Corporate Presentation

July 2023

SpringWorks® THERAPEUTICS

Forward-Looking Statements

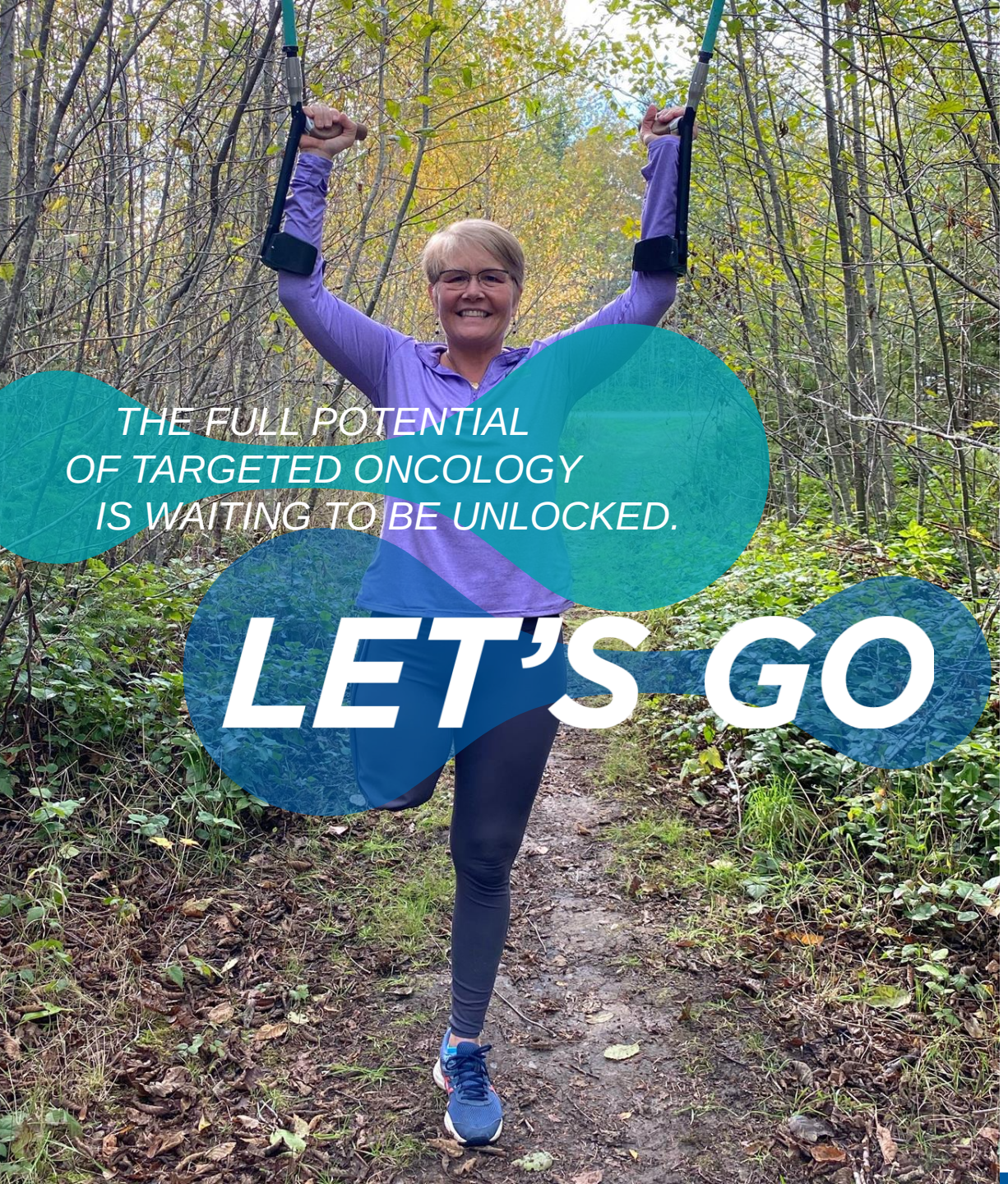
Note: Unless otherwise indicated, the information presented herein is as of July 2023 and made publicly available on July 27, 2023.

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 nirogacestat to become an important new treatment for adult patients with desmoid tumors, the potential for a Marketing Authorization Application for nirogacestat, expectations regarding the timing and results of the FDA’s review of the NDA for nirogacestat, including the FDA's PDUFA target action date for the NDA, and the adequacy of the data contained in the NDA to serve as the basis for an approval of nirogacestat for the treatment of adults with desmoid tumors, 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, expectations regarding the timing and results of topline data from the Phase 2b ReNeu clinical trial, our plans to file an Investigational New Drug Application for SW-682 in 2023, our plans to report additional clinical data of nirogacestat in combination with BCMA-directed therapies and initiate additional planned Phase 1 collaborator studies, our expectations regarding the potential for the Phase 1b dose expansion phase of brimarafenib, expectations about whether our patents for our lead assets will adequately protect SpringWorks against competition, 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 and our ability to realize the benefits expected from such collaborations, (ix) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, (x) the adequacy of our cash position to fund our operations through any time period indicated herein, (xi) our ability to establish manufacturing capabilities, and our and our collaboration partners’ abilities to manufacture our product candidates and scale production, and (xii) our ability to meet any specific milestones set forth herein.

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 protection extending beyond 2040
- **Experienced leadership team** with end-to-end expertise spanning drug development and commercialization
- **Robust balance sheet** with $528M in cash and disciplined capital allocation approach(1)

(1) Cash balance as of March 31, 2023.

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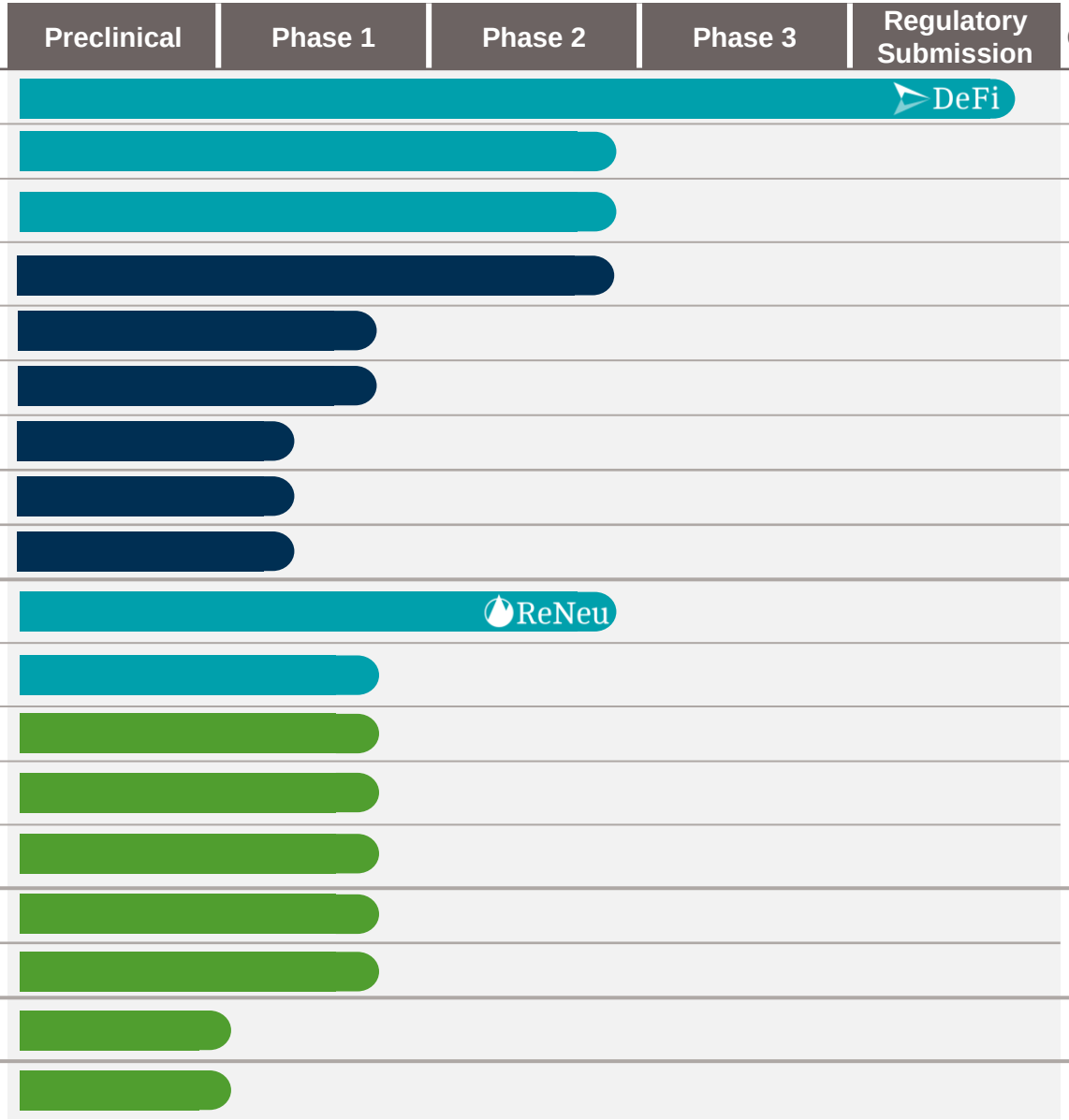
Diversified Targeted Oncology Pipeline Spanning Solid Tumors and Hematological Cancers

Compound	Indication	Development Approach	Collaborator(s)
Nirogacestat Gamma Secretase Inhibitor	Desmoid Tumors*	Monotherapy (adult)	DeFi
		Monotherapy (pediatric)	Children's Oncology Group
	Ovarian Granulosa Cell Tumors	Monotherapy	
	Multiple Myeloma *(BCMA Combinations)*	+ Belantamab mafodotin (belamaf) (ADC)	GSK
		+ Teclistamab (Bispecific)	Janssen
		+ Elranatamab (Bispecific)	Pfizer
		+ SEA-BCMA (mAb)	Seagen
		+ ABBV-383 (Bispecific)	abbvie
		+ Linvoseltamab (Bispecific)	REGENERON
Mirdametinib MEK Inhibitor	NF1-Associated Plexiform Neurofibromas†	Monotherapy	ReNeu
	Pediatric Low-Grade Gliomas	Monotherapy	St. Jude Children's Research Hospital
	MAPK Mutant Solid Tumors	+ Lifirafenib (Pan-RAF inhibitor)	BeiGene
	ER+ Metastatic Breast Cancer	+ Fulvestrant (SERD)	Memorial Sloan Kettering Cancer Center
	MEK 1/2 Mutant Solid Tumors	Monotherapy	Memorial Sloan Kettering Cancer Center
Brimarafenib(1) RAF Fusion & Dimer Inhibitor	MAPK Mutant Solid Tumors	Monotherapy	Mapkure(1)
	MAPK Mutant Solid Tumors	+ Mirdametinib	Mapkure(1)
SW-682 TEAD Inhibitor	Hippo Mutant Tumors	Monotherapy and combo	
EGFR Program	EGFR Mutant Tumors	Monotherapy and combo	



* Received Orphan Drug, Fast Track and Breakthrough Therapy Designations. † Received Orphan Drug and Fast Track Designations.

(1) Brimarafenib = BGB-3245. Being developed by MapKure, LLC, jointly owned by SpringWorks and BeiGene.

Rare Oncology | BCMA Combos | Biomarker-Defined Solid Tumors

Differentiated Late-Stage Assets With Near-Term Approval Potential in Rare Tumor Types and Broad Indication Expansion Opportunities

Nirogacestat

- On track to become the first FDA-approved therapy for desmoid tumors (PDUFA date: November 27, 2023)
- NDA based on Phase 3 DeFi trial, which achieved statistical significance on primary and all key secondary endpoints
- Significant opportunity to meaningfully impact the desmoid tumor community; ~5,500-7,000 desmoid tumor patients actively receive treatment annually in the U.S.
- Advancing expansion opportunities as monotherapy in ovarian granulosa cell tumors and BCMA combination therapy in multiple myeloma
- Durable patent portfolio with latest expiry in 2042

Mirdametinib

- Best-in-class product potential in late-stage development to serve patients with NF1-PN; topline data from Phase 2b ReNeu trial expected in 2H23
- Potentially optimized clinical profile with opportunity for differentiated activity, safety, and product format to enhance compliance and address unmet patient needs
- Meaningful addressable patient population;~100k patients with NF1 in the U.S. today with a ~30-50% lifetime risk of developing NF1-PN
- Monotherapy and combination studies ongoing in additional indications, including RAS/RAF-mutated solid tumors
- Durable patent portfolio with latest expiry in 2041

Note: NF1-PN: Neurofibromatosis type 1-associated plexiform neurofibroma; OvGCT: Ovarian granulosa cell tumors.

Value-Driving Milestones Across the Pipeline in 2023

Late-Stage Rare Oncology Portfolio	
Nirogacestat *(Gamma Secretase Inhibitor)*	✓ NDA submission in desmoid tumors accepted by FDA in 1Q23 with Priority Review ✓ Published Phase 3 DeFi trial data in a peer-reviewed journal (*NEJM* in March 2023) ✓ Completed enrollment of Phase 2 trial in ovarian granulosa cell tumor patients (May 2023) ✓ Presented additional DeFi analyses on secondary and exploratory endpoints at ASCO 2023 ❑ Secure FDA approval and launch first FDA-approved therapy for desmoid tumor patients (PDUFA: November 27, 2023)
Mirdametinib *(MEK Inhibitor)*	❑ Present topline data from the pediatric and adult cohorts in the Phase 2b ReNeu trial
Emerging Portfolio	
Nirogacestat + BCMA Therapies	✓ Expanded emerging data set with additional clinical data in combination with BCMA-directed therapies (EHA 2023) ❑ Support initiation of additional planned collaboration studies
MAPK Portfolio	✓ Dosed first patient in brimarafenib (BGB-3245) + mirdametinib combination study in MAPK-mutant solid tumors (1Q23) ✓ Reported additional clinical data from BeiGene collaboration programs (AACR 2023)
Preclinical Programs	✓ Presented additional preclinical data for SW-682 (AACR 2023) ❑ File IND for SW-682

Late-Stage Portfolio

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Nirogacestat

Desmoid Tumors

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

- Nirogacestat is an investigational novel oral, small-molecule, selective gamma secretase inhibitor
- NDA for nirogacestat in desmoid tumors accepted by the FDA with Priority Review and being evaluated under the FDA's RTOR program
- Fast Track and Breakthrough Therapy Designations received from FDA and Orphan Drug Designation granted from both FDA and European Commission(1)
- Phase 3 DeFi trial in adult patients with progressing desmoid tumors achieved statistical significance on primary and all key secondary endpoints; data published in March 9, 2023 issue of *New England Journal of Medicine*
- Unlocking additional expansion opportunities, including monotherapy development in ovarian granulosa cell tumors and BCMA combination therapy development in multiple myeloma
- Eight Orange Book-listable patents for nirogacestat with latest expiry in 2042

Nirogacestat in Desmoid Tumors NDA PDUFA Date:	**Nov 27, 2023**
Indications Under Development:	**3**
U.S. Patent Protection:	**2042**

(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.

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 can include lesion ulceration, organ dysfunction, amputation, long-lasting pain, disfigurement; DTs 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

Sources: (1) Penel et al., European Journal of Cancer, 2017; (2) Tsagozis et al., Annals of Medicine & Surgery, 2017; (3) Easter et al., Annals of Surgical Oncology, 1989.

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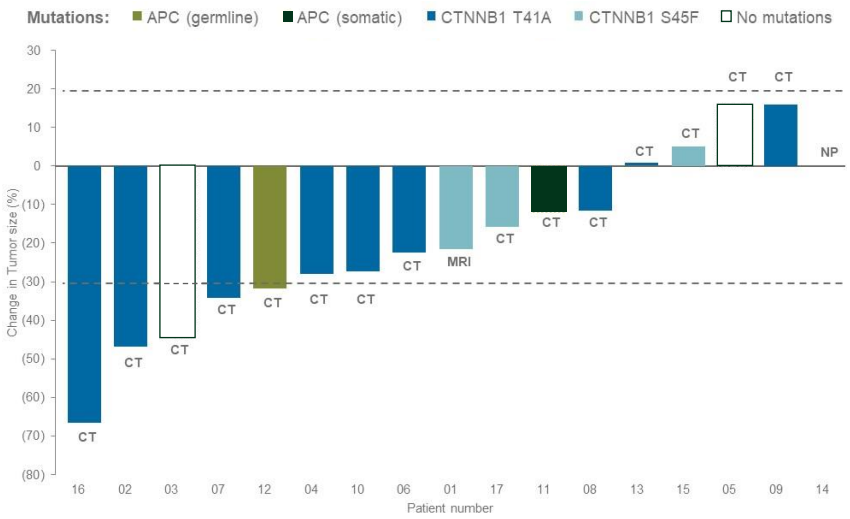
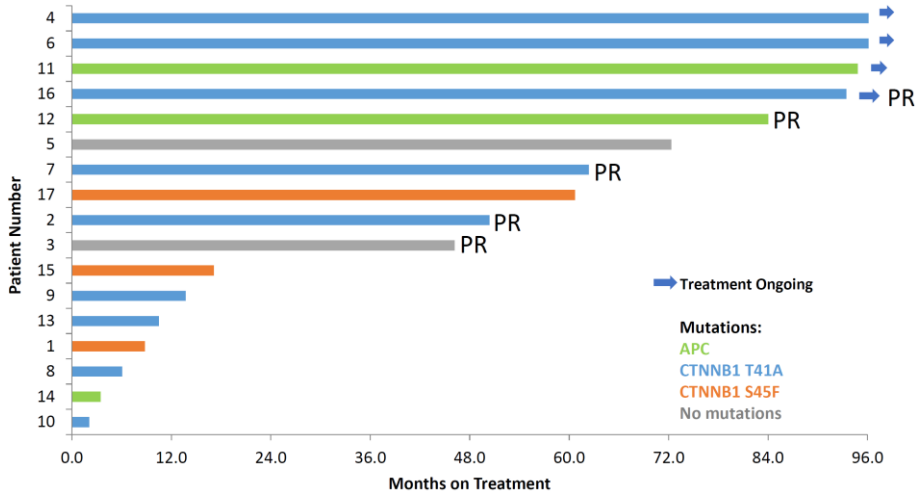
Encouraging Phase 2 Data With Extended Duration of Treatment Set the Stage for Phase 3 DeFi Trial

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

Clinical Responses by RECIST v1.1



Long-Term Progression Free Survival



- **mPFS: Not reached by publication date 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)
  - ORR of 29.4% (5/17) with no progressive disease

- **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; no PD maintained with follow-up
  - Nirogacestat was generally well tolerated
    - > Most commonly (>50%) reported treatment-related AEs included diarrhea, fatigue, nausea, AST increase, lymphocyte decrease, hypophosphatemia, and rash (maculopapular)

Source: Kummar et al., 2017. O'Sullivan; Coyne et al., ASCO, 2022.

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

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

DeFi

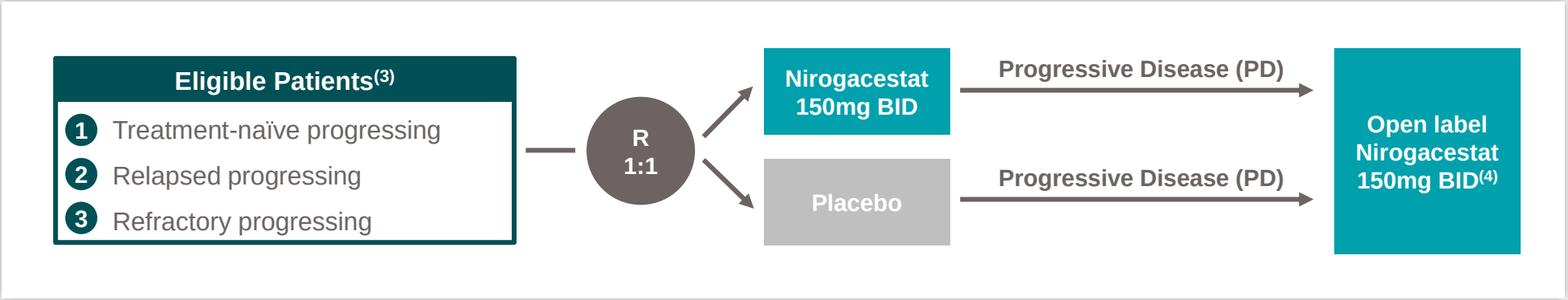
PHASE 1 | PHASE 2 | **PHASE 3**

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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Baseline Demographics and Characteristics

Demographics/Characteristics, ITT Population	Nirogacestat (n=70)	Placebo (n=72)
Age, median (range), y	33.5 (18, 73)	34.5 (18, 76)
Sex, n (%)		
Male	25 (36)	25 (35)
Female	45 (64)	47 (65)
Somatic mutations in analyzed patients, n (%)[a]		
APC	11 (22)	11 (21)
CTNNB1	43 (84)	42 (79)
Tumor location, n (%)		
Intra-abdominal	17 (24)	18 (25)
Extra-abdominal	53 (76)	54 (75)
Focal category, n (%)		
Single	43 (61)	41 (57)
Multifocal	27 (39)	31 (43)
Desmoid tumor treatment status, n (%)		
Treatment naïve	18 (26)	14 (19)
Refractory/Recurrent	52 (74)	58 (81)
Number of lines of any prior therapy, median (range)	2 (0, 14)	2 (0, 19)
Prior therapies, n (%)		
Prior systemic therapy	43 (61)	44 (61)
Chemotherapy	24 (34)	27 (38)
Tyrosine kinase inhibitor	23 (33)	24 (33)
Sorafenib	17 (24)	18 (25)
Prior radiation therapy	16 (23)	16 (22)
Prior surgery	31 (44)	44 (61)
Patients with uncontrolled pain per BPI-SF API >4, n (%)[b]	27 (39)	31 (43)

Source: Kasper et al., *ESMO,* 2022; Gounder et al., *NEJM,* 2023. Data as of the time of primary analysis (04/07/22).
a) Evaluable samples not available for all patients. Samples were analyzed for 51 and 53 patients in the nirogacestat and placebo arms, respectively.
b) Defined as a score of >4 calculated as the average of the daily BPI–SF Item 3 “Worst Pain in Past 24 hours” over the 7-day period before the baseline visit.
Note: API, average pain index; BPI-SF, Brief Pain Inventory–Short Form ITT; intention to treat.

Nirogacestat Demonstrated Highly Significant and Clinically Meaningful Impact on Primary and All Key Secondary Endpoints

DeFi

Clinical Outcome Measures		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

Source: Kasper et al., ESMO, 2022. Data as of the time of primary analysis (04/07/22). Gounder at al., CTOS, 2022.
Note: Differences at Cycle 10 were statistically significant and clinically meaningful. DTSS total symptom score includes pain, fatigue, swelling, muscle weakness, and difficulty moving.
Note: GODDESS: GOunder/Desmoid Tumor Research Foundation DEsmoid Symptom/Impact Scale; EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; PRO: patient-reported outcome.

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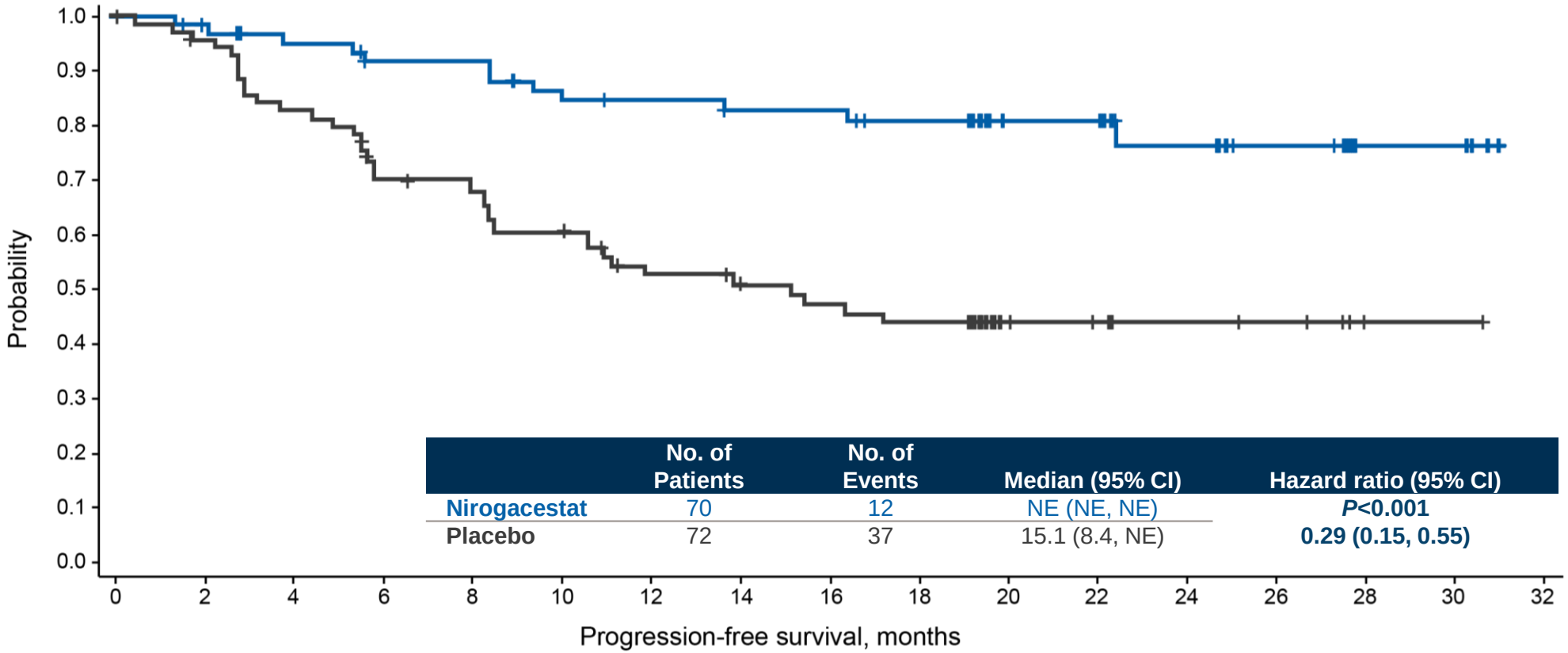
Nirogacestat Significantly Reduced Risk of Disease Progression



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

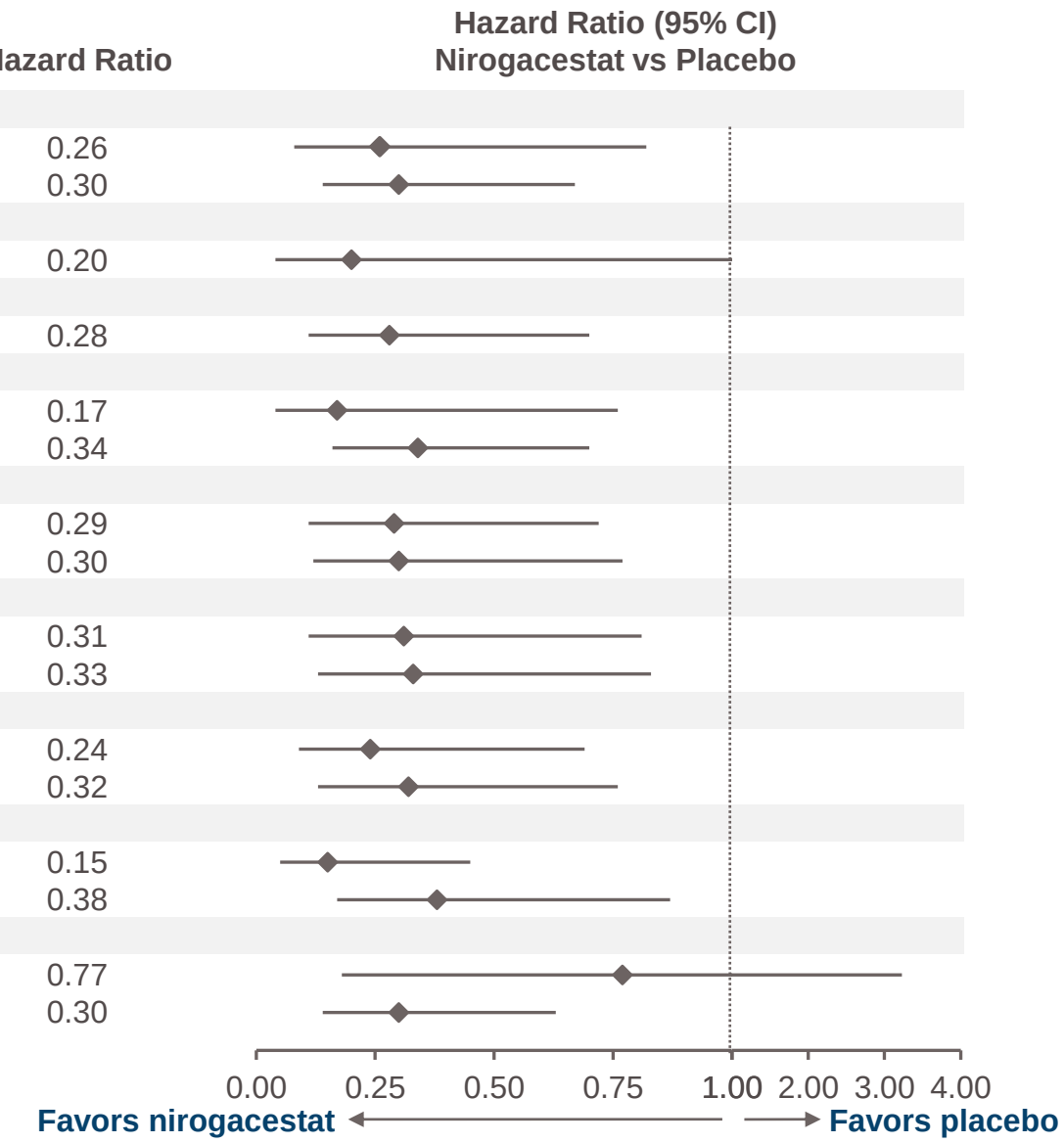
No. of Participants at Risk:

Placebo	72	67	58	47	45	40	32	29	27	25	10	8	6	5	1	1	0
Nirogacestat	70	63	56	52	52	47	46	44	44	41	26	26	17	12	4	4	0

Source: Kasper et al., *ESMO,* 2022. Data as of the time of primary analysis (04/07/22).
Note: Median follow-up time was 19.2 months for nirogacestat and 10.9 months for placebo.
Note: NE: not estimable.

PFS Benefit With Nirogacestat Was Observed Across Prespecified Subgroups

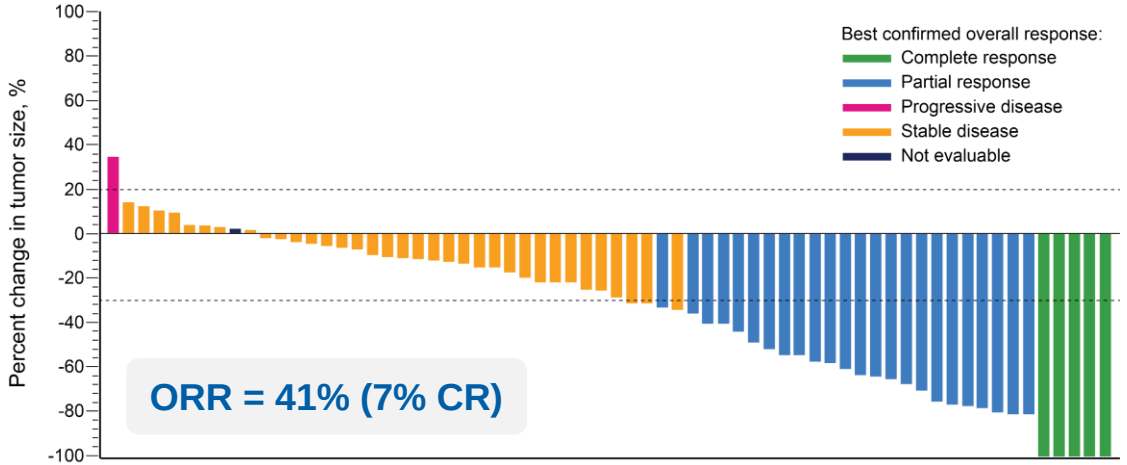
	Nirogacestat	Placebo	Hazard Ratio
	no. of events / no. of patients		
Sex			
Male	4 / 25	11 / 25	0.26
Female	8 / 45	26 / 47	0.30
***APC* mutation**			
Yes	2 / 11	8 / 13	0.20
***CTNNB1* mutation**			
Yes	6 / 43	21 / 42	0.28
Target tumor location			
Intra-abdominal	2 / 17	11 / 18	0.17
Extra-abdominal	10 / 53	26 / 54	0.34
Focality			
Single	6 / 43	19 / 41	0.29
Multifocal	6 / 27	18 / 31	0.30
Prior surgery			
Yes	5 / 31	23 / 44	0.31
No	7 / 39	14 / 28	0.33
Prior chemotherapy			
Yes	5 / 24	17 / 27	0.24
No	7 / 46	20 / 45	0.32
Prior TKI treatment			
Yes	4 / 23	16 / 24	0.15
No	8 / 47	21 / 48	0.38
Treatment status			
No previous treatment	3 / 18	5 / 14	0.77
Refractory or recurrent disease after previous treatment	9 / 52	32 / 58	0.30



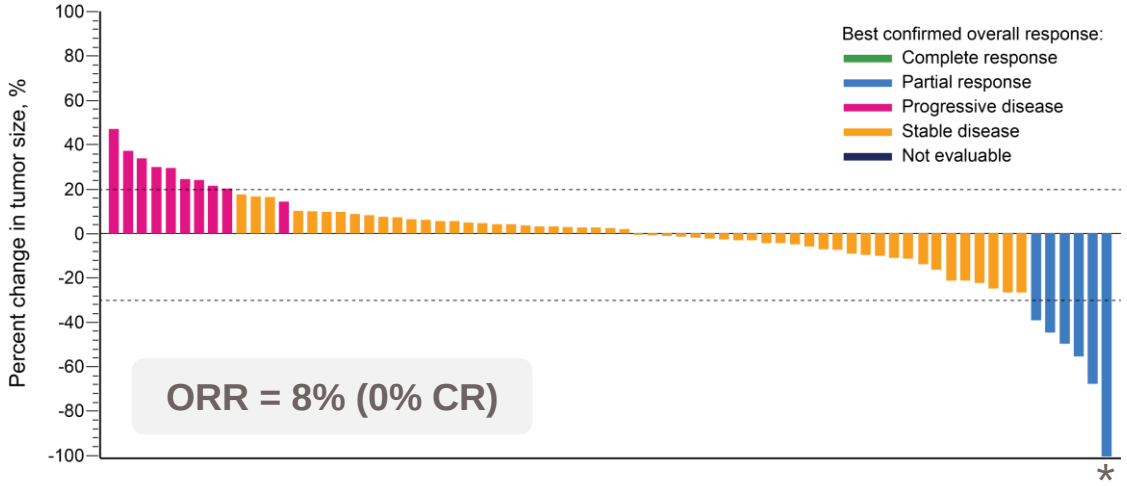
Source: Kasper et al., *ESMO,* 2022; Gounder et al., *NEJM,* 2023. Data as of the time of primary analysis (04/07/22).
Note: PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

Nirogacestat Treatment Resulted in Substantial Reductions in Tumor Size

Nirogacestat (n=70)



Placebo (n=72)

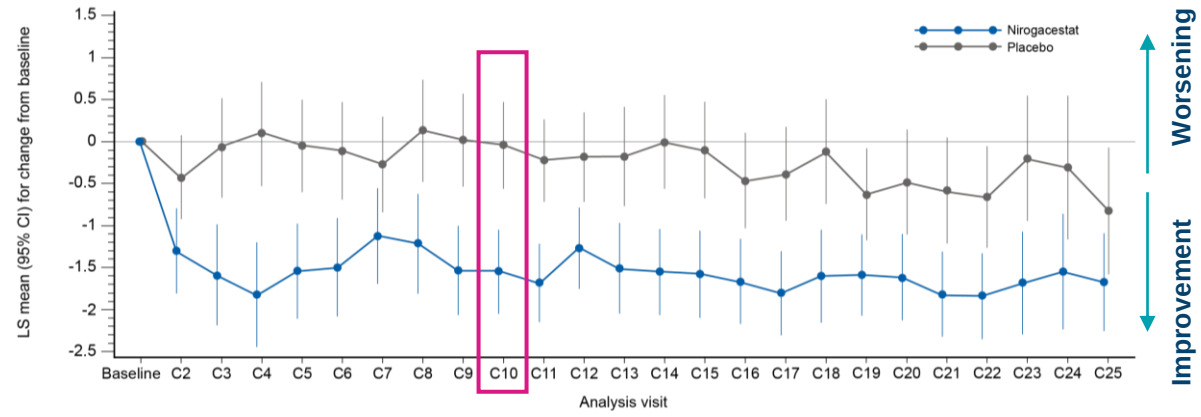


Median time to objective response of 5.6 months for nirogacestat vs. 11.1 months for placebo

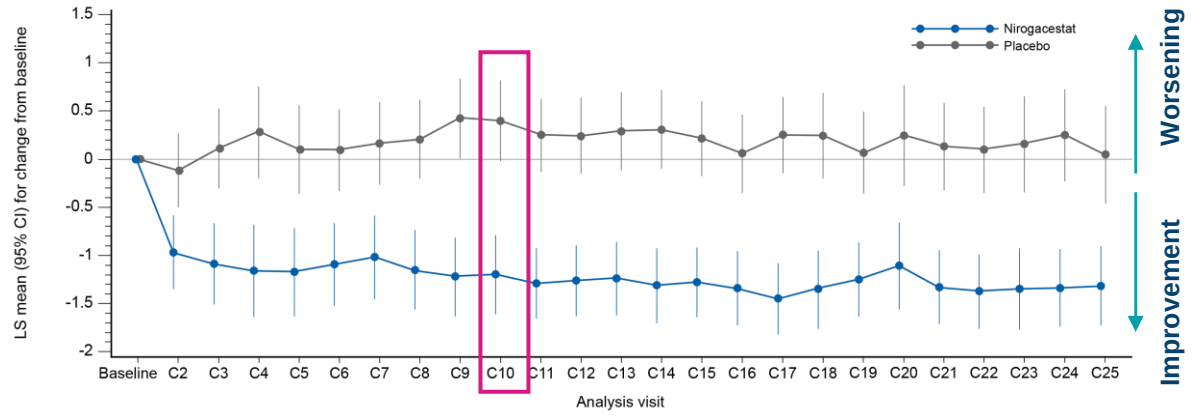
Source: Kasper et al., ESMO, 2022. Data as of the time of primary analysis (04/07/22). Gounder at al., CTOS, 2022.
* Patient had a complete resolution of the target lesion but still had documented non-target lesion; therefore, not a complete response.
Note: Best percent change values are averaged between 2 blinded independent reviewers unless a reader was selected for adjudication, in which case only the adjudicated value is presented.

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

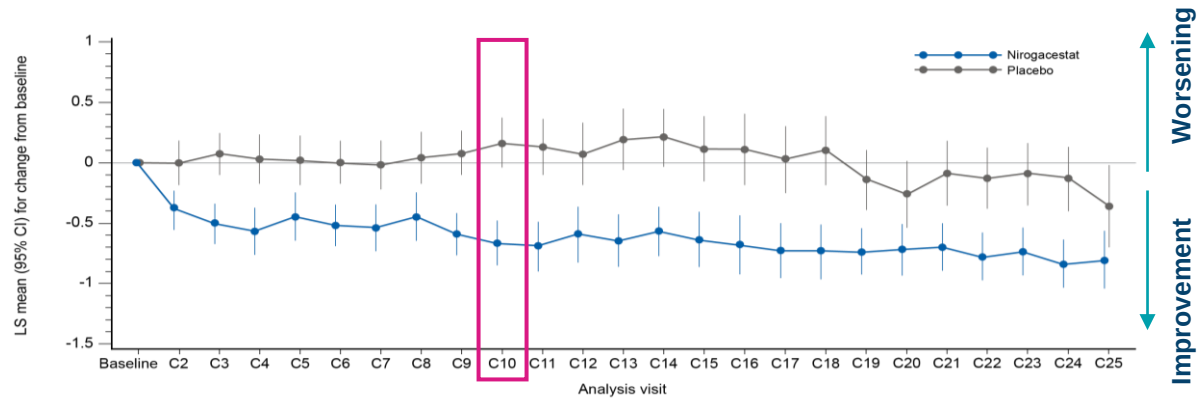
Brief Pain Inventory-Short Form – Average Pain Intensity



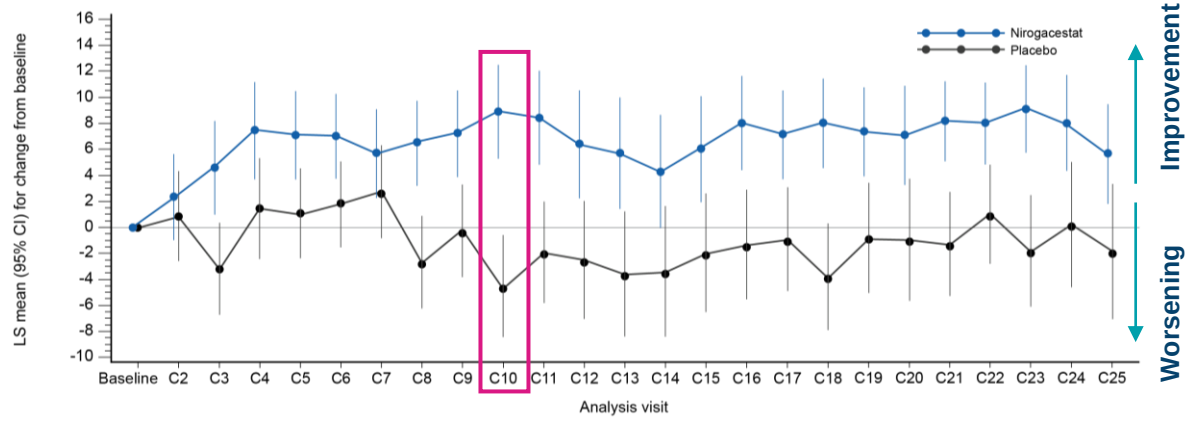
DT-Specific Symptom Severity (GODDESS DTSS)



Physical Functioning Impact Score (GODDESS DTIS)



Physical Functioning (EORTC QLQ-C30)



Source: Kasper et al., ESMO, 2022. Data as of the time of primary analysis (04/07/22).
Note: DTIS: Desmoid Tumor Impact Scale; DTSS: Desmoid Tumor Symptom Score; Symptom/Impact Scale; EORTC QLQ C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; GODDESS: GOunder /Desmoid Tumor Research Foundation DEsmoid Symptom/Impact Scale; LS: least squares.
Mean (SD) baseline scores: nirogacestat, 3.2 (3.26); placebo, 3.3 (3.31). Differences at Cycle 10 were statistically significant and clinically meaningful. LS mean change from baseline represents the 7-day average.

Nirogacestat Safety Profile

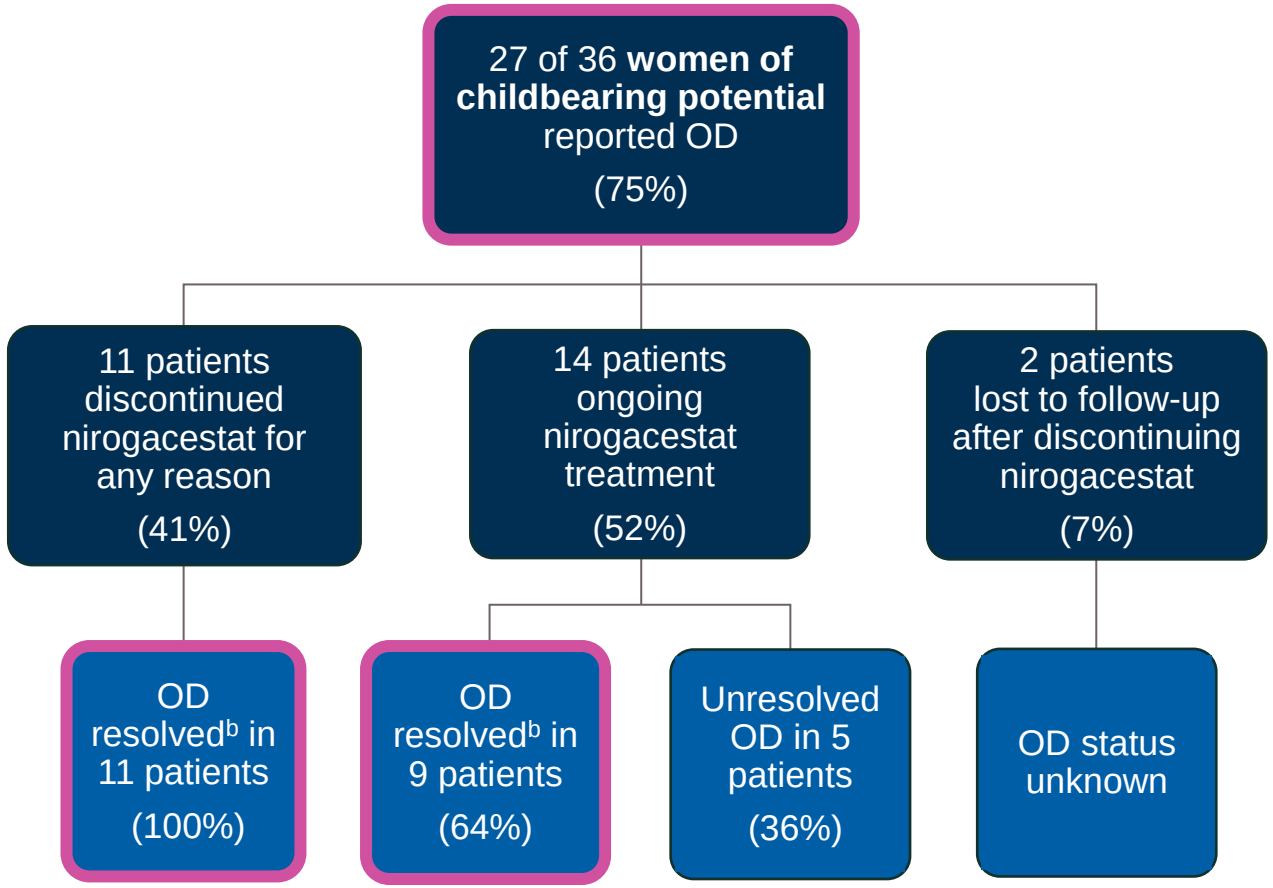
Safety population, n (%)	Nirogacestat (n=69)		Placebo (n=72)	
Duration of study drug exposure, median (range), months	20.6 (0.3, 33.6)		11.4 (0.2, 32.5)	
Dose intensity, median (range), mg/d	288.3 (169, 300)		300.0 (239, 300)	
	Any Grade	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Any TEAE	69 (100)	39 (57)	69 (96)	12 (16)
TEAEs of any grade reported in ≥25% of patients in either arm				
Diarrhea	58 (84)	11 (16)	25 (35)	1 (1)
Nausea	37 (54)	1 (1)	28 (39)	0
Fatigue	35 (51)	2 (3)	26 (36)	0
Hypophosphatemia	29 (42)	2 (3)	5 (7)	0
Rash, maculopapular	22 (32)	4 (6)	4 (6)	0
Headache	20 (29)	0	11 (15)	0
Stomatitis	20 (29)	3 (4)	3 (4)	0
TEAEs leading to death	0		1 (1)[a]	
Dose reductions due to TEAEs	29 (42)		0	
Discontinuations due to TEAEs	14 (20)[b]		1 (1)[b]	

95% of TEAEs were Grade 1 or 2; the first onset of TEAEs in most patients occurred during Cycle 1

Source: Kasper et al., *ESMO,* 2022. Data as of the time of primary analysis (04/07/22).
a) Death due to sepsis.
b) TEAEs leading to discontinuations in ≥1 patient include gastrointestinal disorders (n=5 [4%]), ovarian dysfunction (n=4 [3%]), alanine aminotransferase increase (n=3 [2%]), aspartate aminotransferase increase (n=2 [1%]), and metabolism/nutritional disorders (n=2 [1%]).
Note: TEAE, treatment-emergent adverse event.

Frequency and Resolution of Ovarian Dysfunction Observed With Nirogacestat

- OD is a composite adverse event associated with changes in female reproductive hormone levels and clinical manifestations[1,2]
- Protocol-mandated serum hormone collection at baseline and cycles 1, 2, 4, and every 3 thereafter
- Among women of childbearing potential, OD[a] was observed in 75% receiving nirogacestat and 0% receiving placebo
  - Median time to first onset of OD: 8.9 weeks
  - Median duration of OD events: 21.3 weeks
- No changes in male hormonal levels or TEAEs pertaining to male reproductive potential were reported



Source: Kasper et al., *ESMO,* 2022. Data as of the time of primary analysis (04/07/22). Gounder et al., *CTOS*, 2022. Gounder et al., *NEJM,* 2023.
a) OD among women of childbearing potential was defined by investigators who reported the MedDRA Preferred Terms of amenorrhea, premature menopause, menopause, and ovarian failure.
b) As of July 20, 2022.
c) Resolution of OD events was defined by the investigator.
Note: OD, ovarian dysfunction; TEAE, treatment-emergent adverse event.
1) Thurston et al., *Obstet Gynecol Clin North Am.* 2011;38:489-501; 2) Mauri et al., *Front Endocrinol (Lausanne).* 2020;11:572388.

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

DeFi

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.
(2) Sources: Messersmith et al., Clin Cancer Res., 2015; O'Sullivan Coyne et al., ASCO, 2022.

SpringWorks THERAPEUTICS

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

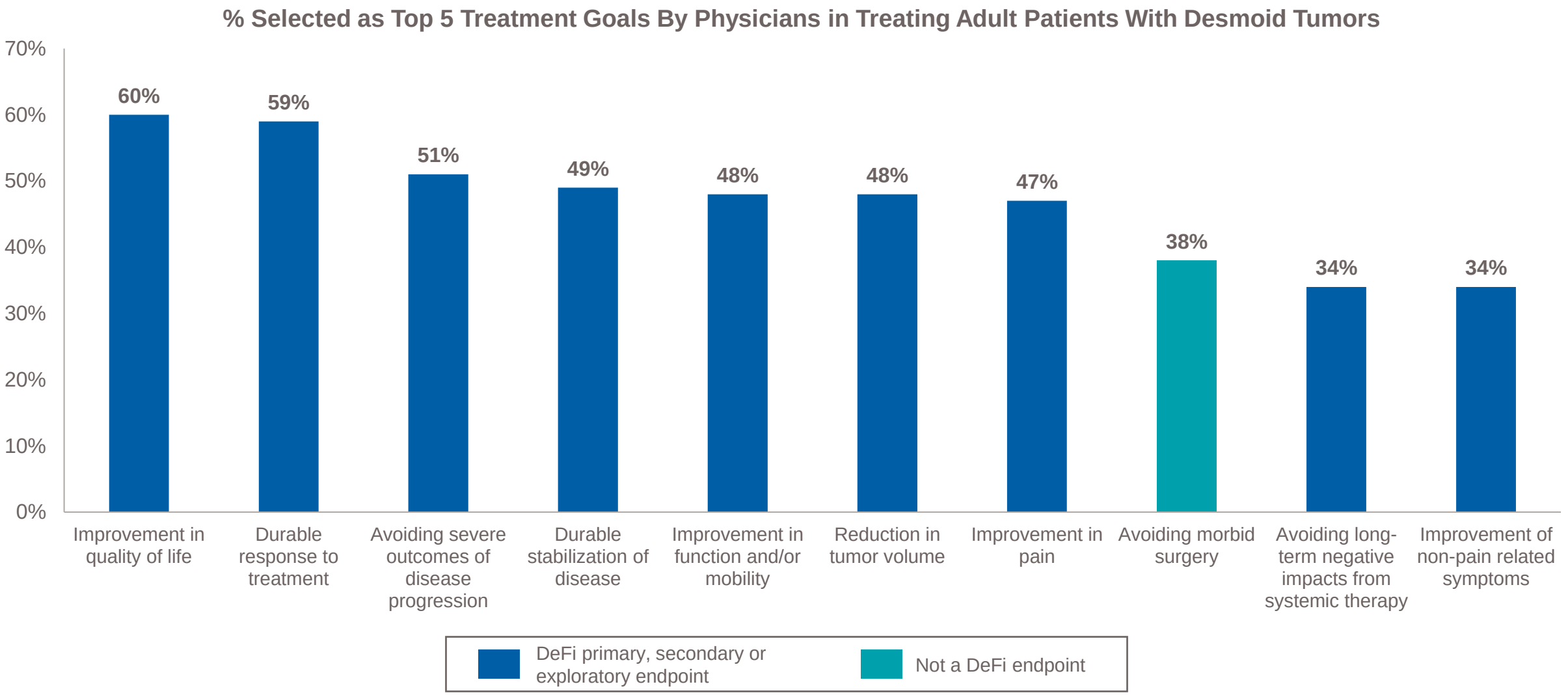
- Meaningful proportion of the diagnosed prevalent population could be addressed with a new treatment option

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

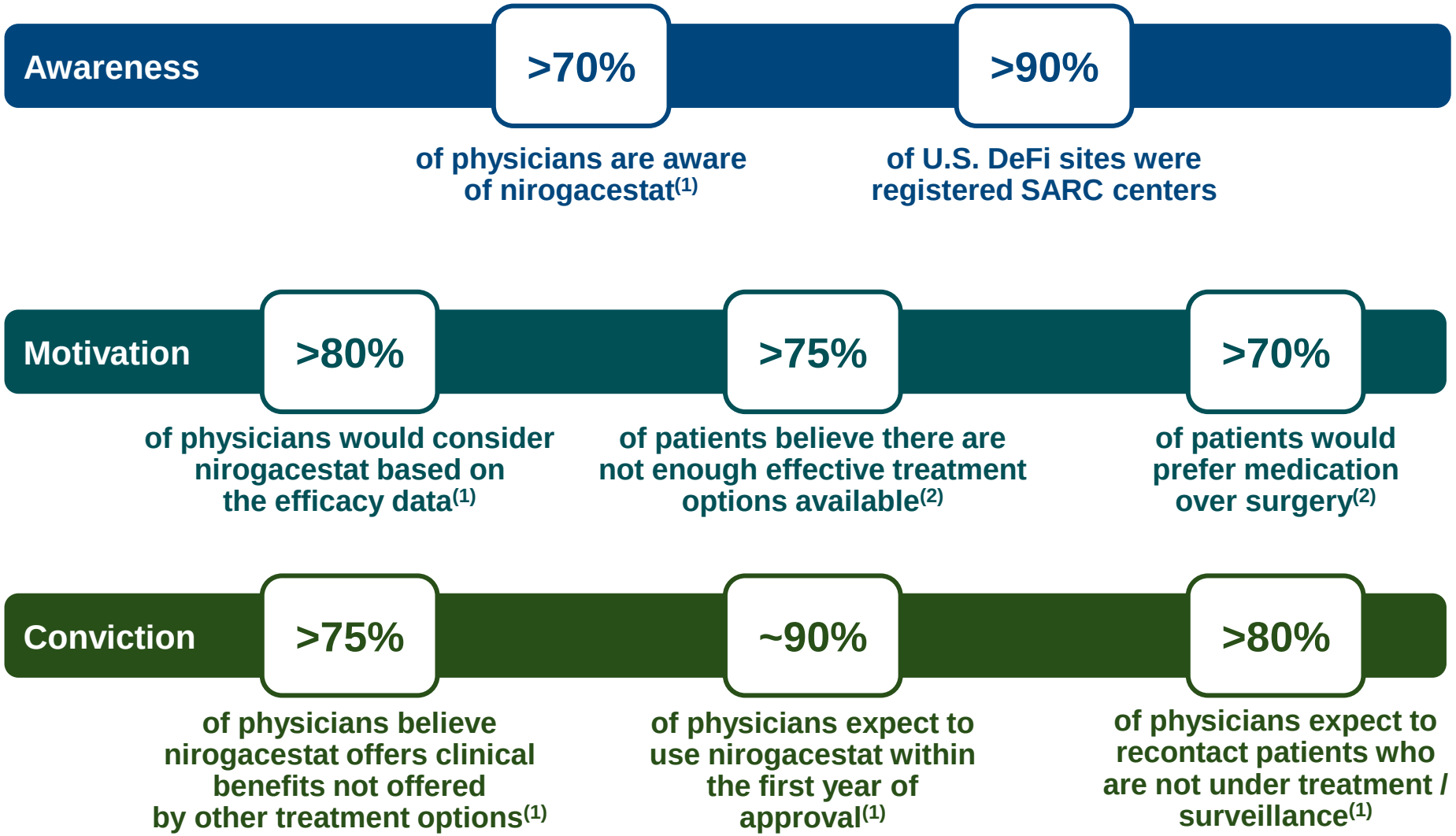
Sources: (1) Van Broekhoven et al., Annals of Surgical Oncology, 2015; (2) Reitamo et al., American Journal of Clinical Pathology, 1982; (3) Anneberg et al., Cancer Epidemiology, 2022; (4) EMR data and KOL Qualitative interviews; (5) Skubitz et al., Mayo Clin Proc, 2017; (6) Easter DW, Halasz NA, Annals of Surgical Oncology, 1989.

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



Source: SWTX Primary Market Research, 2Q22 (n=100 oncologists).

Physician and Patient 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

Source: (1) SWTX Primary Market Research, 2022 (n=200 oncologists).

SpringWorks THERAPEUTICS

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 accepted in 1Q23 with Priority Review; potential to be first FDA-approved therapy in desmoid tumors (November 27, 2023 PDUFA date)
Commercial Execution	Launch activities rapidly advancing to ensure successful preparation of market, organization and brand

Note: NDA: New Drug Application; QoL: quality of life.

Mirdametinib

NF1-PN

SpringWorks® THERAPEUTICS

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
- Topline data from Phase 2b ReNeu trial in NF1-PN is expected in 2H23; NF1 is one of the largest genetic tumor predisposition syndromes with ~100k patients in the U.S. 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

Topline Data from ReNeu Trial Expected:	**2H23**
Clinical Trials Ongoing or On Track for 2023 Initiation:	**6**
U.S. Patent Protection:	**2041**

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

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

Kendall
NF1 Patient

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 US[1]
- NF1 pts have a ~30-50% lifetime risk of developing NF1-PN[2]

TREATMENT PARADIGM

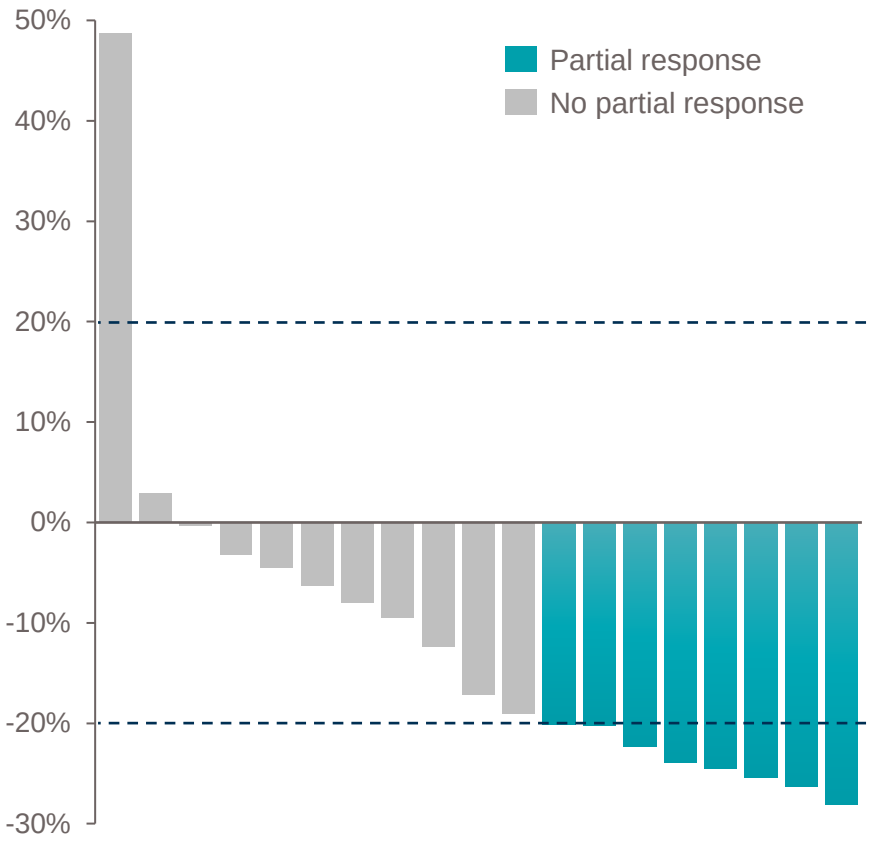
- In a physician survey, ~70% indicated that high unmet needs remain for adult and pediatric NF1-PN patients[3]
- Surgical resection is difficult due to the infiltrative tumor growth pattern along nerves and is rarely performed[3,4]
- Up to ~50% of NF1-PN patients receive systemic treatment based on physician surveys[3]
- 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[3,5]
  - 50%+ of patients discontinued treatment within 1 year[6]

Sources: (1) Lammert et al., Arch Dermat, 2005. U.S. Census Data; (2) Fisher et al., Neuro-Oncology, 2022; (3) SpringWorks Market Research; (4) Korf, American Journal of Medical Genetics, 1999; (5) Koselugo prescribing information; (6) Yang et al., SNO, 2022.

ReNeu Trial Builds Upon Encouraging Phase 2 Results, Which Demonstrated Initial Clinical Activity, QoL Improvement for NF1-PN Patients and a Differentiated Safety Profile vs. Other MEK Inhibitors

PHASE 2 | PHASE 2B

Maximum Tumor Volume Change from Baseline



Trial Design and Clinical Activity

- N = 19 patients with inoperable and symptomatic or growing PNs, aged 16-39 years (median age: 24)
- 2 mg/m^2 (up to 4 mg) BID without regard to food dosed intermittently (3 weeks on/1 week off) for maximum 24 cycles[1]
- 8 patients (42%) achieved a PR[2] by cycle 12; 10 patients (53%) had SD
- PRO measures[3] showed statistically significant improvement with mirdametinib treatment in the following areas:
  - Pain reduction for all patients on treatment by cycle 4
  - Cognitive function improvement for all patients on treatment at cycle 8
  - QoL improvement for patients who achieved a PR by cycle 8

Safety and Tolerability

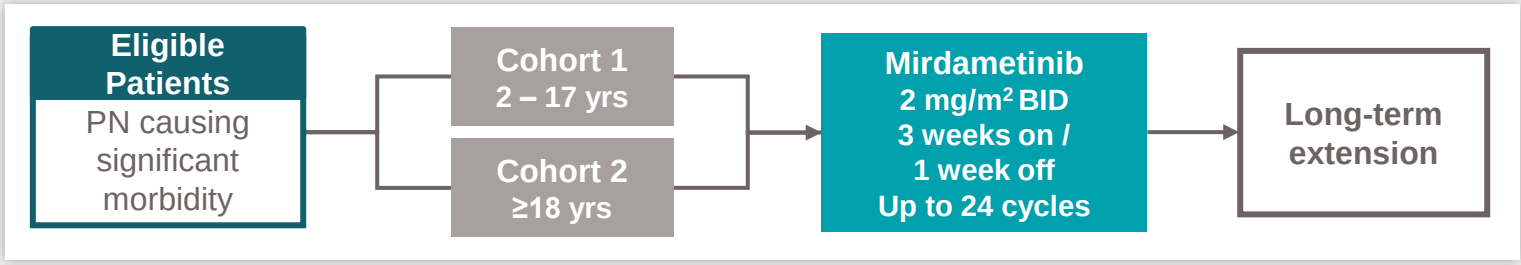
- Dose and schedule minimized historical class toxicities
  - Most common adverse events were Gr1 and Gr2 acneiform rash, fatigue, and nausea
  - No Gr4 or Gr5 events; two Gr3 treatment-related events reported (pain events occurring in the same patient)
- 5 patients required dose reductions; no patient discontinued due to dose limiting toxicity
  - Gr1 rash (n = 2), Gr2 nausea (n = 1), Gr2 fatigue (n = 1), and Gr3 abdominal and/or back pain (n = 1)

Source: Weiss et al., *Journal of Clinical Oncology,* 2021.
(1) Patients without at least 15% reduction in target tumor volume after 8 courses or at least 20% reduction after 12 courses were removed from therapy;
(2) Partial response (PR) defined as a ≥20% reduction in the volume of the target plexiform neurofibroma lesion for ≥4 weeks;
(3) Patient-reported outcome (PRO) measures include the Numerical Rating Scale-11 to assess pain intensity, Brief Pain Inventory Pain Interference subscale to assess impact of pain on daily functioning, and the Pediatric Quality of Life (QoL) Inventory NF1 module to assess disease-specific health-related QoL measures.

Mirdametinib for NF1-PN: ReNeu Trial On Track for Topline Readout in 2H23

Phase 2b ReNeu Trial Summary

TRIAL DESIGN	▪ Phase 2b open-label; n = 114 patients in 2 cohorts (pediatric and adults) across ~50 U.S. sites ▪ 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 ▪ Pediatric formulation (dispersible tablet) introduced in 2H20
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



Clinical / Regulatory Milestones

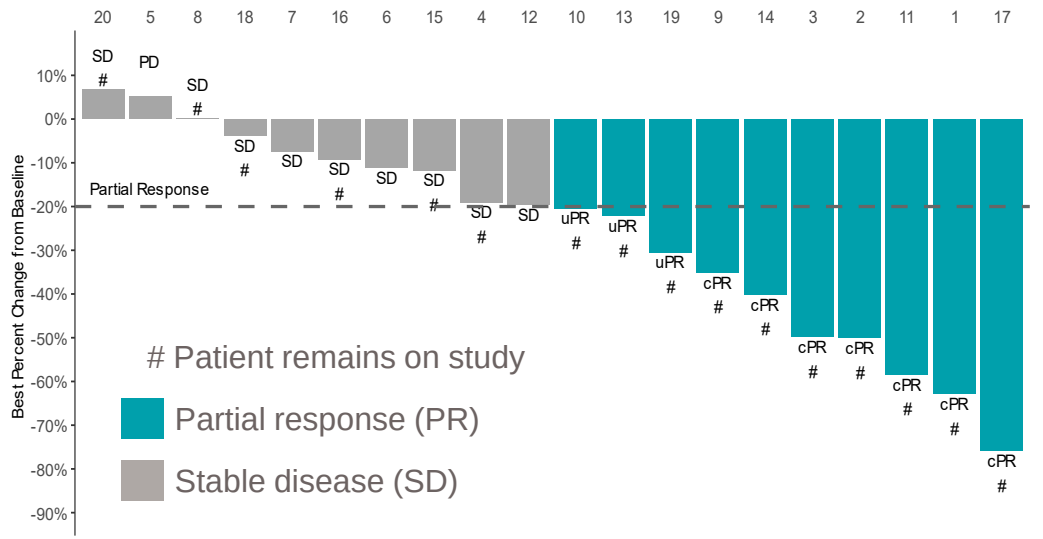
- ✓ Initiate Phase 2b trial in children and adults with NF1-PN (2H19)
- ✓ Achieve full enrollment (n=114) in Phase 2b trial (2H21)
- ✓ Complete FDA Type C Meeting and receive agreement on proposed statistical analysis plan, as well as guidance on NDA submission expectations (4Q22)
- ❑ **Planned disclosure of topline data (2H23)**
- ❑ **Anticipated NDA submission to FDA (1H24)**

Note: BICR: blinded independent central review; BID: twice daily; QoL: quality of life.

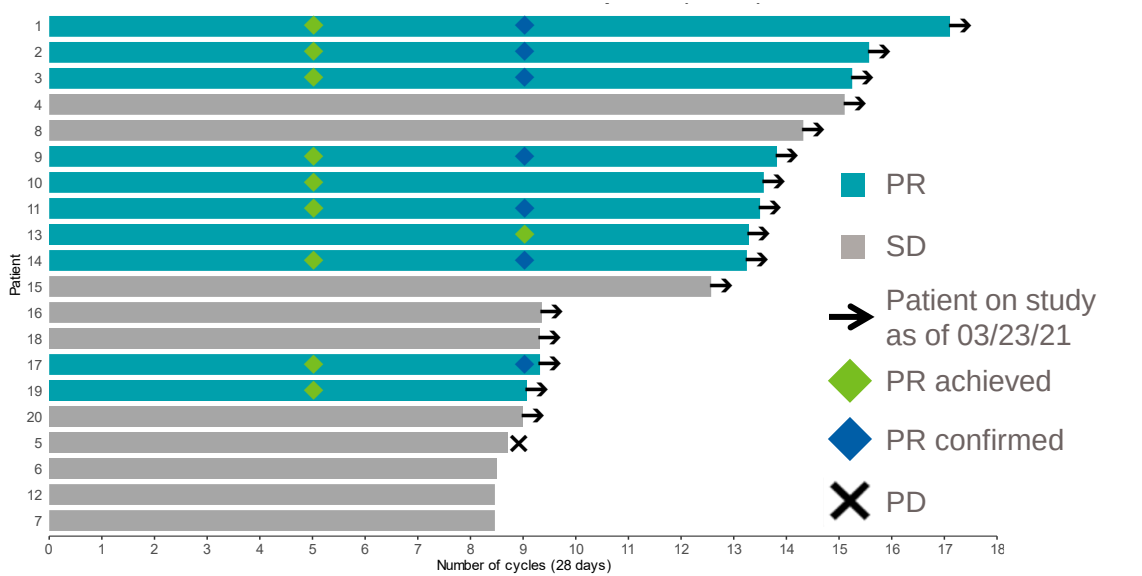
Interim Data Update From ReNeu Trial Adult Stratum Presented at CTF in June 2021

PHASE 2 | PHASE 2B

Best Tumor Responses



Treatment Duration and Response



- **50% of patients have achieved an objective response by BICR (n = 20)**
  - 10 of the first 20 patients enrolled have achieved a PR by BICR
  - 7/10 patients had their PRs confirmed
  - Responders had a median tumor volume reduction of 45%
- **Median time on treatment for these 20 patients was 13 cycles (approximately 12 months)**
  - 80% of patients remain on study as of data cutoff
  - All patients with objective responses continue on study
  - Reason for patients discontinuing therapy include: (1) PD, (1) participant decision, (1) AE[1] and (1) other[2]

Source: Moertel et al., Children's Tumor Foundation (CTF) 2021 Presentation.
BICR: Blinded Independent Central Review; cPR: confirmed partial response; PD: progressive disease; PR: partial response (defined as a ≥20% reduction in tumor volume); SD: stable disease; uPR: unconfirmed partial response
Note: Data are from the first 20 adult patients enrolled in the Phase 2b ReNeu trial (data cutoff: March 23, 2021), representing a database snapshot, and may change based on ongoing routine data monitoring. The ReNeu trial is ongoing, and these results may not be predictive of future data presentations or the final study results. Confirmed PR means subsequent scan confirmed (20%) reduction in tumor volume.
(1) Due to Grade 1 diarrhea.
(2) Patient unable to undergo required MRI imaging due to titanium rod implant from non-treatment related worsening of scoliosis.

Safety Summary From Interim Update: Treatment-Emergent and Treatment-Related AEs

PHASE 2 | PHASE 2B

	Treatment-Emergent AEs (≥15% of patients)			Treatment-Related AEs	
	All Grades	Grade 3	Grade 4	Grade 3	Grade 4
Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)
At least 1 AE	20 (100)	3 (15)	-	1 (5)	-
Dermatitis acneiform / Rash maculopapular	18 (90)	1 (5)	-	1 (5)	-
Nausea	12 (60)	-	-	-	-
Diarrhea	10 (50)	-	-	-	-
Abdominal Pain	6 (30)	-	-	-	-
Fatigue	6 (30)	-	-	-	-
Vomiting	5 (25)	-	-	-	-
Dry skin	4 (20)	-	-	-	-
Ejection fraction decreased	4 (20)	-	-	-	-
Constipation	3 (15)	-	-	-	-
Dyspnea	3 (15)	1 (5)	-	-	-
Gastroesophageal reflux disease	3 (15)	-	-	-	-
Arthralgia	3 (15)	-	-	-	-
Ear pain	3 (15)	-	-	-	-
Urinary tract infection	3 (15)	-	-	-	-
Coronavirus infection	-	1 (5)	-	-	-
Coronavirus test positive	-	1 (5)	-	-	-
Headache	-	1 (5)	-	-	-
Non-cardiac chest pain	-	1 (5)	-	-	-
Scoliosis	-	1 (5)	-	-	-

- Mirdametinib has been generally well tolerated
- Most adverse events (AEs) have been Grade 1 or 2
- Only one Grade 3 treatment-related AE (rash) and no Grade 4 or Grade 5 AEs
- One patient had a dose reduction required due to Grade 3 rash

Note: Data are from the first 20 adult patients enrolled in the Phase 2b ReNeu trial (data cutoff: March 23, 2021), representing a database snapshot, and may change based on ongoing routine data monitoring. The ReNeu trial is ongoing, and these results may not be predictive of future data presentations or the final study results.

With the ReNeu Trial, Mirdametinib Has the Opportunity to Address the Substantial Unmet Needs That Remain for NF1-PN Patients

Opportunities for Differentiation

- Therapeutic option for broader age spectrum (pediatric and adult patients)
- Enhanced efficacy
- Improved safety and tolerability
- More convenient therapy to drive compliance (lack of food effect, limited drug-drug interactions, optimized dose/schedule)
- Differentiated product formulation for pediatric population therapy

Nirogacestat

Ovarian Granulosa Cell Tumors

SpringWorks® THERAPEUTICS

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 U.S. incidence: 1,000-1,500 per year Significant prevalent population: ~10,000-15,000[4,5]

NO APPROVED TREATMENTS

- Early-stage disease managed with surgery; however, ~45% of patients experience post-surgical recurrence[1]
- No currently approved therapies; limited effective treatment options in recurrent setting

Phase 2 Trial Summary

TRIAL DESIGN

- Single-arm open label study, enrolling ~40 patients with recurrent OvGCT with ≥ one line of prior systemic therapy
- 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; announced full enrollment in May 2023

Sources: (1) Klar et al., J Surg Oncol., 2023; (2) Li et al., Journal of Ovarian Research, 2018; (3) Irusta et al., Biol Reprod, 2013; (4) SEER; (5) Torre L. et al., CA Cancer J Clin, 2018.

Gamma Secretase Inhibitors Could Address Need for Targeted Therapy Option 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*, which 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

NCCN Guidelines Highlight Substantial Unmet Need for OvGCT Patients Given 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

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

- Key insights related to unmet need 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: 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. SpringWorks market research.

Emerging Portfolio

SpringWorks® THERAPEUTICS

Broad Emerging Pipeline Continues to Advance and Offers Substantial Upside Potential

Multiple Myeloma – Nirogacestat + BCMA-Directed Therapy Combinations

+ Belantamab mafodotin (ADC)	Phase 2 ongoing
+ Teclistamab (Bispecific)	Phase 1 ongoing
+ Elranatamab (Bispecific)	Phase 1b/2 ongoing
+ SEA-BCMA (mAb)	Phase 1 planned
+ ABBV-383 (Bispecific)	Phase 1b planned
+ Linvoseltamab (Bispecific)	Phase 1b planned

MAPK-Mutant Solid Tumors

Pediatric Low-Grade Gliomas	**Mirdametinib**: Phase 1/2 ongoing
MAPK Mutant Solid Tumors	**Mirda + Lifirafenib:** Ph 1/2 ongoing
ER+ Metastatic Breast Cancer	**Mirda + Fulvestrant:** Ph 1b/2a ongoing
MEK 1/2 Mutant Solid Tumors	**Mirdametinib:** Phase 1b/2a ongoing
MAPK Mutant Solid Tumors	**Brimarafenib:** Phase 1 ongoing
MAPK Mutant Solid Tumors	**Mirda + Brimarafenib:** Ph 1/2a ongoing

Preclinical Programs

Hippo Mutant Tumors	**SW-682:** IND-enabling
EGFR Mutant Tumors	Discovery

2023 Milestones

- ✓ Highlight clinical data for various programs at EHA 2023
- ▪ Support initiation of trials across modalities

- ✓ Dose first patient in mirdametinib + brimarafenib (BGB-3245) study (1Q23)
- ✓ Present data from brimarafenib and mirdametinib + lifirafenib at AACR 2023

- ✓ Present preclinical data for SW-682 at AACR 2023
- ▪ File IND for SW-682

Nirogacestat

BCMA Combination Therapy Development in Multiple Myeloma

SpringWorks® THERAPEUTICS

Nirogacestat in Multiple Myeloma: A Potential 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 multiple myeloma

- ~40,000 MM patients receiving 1L and 2L therapy annually in the U.S.(1)
- ~15,000 r/r MM patients receiving 3L+ therapy annually in the US(1)

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

- Preclinically validated across all key modalities:
  - ✓ Antibody-drug conjugates
  - ✓ Bispecific antibodies
  - ✓ CAR-T cell therapies
  - ✓ Monoclonal antibodies

Industry Collaborators

abbvie

GSK

janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson

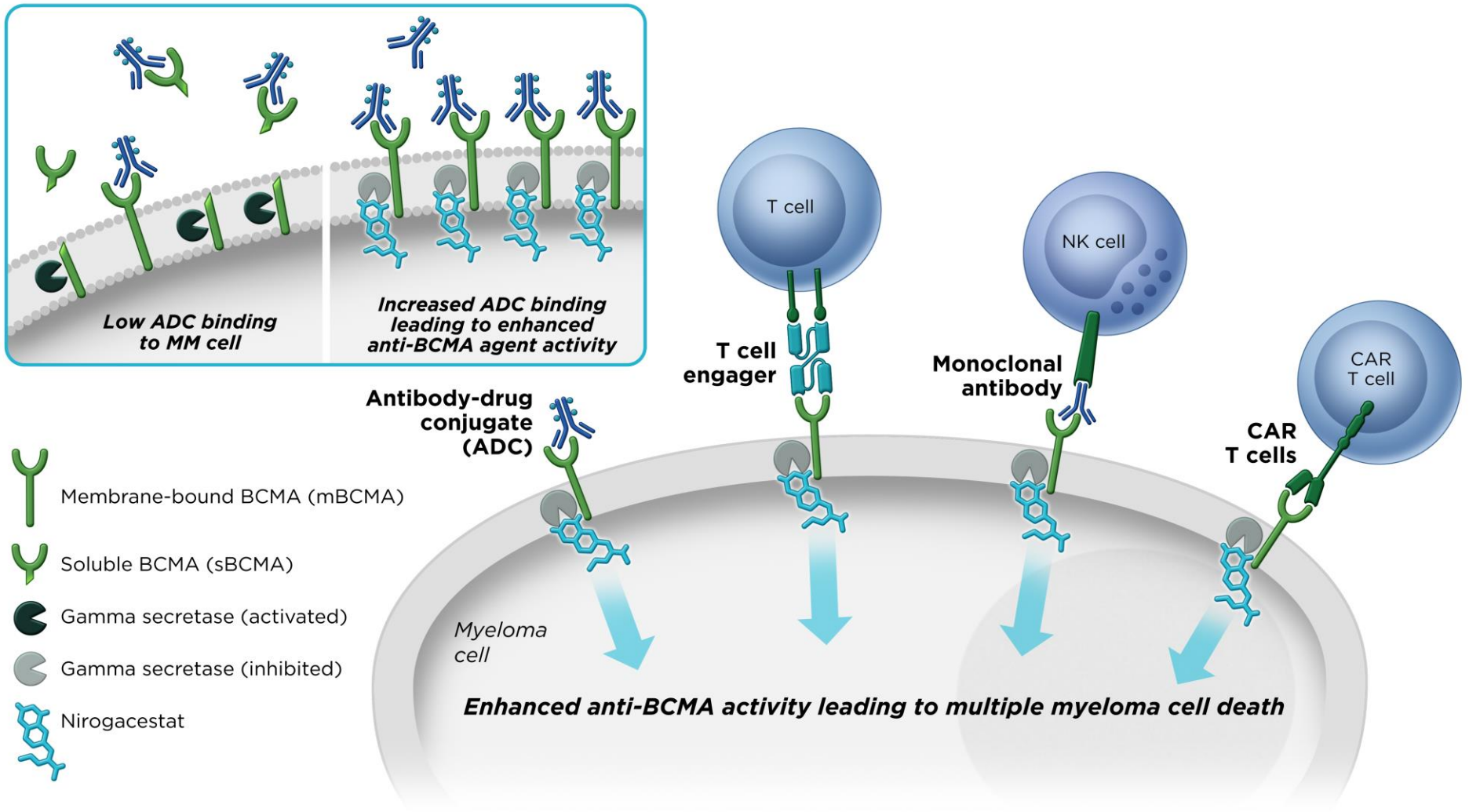
Pfizer

REGENERON

Seagen®

Source: (1) Siegel et al., 2022; DRG market research.
Note: MM: multiple myeloma; r/r: relapsed / refractory.

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

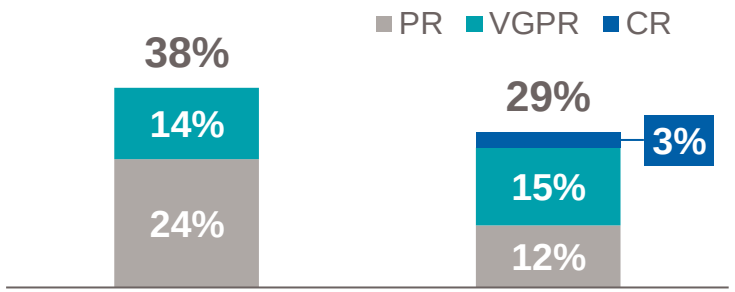


Note: GSI: gamma secretase inhibitor.

Emerging Clinical Data With Nirogacestat Supports Validation of BCMA Combination Development Approach Across Modalities

Nirogacestat + Belamaf Ph 1/2

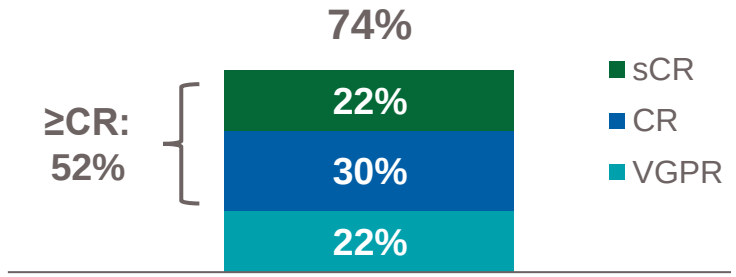
Overall Response Rate (ORR)



- Comparable efficacy with substantial reduction in Grade 3 ocular adverse events observed
- Posterior probability ORR(1) of 36% for nirogacestat + belamaf combo vs. 33% for belamaf alone
- Additional trials with SoC agents and investigator-sponsored studies ongoing
- Expanded non-exclusive collaboration announced in September 2022 enables potential development into earlier treatment lines

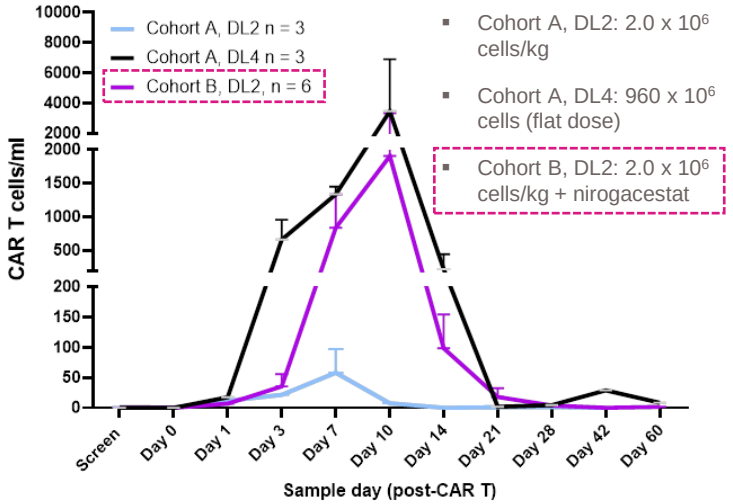
Nirogacestat + Teclistamab Ph 1b

Overall Response Rate (ORR)



- High and deep response rates observed with teclistamab + nirogacestat in patients with relapsed/refractory multiple myeloma
- Safety profile optimized with delayed administration of lower-dose nirogacestat
- Initial profile established for nirogacestat + BCMA bispecific combination

Nirogacestat + BCMA CAR-T Ph 1/2



- Similar level of expansion and persistence observed with nirogacestat + low-dose allogeneic BCMA CAR-T cells vs. monotherapy CAR-T cells
- Improved cell expansion correlated with increased clinical activity

(1) Incorporating prior ORR for low-dose belamaf + nirogacestat from DREAMM-5 sub-study 3 DE cohort (observed ORR 60% [6/10]) and for monotherapy from DREAMM-2 2.5mg/kg monotherapy cohort (observed ORR 31% [30/.97] per prespecified analysis plan.

(2) Dose level 1: teclistamab SC 0.72 mg/kg QW + concurrent nirogacestat PO 100 mg BID (n=8); dose level 2: teclistamab SC 0.72 mg/kg QW + delayed nirogacestat PO 100 mg QD (n=7); dose level 3: teclistamab SC 1.5 mg/kg QW + delayed nirogacestat PO 100 mg QD (n=13).

Note: PR: partial response; VGPR: very good partial response; CR: complete response; sCR: stringent complete response; CE: cohort expansion; DE: dose exploration; BID: twice daily; SoC: standard of care.

Source: Lonial et al., EHA, 2023. Offner et al., EHA, 2023. Precision BioSciences investor materials (ASH 2021 presentation on December 11, 2021; Allogeneic CAR-T Update presentation on June 8, 2022; 3Q 2022 Earnings Release as of November 8, 2022); preliminary data from Precision-sponsored trial (NCT04171843).

SpringWorks THERAPEUTICS

Mirdametinib

Additional Expansion Opportunities

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Expansion Opportunities for Mirdametinib in Rare Oncology and Biomarker-Defined Solid Tumors

Pediatric Low-Grade Glioma

- Open-label, multi-center study evaluating single agent mirdametinib, a brain penetrant MEK 1/2 inhibitor, in pediatric low-grade gliomas (pLGG) in collaboration with St. Jude Children's Research Hospital
- Favorable safety and blood-brain barrier penetration properties set the stage for development approach in pLGG
- Data from first 11 patients in Phase 1 dose escalation presented at ISPNO 2022, showing promising clinical activity with 1 patient with partial response, 7 patients with minor response, and 3 patients with stable disease

ER+ Breast Cancer

- MAPK mutations in ER+ mBC cells can lead to fulvestrant resistance, which can be reversed with MEK inhibition(1)
- ~25% of ER+ mBC patients progress on endocrine therapy and up to 15% of mBC harbor MAPK pathway mutations, including NF1 loss-of-function
- NF1 deficiency has been shown to enhance ER transcriptional activity leading to hormone resistance(2)
- Phase 1 trial ongoing in collaboration with Memorial Sloan Kettering Cancer Center

MEK1/2 Mutant Solid Tumors

- Mirdametinib shows potent preclinical activity against Class 1 and Class 2 mutations in MEK1 and MEK2(3)
- MEK1 and MEK2 have been validated as oncogenic targets with mutations present in ~2% of solid tumors(4)
- Clinical case reports with allosteric MEK inhibitors also support utility of mirdametinib in tumors driven by MEK mutation
- Phase 1 trial ongoing in collaboration with Memorial Sloan Kettering Cancer Center

Note: ISPNO: International Symposium on Pediatric Neuro-Oncology; mBC: metastatic breast cancer;.
Sources: (1) Zheng et al., 2020; (2) Sokol et al., 2019; (3) Gao et al., 2018; (4) Hanrahan et al., 2020.

Mirdametinib + Lifirafenib: Antitumor Activity in Various KRAS, NRAS, and BRAF Mutations Across Solid Tumor Types

- Lifirafenib is a pan-RAF inhibitor under study as combination therapy with mirdametinib through collaboration with BeiGene
- Combination led to sustained inhibition of MAPK pathway signaling and significant tumor regression in preclinical models
- Clinical data for Phase 1b dose-escalation presented at AACR 2023, with dose-expansion portion of the study expected to commence in 2H23

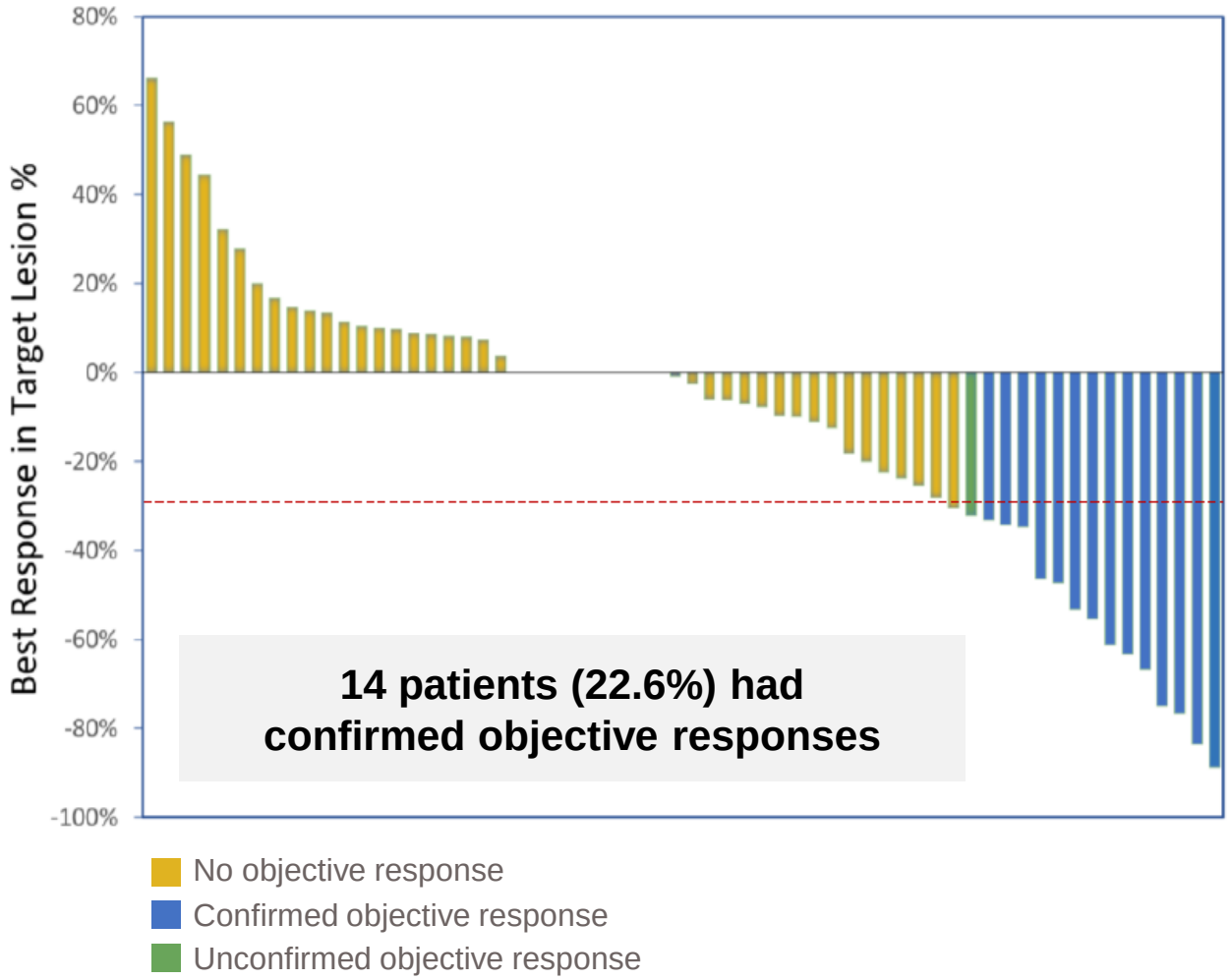
Key Highlights from Initial Phase 1b Clinical Data

SAFETY	▪ Lifirafenib in combination with mirdametinib demonstrated a favorable safety profile, with limited dose-limiting toxicities and discontinuations
EFFICACY	▪ Antitumor activity demonstrated across several solid tumor types: – LGSOC (deeper and faster responses with BRAF mutations) – NSCLC (especially with NRAS and BRAF mutations) – Endometrial cancer with KRAS and BRAF mutations
NEXT STEPS	▪ The combination of lifirafenib and mirdametinib demonstrated a desirable risk-benefit profile and warrants further clinical investigation ▪ Dose-expansion in NRAS-mutated solid tumors planned to initiate in 2H23

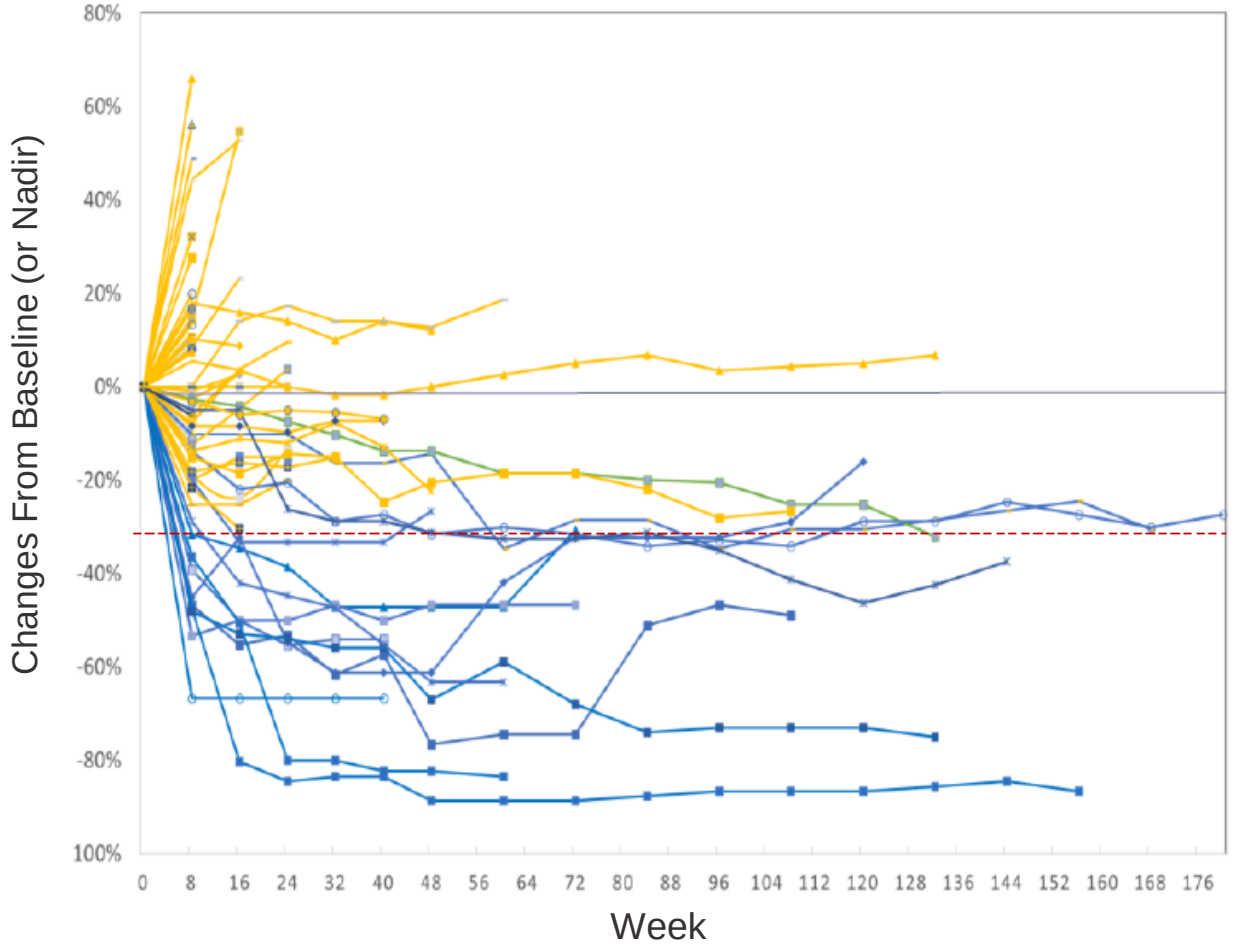
Source: Solomon et al., AACR 2023.
Note: LGSOC: low-grade serous ovarian cancer; NSCLC: non-small cell lung cancer.

Mirdametinib + Lifirafenib: Clinical Activity During Dose Escalation in All Evaluable Patients

Best Overall Response [a] (n=62)



Changes in Tumor Response Over Time [a] (n=62)



Source: Solomon et al., AACR 2023.

[a] According to RECIST v1.1. Data cutoff date: 20 January 2023.

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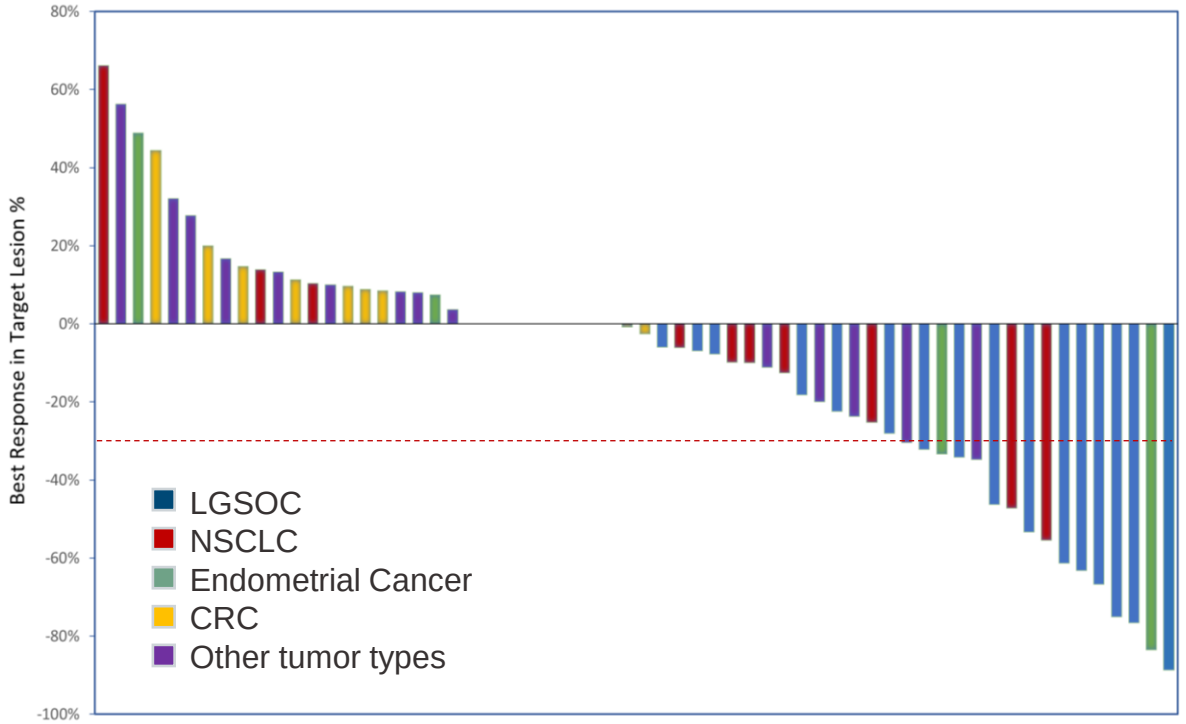
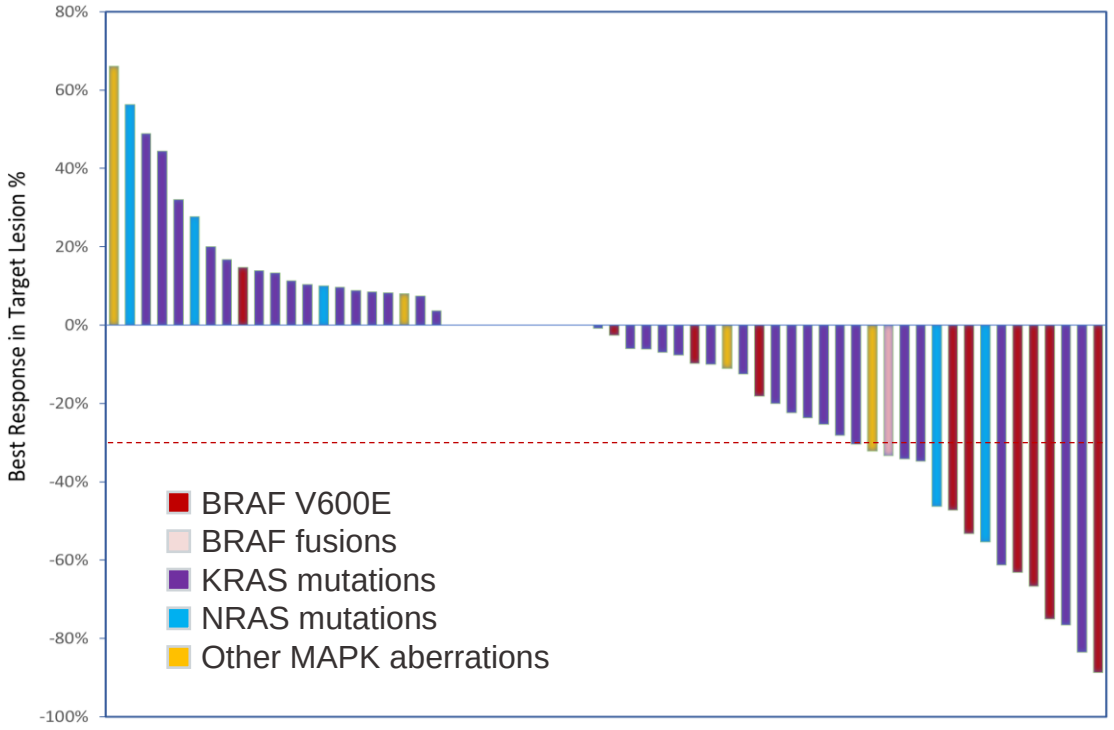
Mirdametinib + Lifirafenib: Clinical Activity During Dose Escalation in All Evaluable Patients By Tumor Types and Mutation

Best Overall Response by Tumor Type [a]
(n=62)



Best Overall Response by Mutation [a]
(n=62)



Source: Solomon et al., AACR 2023.
[a] According to RECIST v1.1.
Data cutoff date: 20 January 2023.

SpringWorks THERAPEUTICS

Brimarafenib (BGB-3245)

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Investigating Brimarafenib (BGB-3245) as Monotherapy and in Combination With Mirdametinib

- Brimarafenib is a RAF fusion and dimer inhibitor under development by MapKure, a joint venture owned by SpringWorks and BeiGene
- Preclinical research of brimarafenib has demonstrated activity against a broad spectrum of BRAF class I/II/III mutations and fusions
- Clinical data for Phase 1 monotherapy trial presented at AACR 2023, with encouraging antitumor activity and efficacy across mutations and tumor types; combination trial initiated 1Q23

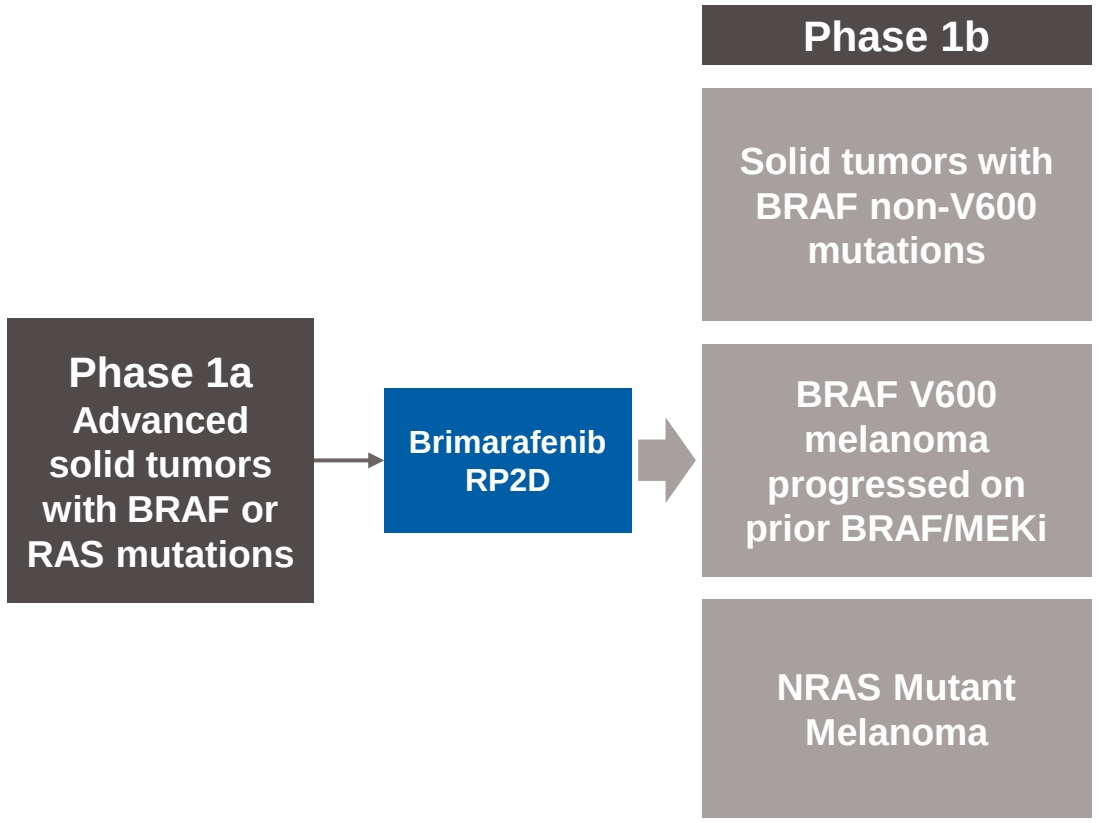
Key Highlights from Initial Phase 1b Monotherapy Clinical Data

SAFETY	▪ Manageable safety profile, with AE findings consistent with those of other MAPK inhibitors ▪ 40 mg was determined to be maximum tolerated dose
EFFICACY	▪ Encouraging antitumor activity was observed in the heavily pretreated heterogeneous patients – ORR (confirmed): 6/33, 18%; CBR: 14/33, 42%; DCR: 26/33 (79%) ▪ Efficacy in patients with tumors harboring BRAF V600E progressed on prior BRAF/MEK inhibitors, BRAF Class II mutations, BRAF fusions, and NRAS mutations
NEXT STEPS	▪ Data support ongoing investigation of brimarafenib in defined cohorts ▪ Evaluation of brimarafenib in combination with the MEK inhibitor, mirdametinib, in MAPK-altered advanced solid tumors has been initiated (NCT05580770)

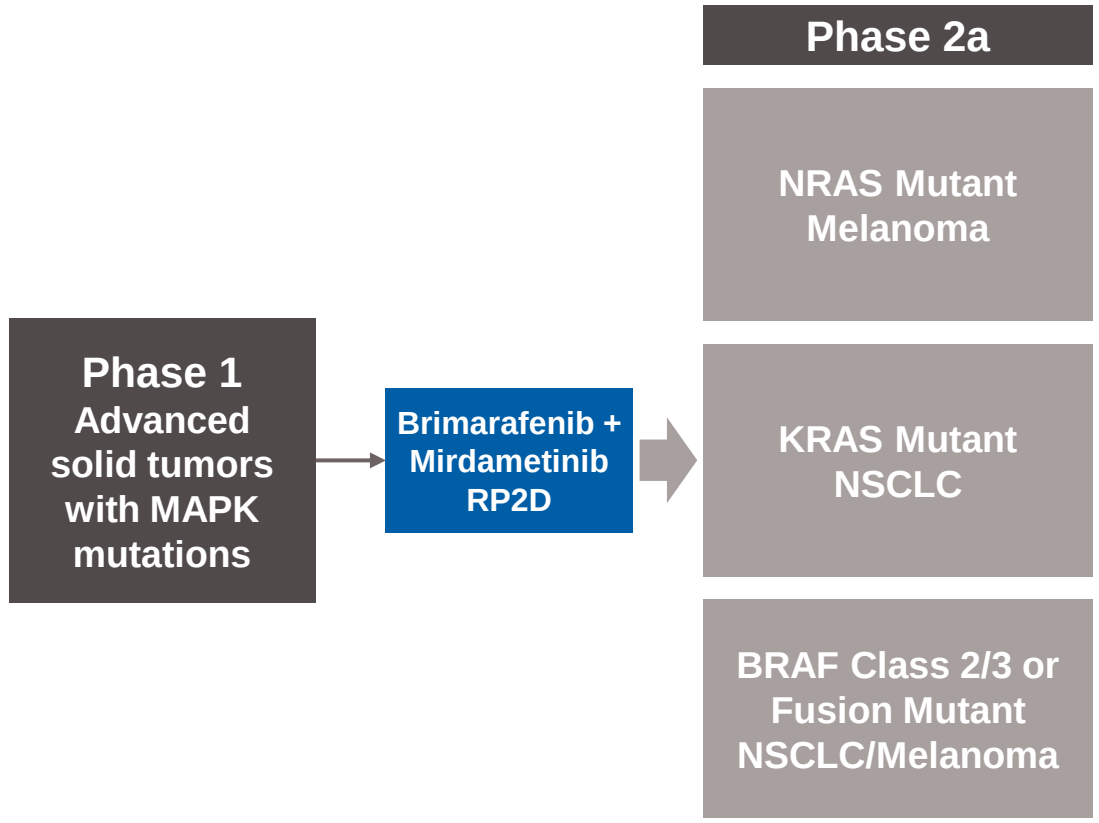
Source: Schram et al., AACR 2023.
Note: AE: adverse event; ORR: overall response rate; CBR: clinical benefit rate; DCR: disease control rate.

Brimarafenib: Ongoing Trials

Ongoing Monotherapy Development



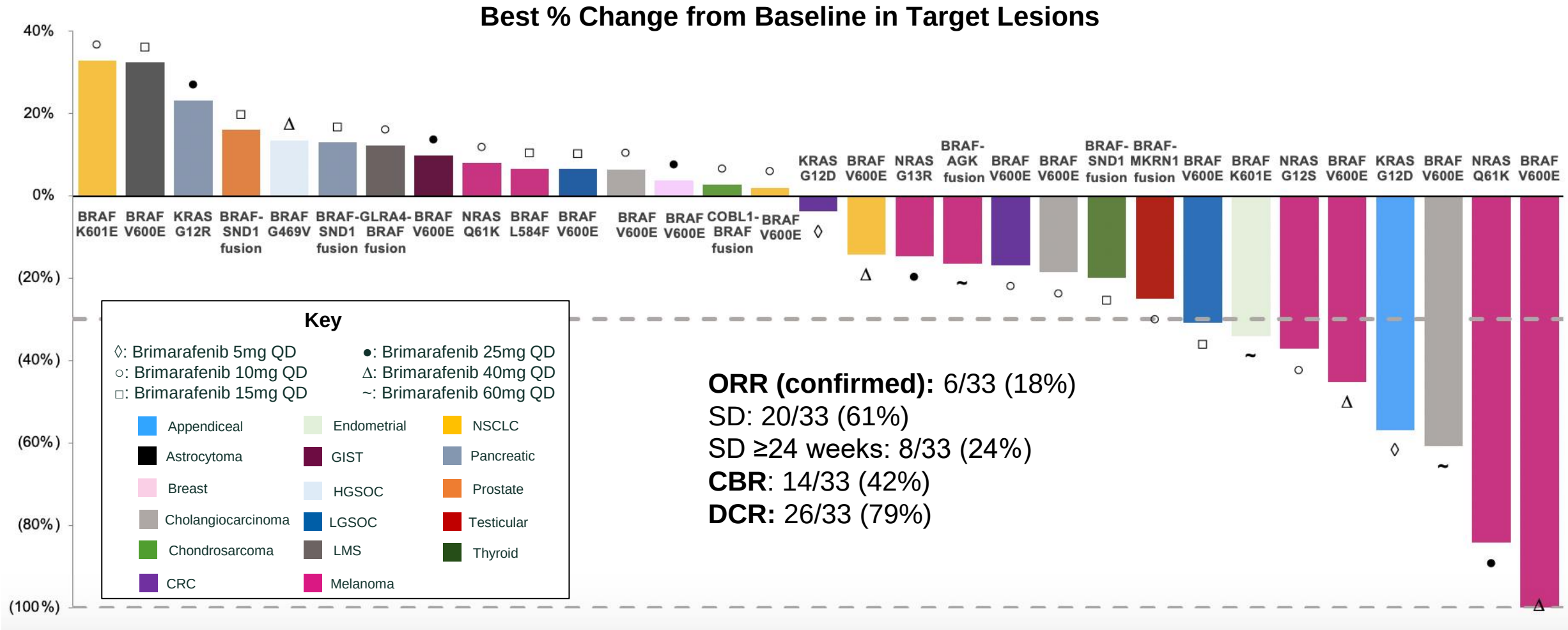
Ongoing Combination Trial with Mirdametinib



Advanced monotherapy trial into Phase 1b in 3Q22; combination trial dosed first patient in 1Q23

Note: RP2D: recommended Phase 2 dose.

Anti-Tumor Activity of Brimarafenib Monotherapy Presented at AACR 2023

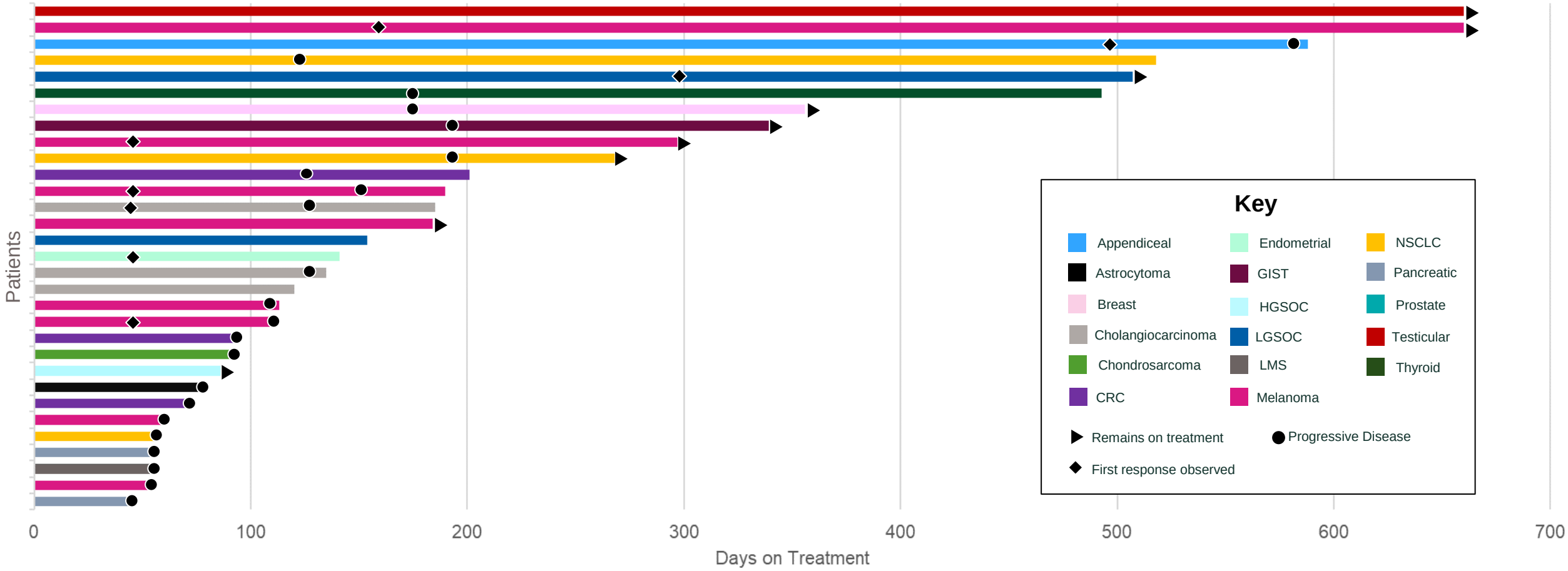


ORR (confirmed): 6/33 (18%)
SD: 20/33 (61%)
SD ≥24 weeks: 8/33 (24%)
CBR: 14/33 (42%)
DCR: 26/33 (79%)

Overall data profile of brimarafenib as monotherapy supports ongoing investigation in defined cohorts

Source: Schram et al., AACR 2023.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Data as of September 1, 2022.
Note: Follow up scans on two patients indicated new lesions with progressive disease (PD) recorded as their best objective response. These follow-up scans did not measure target lesion and therefore are not included in the waterfall plot.
Note: CRC: colorectal cancer; GIST: gastrointestinal stromal tumor; HGSOC: high grade serous ovarian cancer; LMS: leiomyosarcoma; LGSOC: low-grade serous ovarian cancer; NSCLC: non-small cell lung cancer.

Time on Treatment for Brimarafenib Monotherapy Presented at AACR 2023



- As of data cut (September 1, 2022), median time on treatment: 154 days (range: 54 – 660 days)
- 9 patients remain on treatment

Source: Schram et al., AACR 2023.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Data as of September 1, 2022.

Preclinical Pipeline

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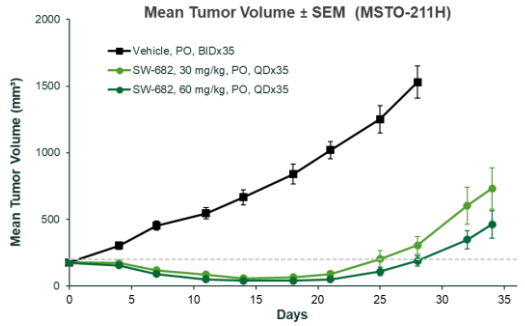
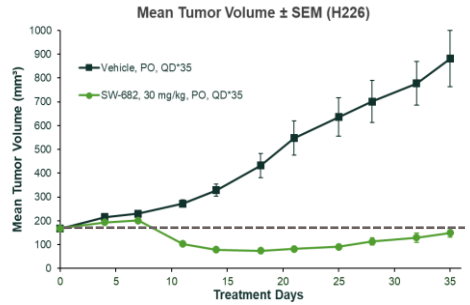
Preclinical Assets Broaden Portfolio Reach With Monotherapy and Combination Opportunities

SW-682

- SW-682 is an investigational novel, potent, and selective antagonist of TEAD dependent transcription, with activity against all TEAD isoforms
- Potent and selective inhibition of proliferation of Hippo-mutant tumor cell lines
- Demonstrates robust anti-tumor activity in Hippo altered xenograft models in vivo
- Development candidate nominated in 4Q22 and studies underway to enable IND filing in 2023





EGFR Inhibitor Portfolio

- Collaboration with Dana-Farber Cancer Institute and Stanford developing a portfolio of next-generation EGFR inhibitors
- Lead optimization focuses on CNS penetrant, C797S active inhibitors to address osimertinib resistance
- Additional strategies being advanced to address *de novo* EGFR driver and resistance mutations through first-in-class targeting approaches

Dana-Farber Cancer Institute

Stanford Medicine

Research is being conducted in collaboration with Nathanael Gray, PhD (Stanford) and Pasi Jänne, MD, PhD (Dana-Farber)

Source: Chen et al., AACR 2023.
Note: CNS: central nervous system.

SpringWorks THERAPEUTICS

The SpringWorks Opportunity

Well-Capitalized to Execute on Important Value-Driving Milestones

$528.1M

Cash, Cash Equivalents & Marketable Securities(1)

No Debt

NASDAQ: SWTX

62.5M

Common Shares Outstanding(2)

(1) As of March 31, 2023.
(2) Basic common shares outstanding as of April 28, 2023.

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 expected to provide 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

Thank you

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