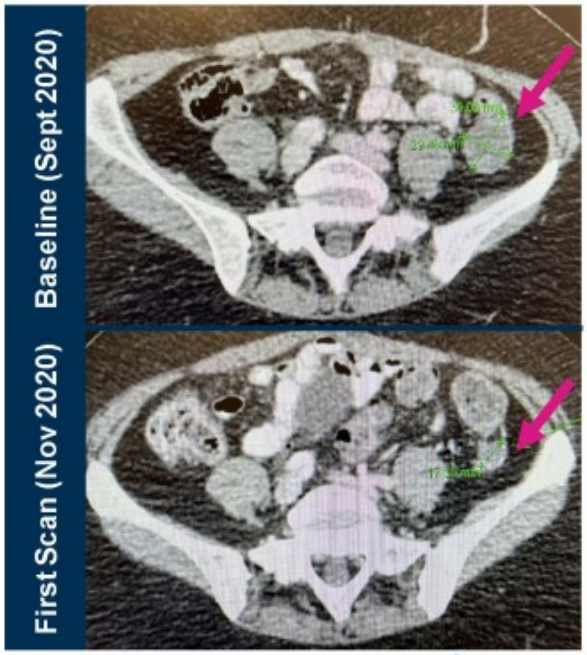
Note: CR: complete response; LGSOC: low grade serous ovarian carcinoma; ORR: overall response; PR: partial response; SD: stable disease.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed; enrollment data as of 05/11/22. Assumes 30 days in one month.

Mirdametinib + Lifirafenib Patient Vignette – KRAS G12D-mutant LGSOC

- Patient initiated therapy in September 2020 and achieved a 77% reduction from baseline at Week 48 (time of first response: Week 8) by RECIST v1.1 with continued stability in tumor size and CA-125 levels
  - 62-year-old female with low grade serous ovarian carcinoma
  - 3 lines of prior treatment
  - Investigator indicated patient experienced rapid symptomatic response
- Patient remains on therapy as of May 2022 (19.6 months on treatment)

CA125 Levels Over Treatment





Note: Data are preliminary, investigator assessed, and have not been centrally reviewed; response data as of 11/05/21. Enrollment data as of 05/11/22. Assumes 30 days in one month.

SpringWorks THERAPEUTICS

Evidence of Acceptable Safety and Tolerability Profile with Multiple Patients Exposed for >2 Years

Grade ≥3 TEAE – All Cause	
MedDRA PT	Grade ≥3 / n (%)
Overall	15 (42.9)
Thrombocytopenia + platelet count decrease	4 (11.4)
Intestinal obstruction	4 (11.4)
ALT increased	3 (8.6)
Hypertension	2 (5.7)
Abdominal pain	1 (2.9)
Anemia	1 (2.9)
AST increased	1 (2.9)
Febrile neutropenia	1 (2.9)
Hypertriglyceridemia	1 (2.9)
Other[1]	1 (2.9) each

Grade ≥3 TEAE – Related	
MedDRA PT	Grade ≥3 / n (%)
Overall	8 (22.9)
Thrombocytopenia + platelet count decrease	4 (11.4)
ALT increased	2 (5.7)
Hypertension	2 (5.7)
Abdominal pain	1 (2.9)
Anemia	1 (2.9)
AST increased	1 (2.9)
Febrile neutropenia	1 (2.9)
Hypertriglyceridemia	1 (2.9)

All-cause adverse event profile aligns with relapsed/refractory cancer patients generally; related TEAEs have been manageable with few treatment discontinuation due to adverse events; expected publication at a future medical conference

Note: MedDRA PT: Medical Dictionary for Regulatory Activities Preferred Term; TEAE: treatment-emergent adverse event.
(1) One patient each with abnormal LFTs; gamma-GT increased; rash maculopapular; urticaria; biliary infection; urinary tract infection; respiratory tract infection; neoplasm progression; metastasis to spine; acute myocardial infarction; and biliary obstruction.
Data cutoff date of 11/05/21.

Joint Venture with BeiGene Created to Advance BGB-3245 Through Clinical Development

BGB-3245 Profile

- BGB-3245 is an investigational next-generation oral, selective small molecule RAF dimer inhibitor
- BGB-3245 has demonstrated 5-10x greater potency than lifirafenib in inhibiting RAF-dimer activity in preclinical studies, including CRAF kinase activity, dimer-mediated signaling, and cell proliferation
- BGB-3245 has shown greater kinome selectivity than lifirafenib:

Selectivity (Kinases vs. V600E BRAF)	No. of Kinases for BGB-3245	No. of Kinases for Lifirafenib
≤10 fold	5	37

MapKure Background

- MapKure was formed as a joint venture between SpringWorks and BeiGene in 2019
  - MapKure licensed global rights (ex-Asia, including Japan) for BGB-3245 from BeiGene
  - At the time, BGB-3245 had finished preclinical development and was in IND-enabling activities
  - SpringWorks and BeiGene together are the majority equity holders in MapKure
- Clinical development of BGB-3245 has been advanced through the joint venture
  - Cross-functional collaboration using resources and teams from both SpringWorks and BeiGene
- Scientific advisory board comprised of leading industry and academic experts
  - Neal Rosen, MD, PhD – Memorial Sloan Kettering Cancer Center
  - Toni Ribas, MD – University of California, Los Angeles
  - Dejan Juric, MD – Massachusetts General Hospital
  - Kevin Koch, PhD – Founder and CSO, Array Biopharma

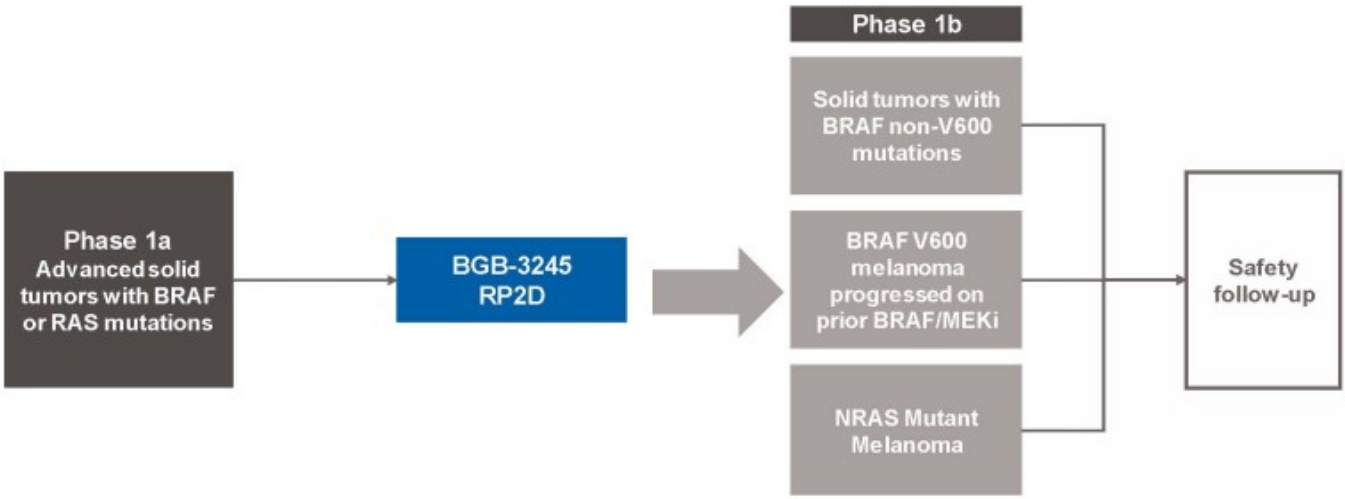
Source: BeiGene.

BGB-3245: Clinical Data Update

Jim Cassidy, MD, PhD, *Chief Medical Officer*

SpringWorks THERAPEUTICS

BGB-3245 Monotherapy Phase 1a/1b Study Design



Note: RP2D: recommended Phase 2 dose.

BGB-3245 Monotherapy Patient Characteristics in Dose Escalation

As of 02/26/22

Baseline Characteristics	Overall, n (%)
Patients treated	38 (100)
Still on Treatment	14 (36.8)
Sex	
Male	22 (57.9)
Female	16 (42.1)
Age	
Mean	58.6
Median (Range)	57 (31-83)
Cancer stage at entry	
III/other	5 (13.2)
IV	33 (86.8)
Prior systemic cancer regimens	
Median (Range)	5 (0-10)

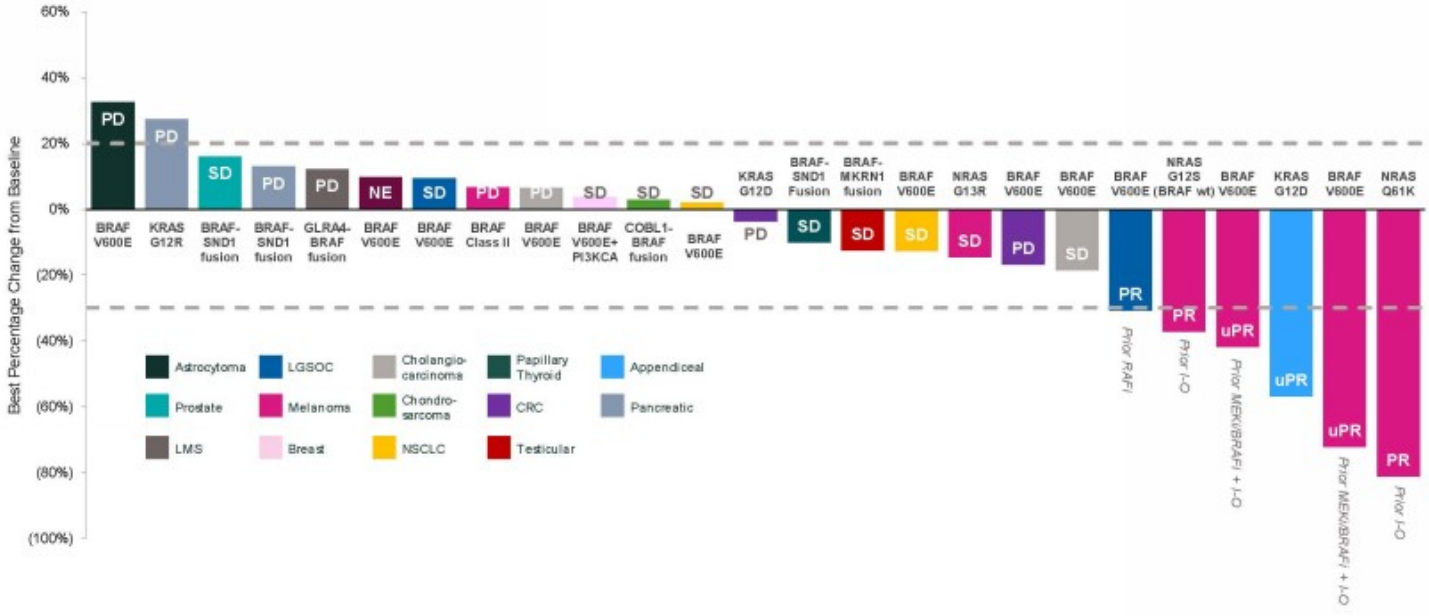
Baseline Characteristics	Overall, n (%)
ECOG status at entry	
0	24 (63.2)
1	13 (34.2)
Undocumented	1 (2.6)
Classification of Tumor	
Gastrointestinal	13 (34.2)
Skin	9 (23.7)
Female genitourinary	4 (10.5)
Lung	4 (10.5)
Thyroid	3 (7.9)
Male genitourinary	2 (5.3)
Brain	1 (2.6)
Breast	1 (2.6)
Other	1 (2.6)
Mutation Status	
RAS	11 (28.9)
RAF	27 (71.1)

Diverse group of solid tumor patients with RAS/RAF mutations enrolled

Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Enrollment as of 02/26/22.

BGB-3245: Early Clinical Efficacy Observed in Dose Escalation

As of 02/26/22



Note: CRC: colorectal cancer; IO: immuno-oncology; LMS: leiomyosarcoma; LGSOC: low-grade serous ovarian cancer; NSCLC: non-small cell lung cancer; PD: progressive disease; PR: partial response; SD: stable disease; TL: target lesion; uPR: unconfirmed partial response; wt: wildtype.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Response data as of 02/26/22.

SpringWorks THERAPEUTICS

Emerging Clinical Data Highlight Rapid Objective Responses in Metastatic BRAF V600 Melanoma Patients Progressed on Existing I-O and MEK + BRAF Treatments

As of 02/26/22

Patient Case Report #1

- 39-year-old man presented with BRAF V600E-mutated melanoma and had **previously received 2 prior lines of treatment, including BRAF + MEK combination (dabrafenib + trametinib) followed by I-O therapy (ipilimumab + nivolumab)**
- Began treatment on November 16, 2021 with 40 mg QD of BGB-3245 dosed continuously
- At the patient's first scan (Week 8), a **72% decrease from baseline in the target lesion** was observed
- Dose and schedule were well tolerated, with Grade 2 rash and Grade 2 ALT elevation noted
- The patient remained on treatment at the time of data cutoff

Patient Case Report #2

- 57-year-old woman presented with BRAF V600E-mutated melanoma and had **previously received 3 prior lines of treatment, including BRAF + MEK combination (dabrafenib + trametinib) and I-O therapy (ipilimumab + nivolumab)**
- Began treatment on November 8, 2021 with 40 mg QD of BGB-3245, dosed continuously
- At the patient's first scan (Week 8), a **42% decrease from baseline in target lesions** was observed – this radiological response also coincided with symptomatic relief
- Dose and schedule were well tolerated, with Grade 2 fever, Grade 1 diarrhea and Grade 1 rash noted
- The patient remained on treatment at the time of data cutoff

We are anticipating monotherapy RP2D declaration 2H 2022 and expansion cohorts to commence thereafter

Note: IO: immuno-oncology; QD: once daily.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed; data as of 2/26/22.

BGB-3245 Emerging Safety Profile Manageable and Consistent with MAPK Pathway Inhibitors

As of 01/10/22

Grade ≥3 TEAE – All Cause	
MedDRA PT	Grade ≥3 / n (%)
Overall	14 (41.2)
Rash maculopapular	2 (5.9)
Dyspnea	2 (5.9)
ALT increased	3 (8.8)
AST increased	2 (5.9)
Abdominal pain	2 (5.9)
Pyrexia	1 (2.9)

Grade ≥3 TEAE – Related	
MedDRA PT	Grade ≥3 / n (%)
Overall	4 (11.8)
Rash maculopapular	2 (5.9)

Note: TEAE: treatment-emergent adverse event.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Safety data as of 01/10/22.

Future Development for Portfolio of BeiGene Collaborations

Mirdametinib + Lifirafenib

- Complete Phase 1 dose finding 2H 2022 prior to expansion studies
- Data from ongoing study expected to be presented at a medical conference in 2H 2022

BGB-3245

- Complete dose escalation and determine RP2D in 2H 2022
- Data from ongoing study expected to be presented at a medical conference in 2H 2022
- Continue monotherapy development in BRAF non-V600 mutant solid tumors, post-BRAF/MEKi exposed BRAF V600 mutant melanoma and NRAS melanoma tumor types
- Commence proof of concept combination study with mirdametinib, focusing on KRAS (non-G12C) mutant tumors
  - Combination study sponsored by SpringWorks
- MapKure equity financing completed in early June to further advance development for BGB-3245
  - Participation from SpringWorks, BeiGene and other original investors in the joint venture

Note: RP2D: recommended phase 2 dose.

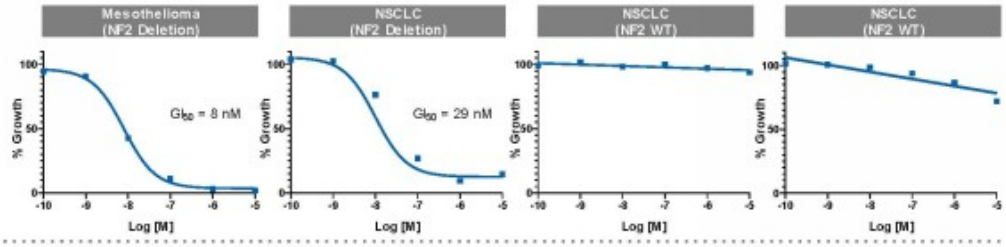
Preclinical Pipeline

Mike Burgess, MBChB, PhD, *Head of Research and Development*

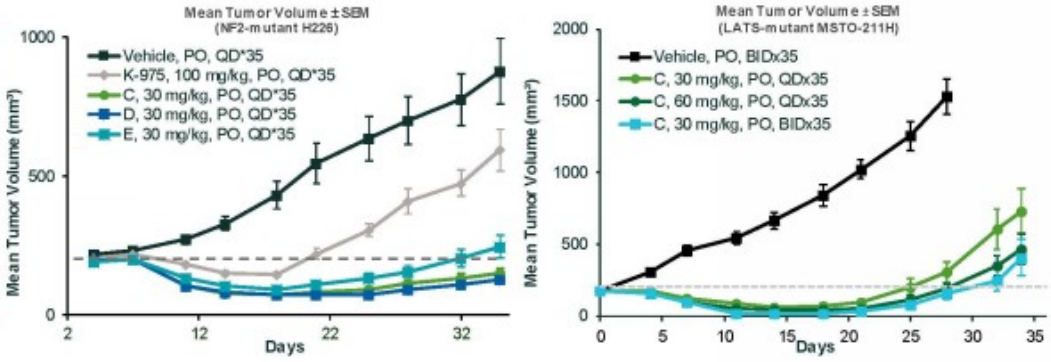
SpringWorks THERAPEUTICS

TEAD Inhibitor: Program in Lead Optimization With Selectivity, Potency and In Vivo Tumor Growth Inhibition Demonstrated in Hippo-Driven Models

1 TEAD inhibitors potently and selectively inhibit growth of cancer cell lines driven by Hippo pathway mutations



2 Compounds have shown good tolerability and oral bioavailability *in vivo*, with dose dependent tumor growth inhibition in Hippo altered xenografts



Note: GI50 = drug concentration producing 50% maximal growth inhibition; P.O. = by mouth; QD = once a day; BID = twice a day.

SpringWorks THERAPEUTICS

EGFR Inhibitor Portfolio: Developing Several Novel Targeting Approaches to Address De Novo Oncogenic Drivers and Resistance Mechanisms

SpringWorks THERAPEUTICS

Three EGFR Inhibitors

First program targeting C797S mutants
Two additional first-in-class approaches

EGFR Mutant Tumors

- EGFR inhibition is a validated therapeutic approach – limitations of existing agents center on development of resistance and subgroups with suboptimal responses
- SpringWorks is working with Dana-Farber Cancer Institute and Stanford on a portfolio of next-generation EGFR inhibitors
- Most advanced program is addressing EGFR C797S-mediated osimertinib resistance utilizing a novel chemical strategy and is currently in lead optimization
- Additional strategies being advanced to address *de novo* EGFR driver and resistance mutations through first-in-class targeting approaches
- Research will be conducted in collaboration with Dr. Nathanael Gray (Stanford) and Drs. Pasi Janne, Michael Eck, and Jarrod Marto (Dana-Farber)

The SpringWorks Opportunity

Foundation in Place to Drive Sustainable Growth and Value Creation in 2022+

Focus Areas

2022+

- **Executing** late-stage development programs for nirogacestat and mirdametinib, with positive DeFi readout expected to yield first FDA-approved therapy for DT patients
- **Advancing** nirogacestat as a cornerstone of BCMA combination therapy across modalities with data readouts expected throughout 2022
- **Building** commercial infrastructure to support first potential commercial launch in 2023
- **Bolstering** R&D capabilities to advance preclinical portfolio into the clinic
- **Enhancing** exclusivity position through regulatory designations and IP portfolio development
- **Expanding** portfolio of opportunities as a partner of choice to industry and academia
- **Maintaining** strong financial position with disciplined capital allocation strategy and multi-year cash runway

Value-Driving Data Readouts and Program Updates Anticipated Across the Pipeline in 2022

Milestone	Expected Timing
Nirogacestat	
Phase 3 DeFi topline readout in desmoid tumors	✓
Nirogacestat + BCMA therapies	
Phase 1 trial initiation with AbbVie (ABBV-383)	2H
Initial clinical data from Phase 1 combo trial with GSK (BLENREP)	✓
Mirdametinib in pLGG	
Phase 1b/2 initial data to be presented at the ISPNO Conference	June 13-14
Mirdametinib + Lifirafenib	
Phase 1b/2 initial data readout in RAS/RAF-mutant solid tumors	✓
BGB-3245	
Phase 1 initial data readout in RAF-mutant solid tumors	✓
TEAD inhibitor program	
Preclinical data at AACR	✓
Potential for additional data readouts and updates from other programs ▪ Additional clinical data from BCMA combo trials in RRMM ▪ ReNeu trial for mirdametinib in NF1-PN	Full year

Note: ISPNO: International Symposium on Pediatric Neuro-Oncology; RRMM = relapsed/refractory multiple myeloma; LGG = low-grade glioma.

Q&A

Instructions

- Call the appropriate participant dial-in number
- Provide the operator with the conference ID

Dial-in numbers

- US: (844) 946-0285
- International: (602) 585-9676

Conference ID

- 4453188

Helpful keypad commands

- *0 - Operator assistance
- *6 - Self mute/unmute

Participants in Today's Q&A Session

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Badreddin Edris, PhD
Chief Operating Officer

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Chief Development Officer

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Thank you
SpringWorks
THERAPEUTICS