Phase 3 DeFi Trial Results
ESMO 2022 Investor Webcast

September 11, 2022

SpringWorks THERAPEUTICS

Forward-Looking Statements

Note: Unless otherwise indicated, the information presented herein is as of September 2022 and made publicly available on September 11, 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, the potential for nirogacestat to become an important new treatment for patients with desmoid tumors, 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, our plans for seeking regulatory approval for and making nirogacestat available to desmoid tumor patients, if approved, expectations regarding cash and cash equivalents following the closing of the private placement transaction and the equity investment from GSK that were each announced on September 7, 2022, and the anticipated use of proceeds from such transactions as well as the expectation that such proceeds will fund SpringWorks operational plans into 2026, 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) our expectations regarding the potential clinical benefit to patients with desmoid tumors based upon the results of our DeFi trial, (iii) the fact that topline data from the Phase 3 DeFi trial or topline or interim data from 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, (iv) the success and timing of our collaboration partners’ ongoing and planned clinical trials, (v) 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; (vi) 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, (vii) our ability to obtain and maintain regulatory approval of any of our product candidates, (viii) our plans to research, discover and develop additional product candidates, (ix) our ability to enter into collaborations for the development of new product candidates, (x) our ability to establish manufacturing capabilities, and our and our collaboration partners’ abilities to manufacture our product candidates and scale production, (xi) our ability to meet any specific milestones set forth herein, and (xii) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks’ business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines.

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

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

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

SpringWorks Leadership Team and External Speaker Participating Today

SpringWorks Participants

Saqib Islam
Chief Executive Officer

Badreddin Edris, PhD
Chief Operating Officer

Bhavesh Ashar
Chief Commercial Officer

Jim Cassidy, MD, PhD
Chief Medical Officer

External Key Opinion Leader

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

Opening Remarks

Saqib Islam

Chief Executive Officer

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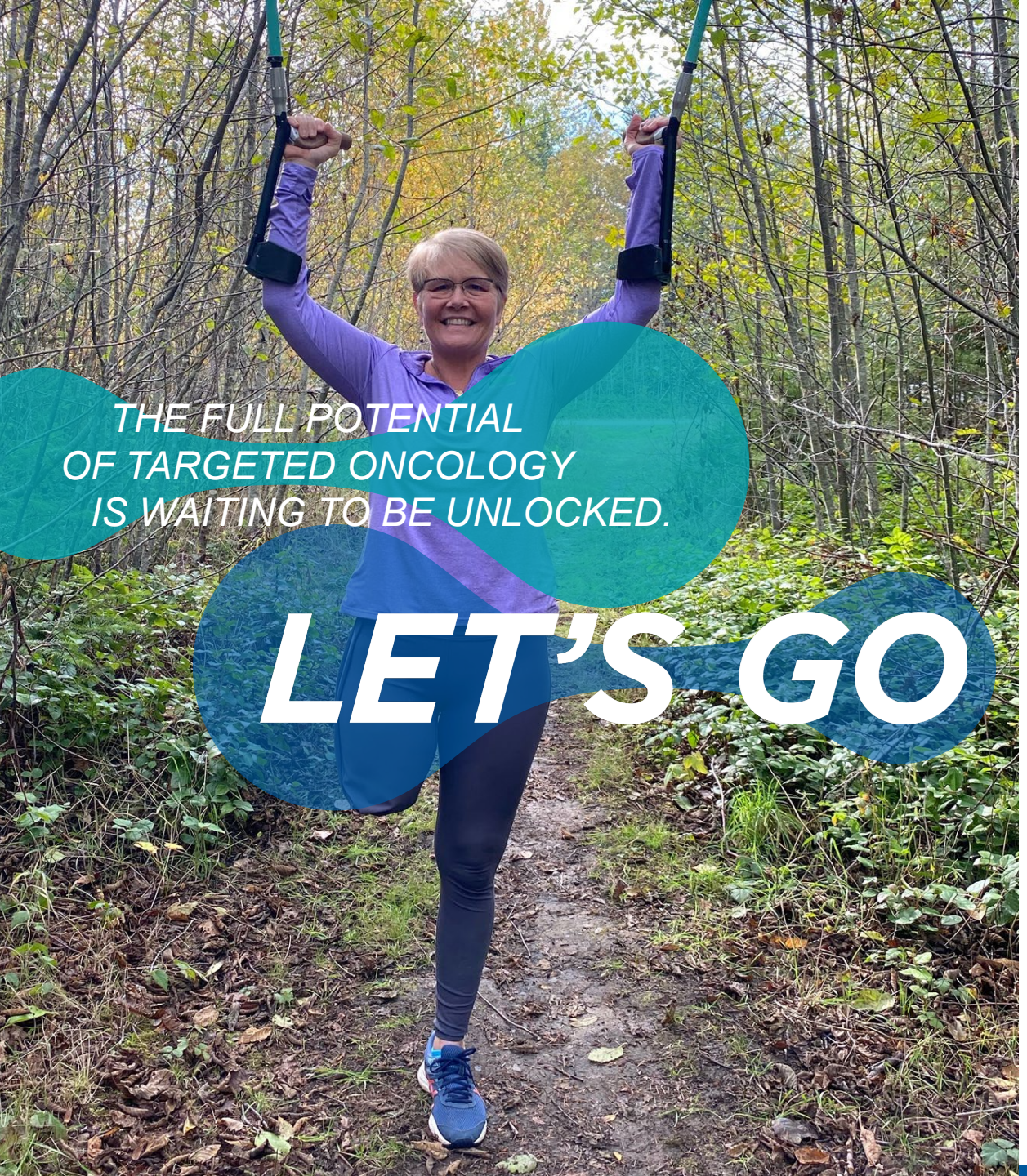

At SpringWorks our singular goal is to make a profound impact on the lives of people living with devastating rare diseases and cancers

2022	**Multiple late-stage opportunities with first NDA filing expected this year**
2	**Marketed products expected by 2025 with the potential to serve patients across 4 indications**
$600M+ in cash	**Robust balance sheet and disciplined approach to capital allocation with cash runway into 2026(1)**

Unlocking opportunities for patients with a deep portfolio of pipeline-in-a-product molecules and collaborative relationships

(1) Preliminary estimate of cash, cash equivalents and marketable securities balance as of September 11, 2022, accounting for net proceeds received as a result of (a) the $225M private placement transaction announced on September 7, 2022, and (b) the $75M equity investment by GSK announced on September 7, 2022, as well as information available to management as of the date of this presentation; actual cash on-hand may vary from this estimate.

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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)*	+ *Blenrep* (belantamab mafodotin) (ADC)	GSK
		+ ALLO-715 (CAR-T)(2)	Allogene Therapeutics
		+ Teclistamab (Bispecific)	Janssen
		+ PBCAR269A (CAR-T)	Precision Biosciences
		+ Elranatamab (Bispecific)	Pfizer
		+ SEA-BCMA (mAb)	Seagen
		+ ABBV-383 (Bispecific)	abbvie
		+ REGN5458 (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	
BGB-3245 RAF Fusion & Dimer Inhibitor	MAPK Mutant Solid Tumors	Monotherapy and combo	Mapkure(1)
TEAD Inhibitor Program	Hippo Mutant Tumors	Monotherapy and combo	
EGFR Inhibitor Program	EGFR Mutant Tumors	Monotherapy and combo	

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.
(2) No further enrollment expected in ongoing Phase 1 study with Allogene per study update disclosed in Allogene press release on 08/09/22.

Rare Oncology | BCMA Combos | Biomarker-Defined Solid Tumors

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
- 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(2) representing all major modalities
- Unlocking additional expansion opportunities, including monotherapy development in ovarian granulosa cell tumors

Anticipated NDA Filing in Desmoid Tumors Through RTOR:	**2H 2022**
Clinical Trials Ongoing or on Track for 2022 Initiation:	**11**
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.
(2) No further enrollment expected in ongoing Phase 1 study with Allogene per study update disclosed in Allogene press release on 08/09/22.

Phase 3 DeFi Data Presentation: ESMO 2022

Bernd Kasper, MD, PhD

University of Heidelberg, Mannheim Cancer Center, Mannheim, Germany

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

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

September 10, 2022

Declaration of Interests

- Bernd Kasper's declaration of interests:
  - Financial interests
    - Ayala (advisory board, personal), Bayer (advisory board, personal), Blueprint, (advisory board, personal), Boehringer Ingelheim (advisory board, personal), GSK (advisory board, personal), PharmaMar (advisory board, personal), SpringWorks Therapeutics (advisory board, personal)
  - Nonfinancial interests
    - Ayala (coordinating PI, institutional, no financial interest), PharmaMar (coordinating PI, institutional, no financial interest), SpringWorks Therapeutics (coordinating PI, institutional, no financial interest), European Organisation for Research and Treatment of Cancer (EORTC; leadership role, Chair of the EORTC Soft Tissue and Bone Sarcoma Group [STBSG])

Gamma Secretase Inhibition in Desmoid Tumors

- Desmoid tumors (DT) are rare, locally aggressive, and invasive soft-tissue tumors that are challenging to manage due to variable presentation, unpredictable disease course, and a lack of approved therapies[1,2]
- Treatment should be individualized to optimize tumor control and improve symptom burden, including pain, physical function, and overall quality of life[3]
  - A global consensus initiative has been launched by The Desmoid Tumor Working Group aiming to harmonize management strategies[4]
- There is mechanistic rationale for the use of gamma secretase inhibitors (GSI) in DT as these tumors highly express Notch, which can be blocked by GSIs[5,6]
- Nirogacestat is an investigational, oral, selective, small-molecule GSI that has shown evidence of antitumor activity in DT in Phase 1 and 2 trials with a manageable adverse event profile[1,7,8]

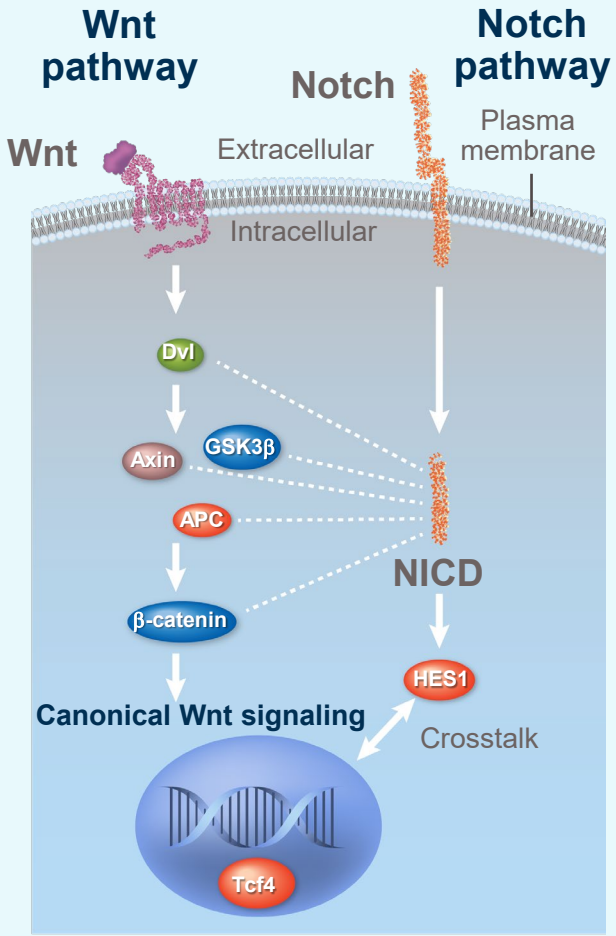


Image adapted from Andersson et al. *Development* (2011) and Bui and Kummar. *Oncotarget* (2017).

DT, desmoid tumor; GSI, gamma secretase inhibitor; NICD, Notch intracellular domain.

1. Villalobos et al. *Ann Surg Oncol.* 2018;25:768-775. **2.** Kasper et al. *Oncologist.* 2011;16:682-693. **3.** Gounder et al. *Cancer.* 2020;126:531-539. **4.** Desmoid Tumor Working Group. *Eur J Cancer.* 2020;127:96-107. **5.** Andersson et al. *Development.* 2011;138:3593-3612. **6.** Gounder et al. *Cancer.* 2015;121:3933-3937. **7.** Messersmith et al. *Clin Cancer Res.* 2015;21:60-67. **8.** Kummar et al. *J Clin Oncol.* 2017;35:1561-1569.

DeFi: Phase 3 Study of Nirogacestat vs Placebo in Adult Patients With DT

Trial Summary

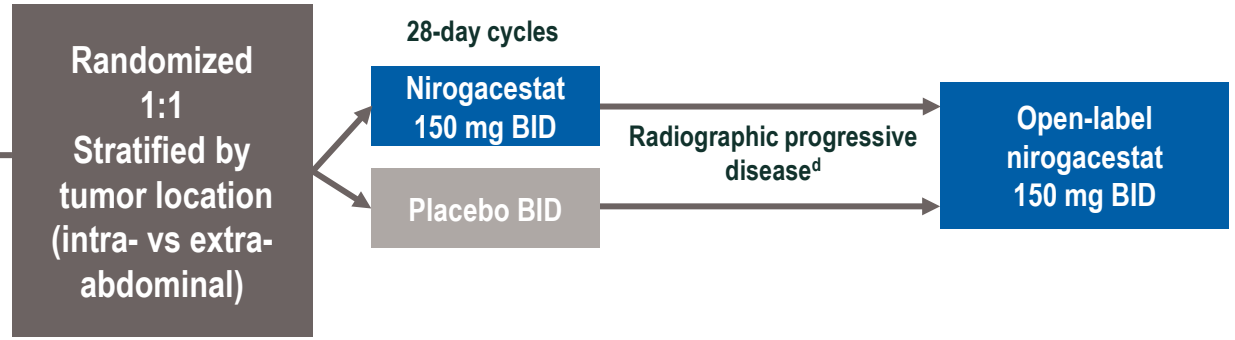
- Global, randomized, double-blind, placebo-controlled, Phase 3 trial comparing the efficacy, safety, and tolerability of nirogacestat vs placebo in adult patients with progressing DT
- 142 patients randomized across 37 sites in North America and Europe

Key Endpoints

- **Primary:** Progression-free survival[b]
- **Secondary:** Objective response rate and patient-reported outcomes, such as pain, symptom burden, physical/role function, and overall quality of life[c]

Adult Eligible Patients

- Histologically confirmed DT with progressive disease per RECIST v1.1[a]
  - Treatment-naïve with DT not amenable to surgery, or
  - Refractory or recurrent disease (after ≥1 line of therapy)



Primary Analysis Data Cutoff: April 7, 2022

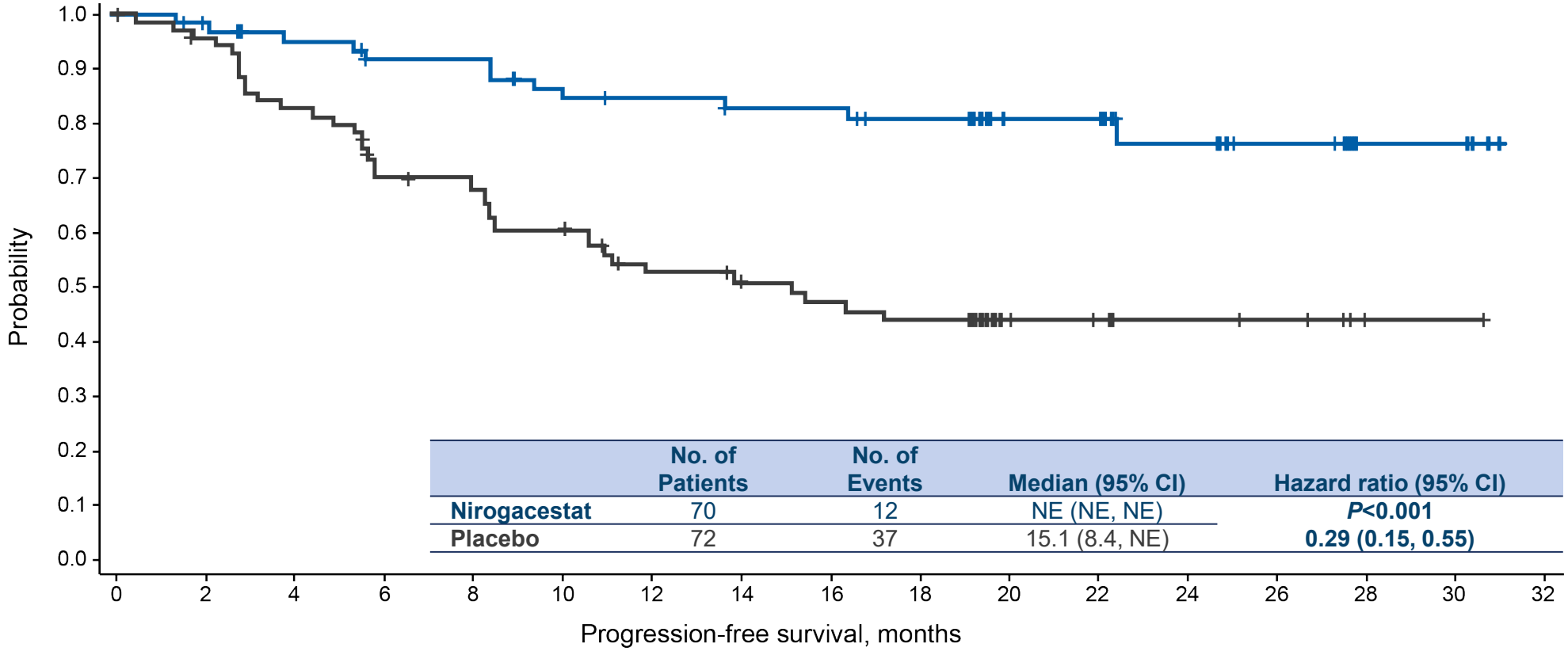
[a]Progressive disease defined by histologically confirmed DT that has progressed ≥20% within the past 12 months by RECIST v1.1. Target tumors identified at screening by the Investigator.
[b]Progression was determined radiographically using RECIST v1.1 or clinically by independent, blinded, central radiologic or clinical review.
[c]As assessed by change from baseline for BPI-SF, GODDESS DTSS, GODDESS DTIS, and EORTC QLQ-C30 at Cycle 10.
[d]Radiographic disease progression or once the required number of events have been observed and the primary progression-free survival analysis has been completed.
BID, twice-daily dosing; BPI-SF, Brief Pain Inventory–Short Form; DT, desmoid tumor; DTIS, GODDESS DT Impact Scale; DTSS, GODDESS DT Symptom 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; RECIST, Response Evaluation Criteria in Solid Tumors.
ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03785964. Accessed August 24, 2022.

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)
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)

[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.
API, average pain index; BPI-SF, Brief Pain Inventory–Short Form ITT; intention to treat.

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:

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

Median follow-up time was 19.2 months for nirogacestat and 10.9 months for placebo.
NE, not estimable.

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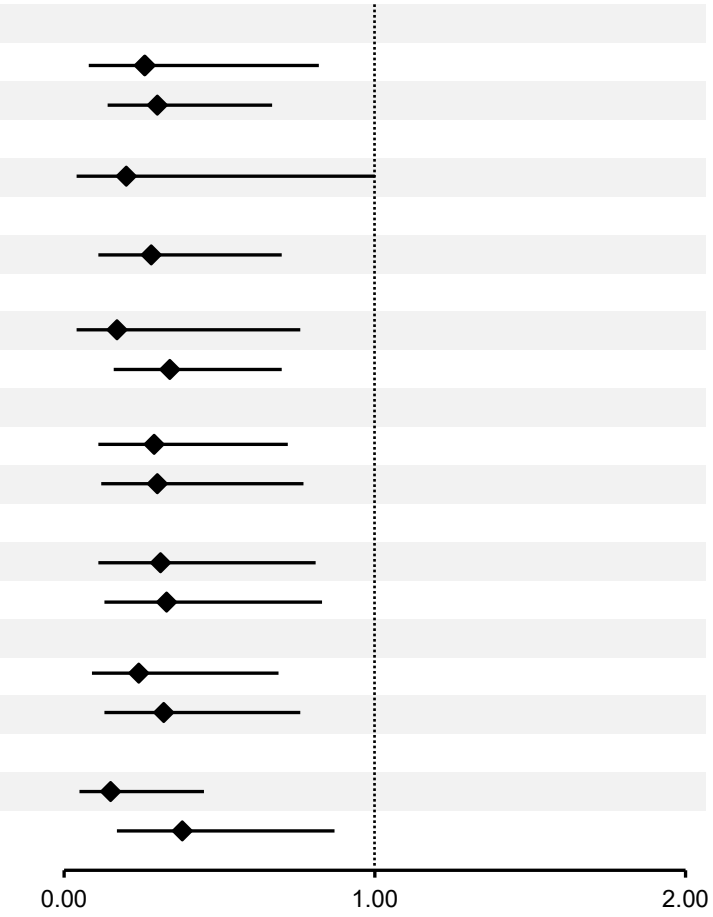
PFS Benefit With Nirogacestat Was Observed Across Prespecified Subgroups

	Hazard Ratio	Nirogacestat Censored/Events	Placebo Censored/Events
Sex			
Male	0.26	21 / 4	14 / 11
Female	0.30	37 / 8	21 / 26
***APC* mutation**			
Yes	0.20	9 / 2	3 / 8
***CTNNB1* mutation**			
Yes	0.28	37 / 6	21 / 21
Target tumor location			
Intra-abdominal	0.17	15 / 2	7 / 11
Extra-abdominal	0.34	43 / 10	28 / 26
Focality			
Single	0.29	37 / 6	22 / 19
Multifocal	0.30	21 / 6	13 / 18
Prior surgery			
Yes	0.31	26 / 5	21 / 23
No	0.33	32 / 7	14 / 14
Prior chemotherapy			
Yes	0.24	19 / 5	10 / 17
No	0.32	39 / 7	25 / 20
Prior TKI treatment			
Yes	0.15	19 / 4	8 / 16
No	0.38	39 / 8	27 / 21



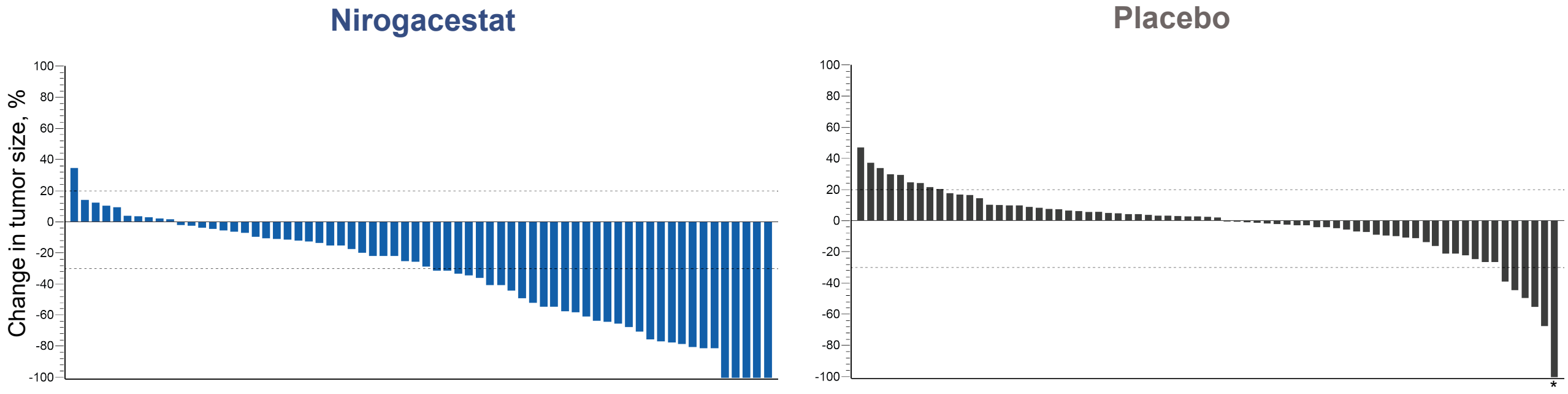
PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

Objective Response Rate by Blinded Independent Central Review

	Nirogacestat (n=70)	Placebo (n=72)
Objective response rate (CR+PR), n (%) 95% CI Two-sided *P* value	**29 (41)** **(30.2, 54.5)** **<0.001**	**6 (8)** **(3.1, 17.3)**
Best overall response, n (%)		
Complete response	5 (7)	0
Partial response	24 (34)	6 (8)
Stable disease	35 (50)	55 (76)
Progressive disease	1 (1)	10 (14)
Not evaluable	4 (6)	1 (1)
Time to objective response, median (range), mo	5.6 (2.6, 19.4)	11.1 (2.8, 16.4)
Kaplan-Meier estimate of median duration of objective response (95% CI), mo[a]	NE (NE, NE)	NE (8.3, NE)

[a]Duration of objective response was defined as duration in months from the time CR or PR (which ever came first) was met until the date of progression, death, or censoring.
CR, complete response; NE, not estimable; PR, partial response.

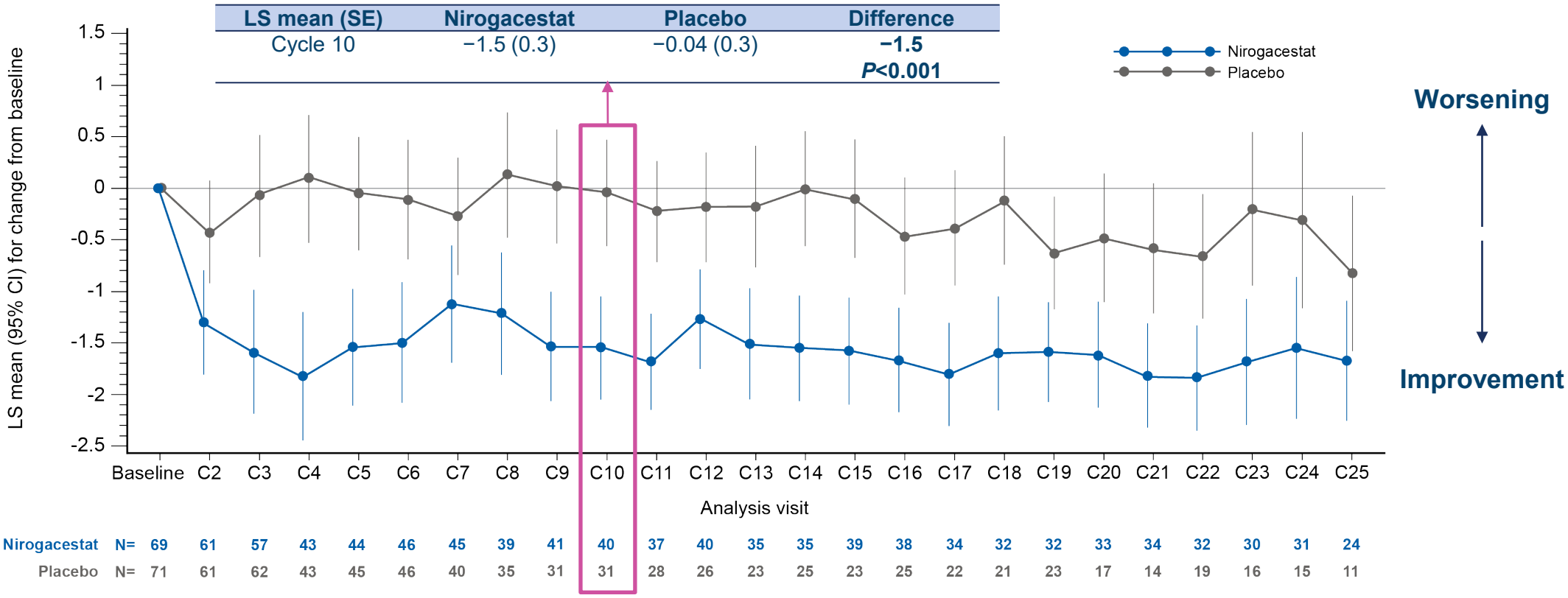
Nirogacestat Treatment Resulted in Substantial Reductions in Tumor Size



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

Nirogacestat Significantly Reduced Pain Severity Compared With Placebo

Brief Pain Inventory-Short Form – Average Pain Intensity



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.
LS, least squares.

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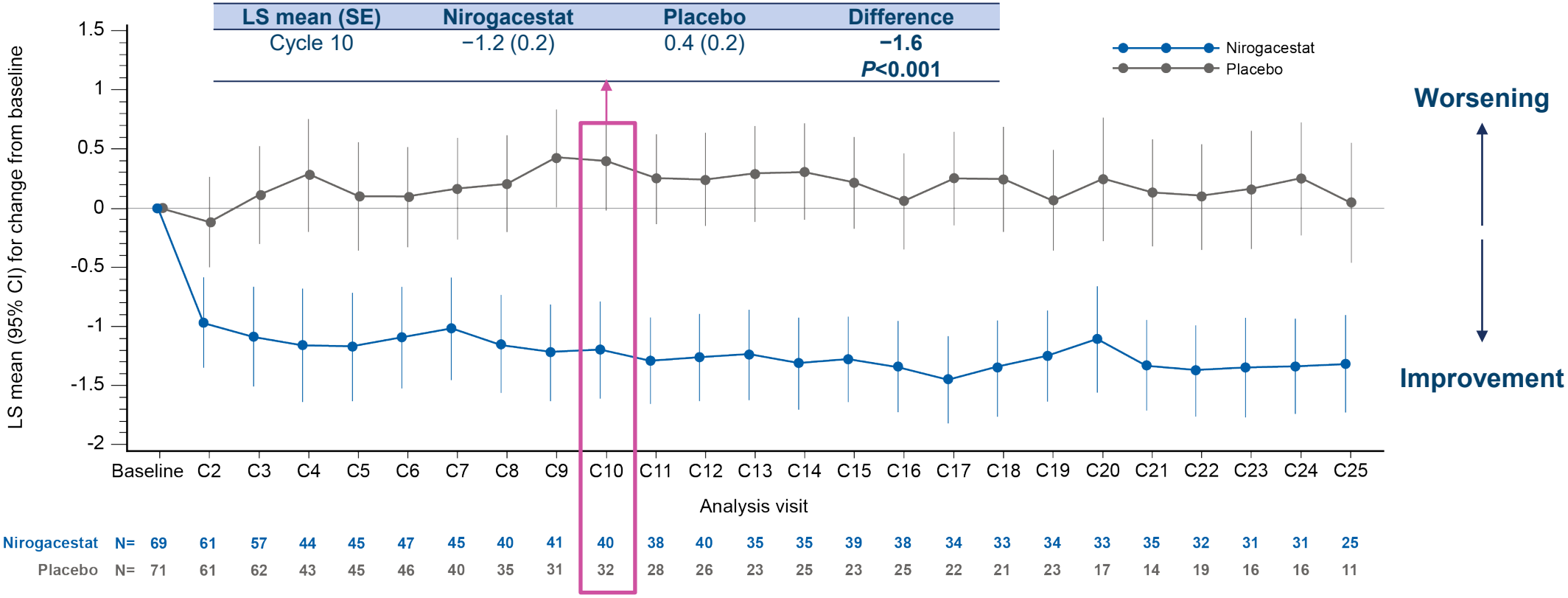
Nirogacestat Significantly Reduced DT-Specific Symptom Severity

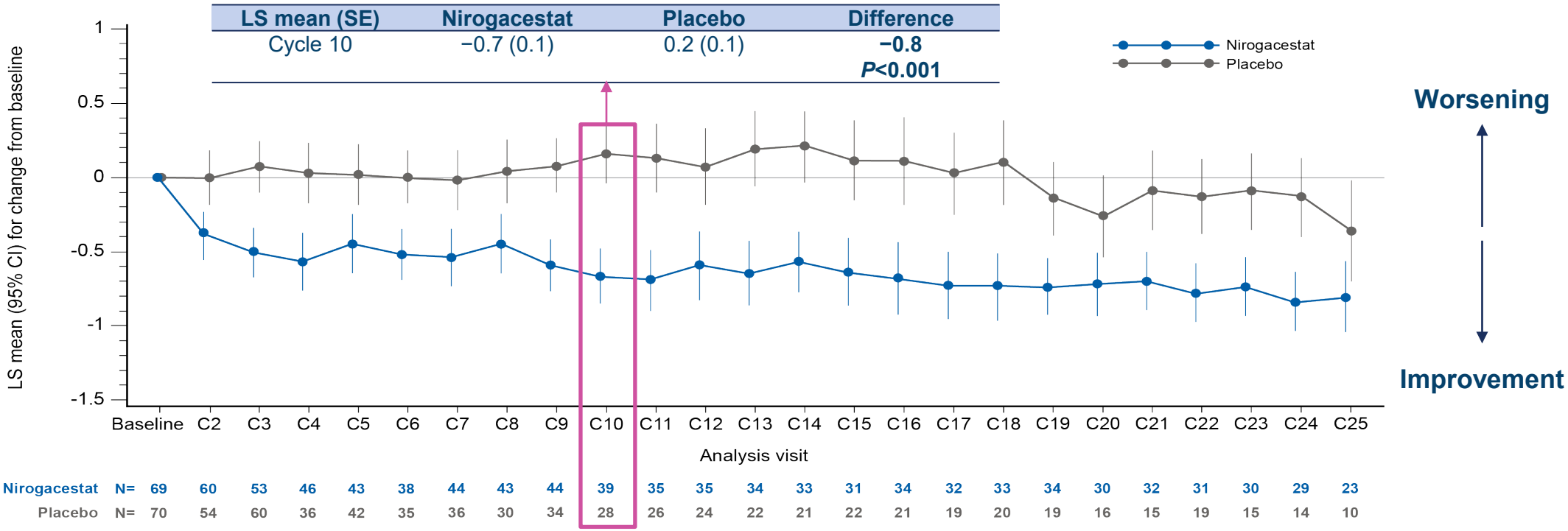
GODDESS DTSS – Total Symptom Score



Mean (SD) baseline scores: nirogacestat, 3.4 (2.34); placebo, 3.5 (2.57). Differences at Cycle 10 were statistically significant and clinically meaningful.
DTSS total symptom score includes pain, fatigue, swelling, muscle weakness, and difficulty moving.
DT, desmoid tumor; DTSS, GODDESS DT Symptom Scale; GODDESS, GOunder/Desmoid Tumor Research Foundation DEsmoid Symptom/Impact Scale; LS, least squares.

Nirogacestat Significantly Improved Physical/Role Functioning and QoL

GODDESS DTIS – Physical Functioning Impact Score



- **Nirogacestat also significantly improved EORTC QLQ-C30 physical functioning (*P*<0.001), role functioning (*P*<0.001), and global health status/QoL (*P*=0.007) at Cycle 10 compared with placebo**

Mean (SD) baseline scores: nirogacestat, 2.8 (1.14); placebo, 2.7 (1.24). Differences at Cycle 10 were statistically significant and clinically meaningful. DTIS physical functioning includes moving, reaching, vigorous activity, moderate activity, accomplishing less.
DT, desmoid tumor; DTIS, GODDESS DT 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; QoL, quality of life.

Nirogacestat Safety Profile

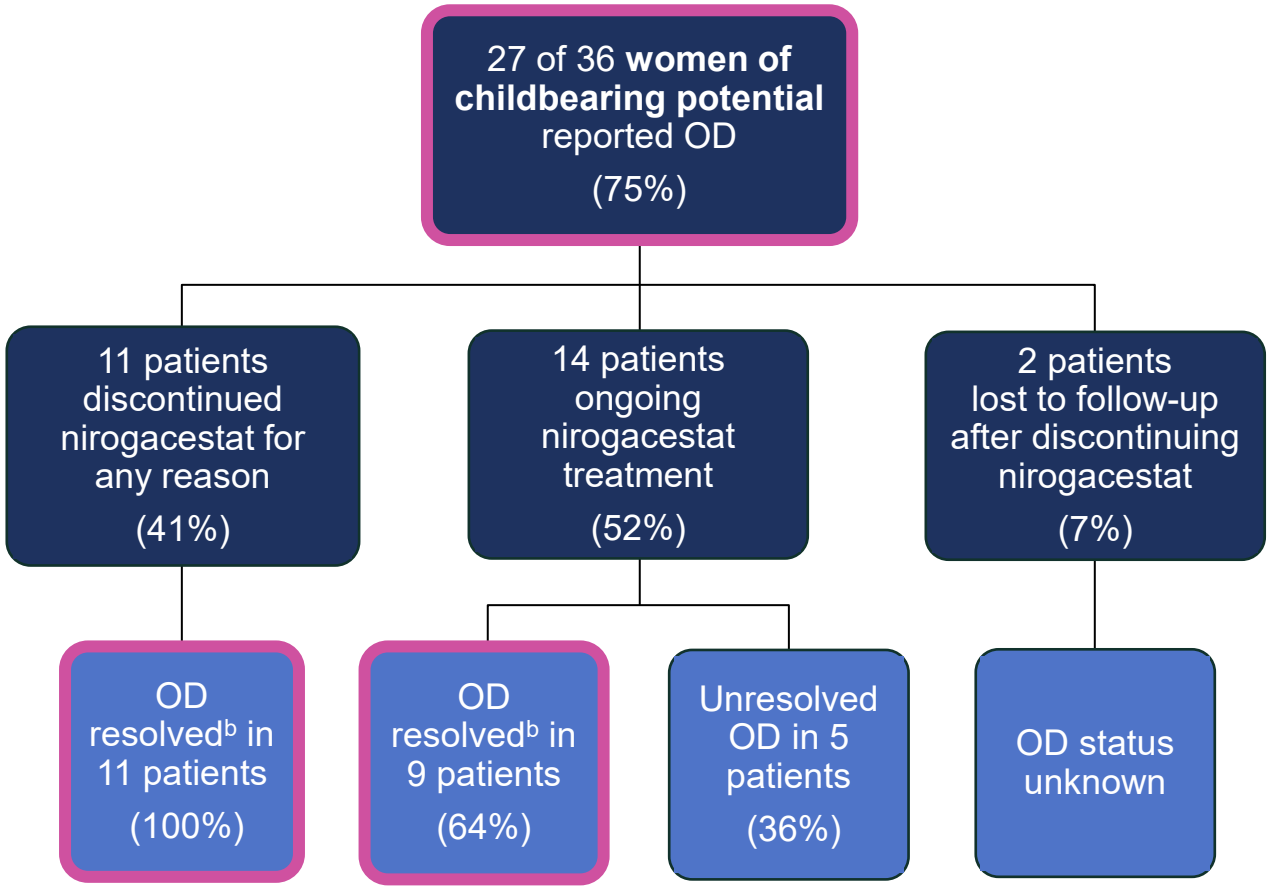
Safety population, n (%)	Nirogacestat (n=69)		Placebo (n=72)	
Duration of study drug exposure, median (range), months	20.6 (0.3, 33.6)		11.4 (0.2, 32.5)	
Dose intensity, median (range), mg/d	288.3 (169, 300)		300.0 (239, 300)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	69 (100)	39 (57)	69 (96)	12 (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**

[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%]).
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



[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.
OD, ovarian dysfunction.

1. Thurston et al. *Obstet Gynecol Clin North Am.* 2011;38:489-501. **2.** Mauri et al. *Front Endocrinol (Lausanne).* 2020;11:572388.

Summary

- **DeFi represents the largest and most rigorous randomized controlled trial conducted to date in DT**
  - DeFi is also the first Phase 3, randomized, controlled trial to demonstrate clinical benefit with a GSI in any indication
- **Nirogacestat demonstrated rapid, sustained, and statistically significant improvements in all primary and secondary efficacy endpoints**
  - 71% reduction in the risk of disease progression as compared with placebo
  - Objective response rate of 41%, including a 7% complete response rate
  - Statistically significant and clinically meaningful improvements in pain, disease-specific symptom burden, physical/role functioning, and overall quality of life ($P \leq 0.007$)
- **Nirogacestat exhibited a manageable safety profile, with 95% of all treatment-emergent adverse events being Grade 1 or 2**
- **Nirogacestat has the potential to become the standard of care for patients with DT requiring systemic treatment**

DT, desmoid tumor, GSI, gamma secretase inhibitor.

Acknowledgments

- We thank the DeFi trial participants, their families, and trial personnel
- We thank these DeFi Principal Investigators for their contributions to participant enrollment and data acquisition: Charlotte Benson, Nam Quoc Bui, Rashmi Chugh, Gabriel Tinoco, John Charlson, Palma Dileo, Lee Hartner, Lore Lapeire, Filomena Mazzeo, Emanuela Palmerini, Peter Reichardt, Silvia Stacchiotti, Howard H. Bailey, Melissa A. Burgess, Gregory M. Cote, Lara E. Davis, Hari Deshpande, Hans Gelderblom, Giovanni Grignani, Elizabeth Loggers, Tony Philip, Joseph G. Pressey
- We thank the former DeFi Principal Investigators for their contributions: Victor Villalobos, Jonathan Trent, Robert Maki, Suzanne George, Michael Nathenson, and Amanda Parkes; and the DeFi Principal Investigators who contributed to the screening of trial participants: Christian Meyer, Mark Agulnik, James Hu, Vicki Keedy, and Jade Homsi
- We thank the data monitoring committee members: Timothy Cripe, Damon Reed, Stephen Skapek, and Barry Turnbull
- We thank The Desmoid Tumor Research Foundation and Sarcoma Patients Advocacy Global Network (SPAGN)
- Medical writing and editorial support was provided by MedThink SciCom
- DeFi was sponsored by SpringWorks Therapeutics, Inc.

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Closing Remarks

Saqib Islam

Chief Executive Officer

SpringWorks® THERAPEUTICS

Promising Phase 3 Results Support NDA Submission in 2H 2022

Robust Improvement in Median PFS

NE	15.1 mo	HR = 0.29 [p<0.001]
Nirogacestat	Placebo	71% reduction in risk of disease progression

Demonstrated ORR Benefit

ORR		CR	
41%	8%	7%	0%
Nirogacestat	Placebo	Nirogacestat	Placebo

Improvement in Key Quality of Life Measures

Significant improvements vs. placebo in reducing pain and DT-specific symptom severity and in improving physical/role functioning and QoL

Manageable Safety Profile

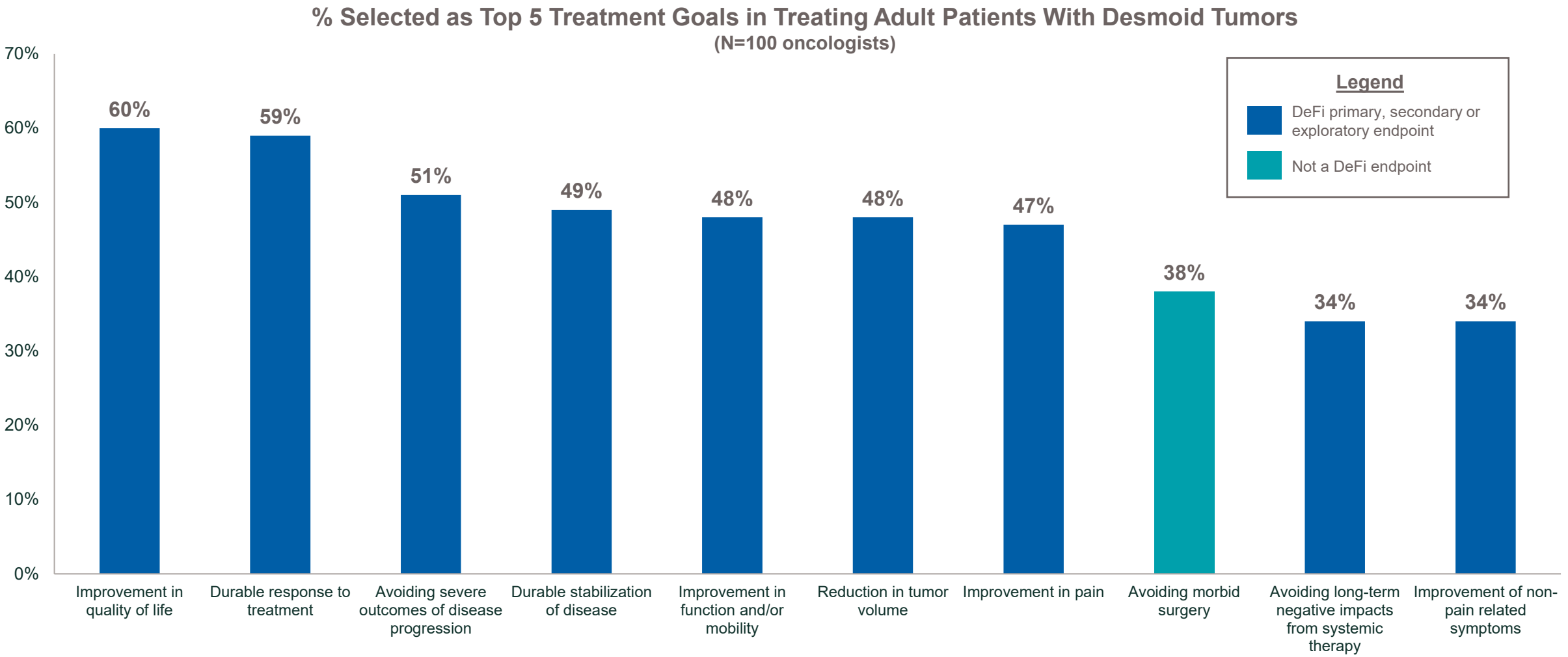
95% of AEs reported were Grade 1 or 2

74% of all OD events resolved(1)

- DeFi is the largest and most robust Phase 3 trial conducted to date in patients with desmoid tumors
- Nirogacestat treatment resulted in rapid, sustained and statistically significant improvements in primary and all key secondary efficacy endpoints
- All patients had RECIST progression at baseline; high proportion of patients with multifocal disease and uncontrolled pain
- Nirogacestat exhibited a manageable safety profile; the most commonly reported adverse events were diarrhea, nausea and fatigue

Note: AE: adverse events; CR: complete response; HR: hazard ratio; NE: not estimable; OD: ovarian dysfunction; ORR: objective response rate
(1) 100% resolution in patients who discontinued treatment; 64% resolution in those remaining on nirogacestat.

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



Desmoid tumor physician treatment goals are driven by efficacy, durability and patient QoL

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

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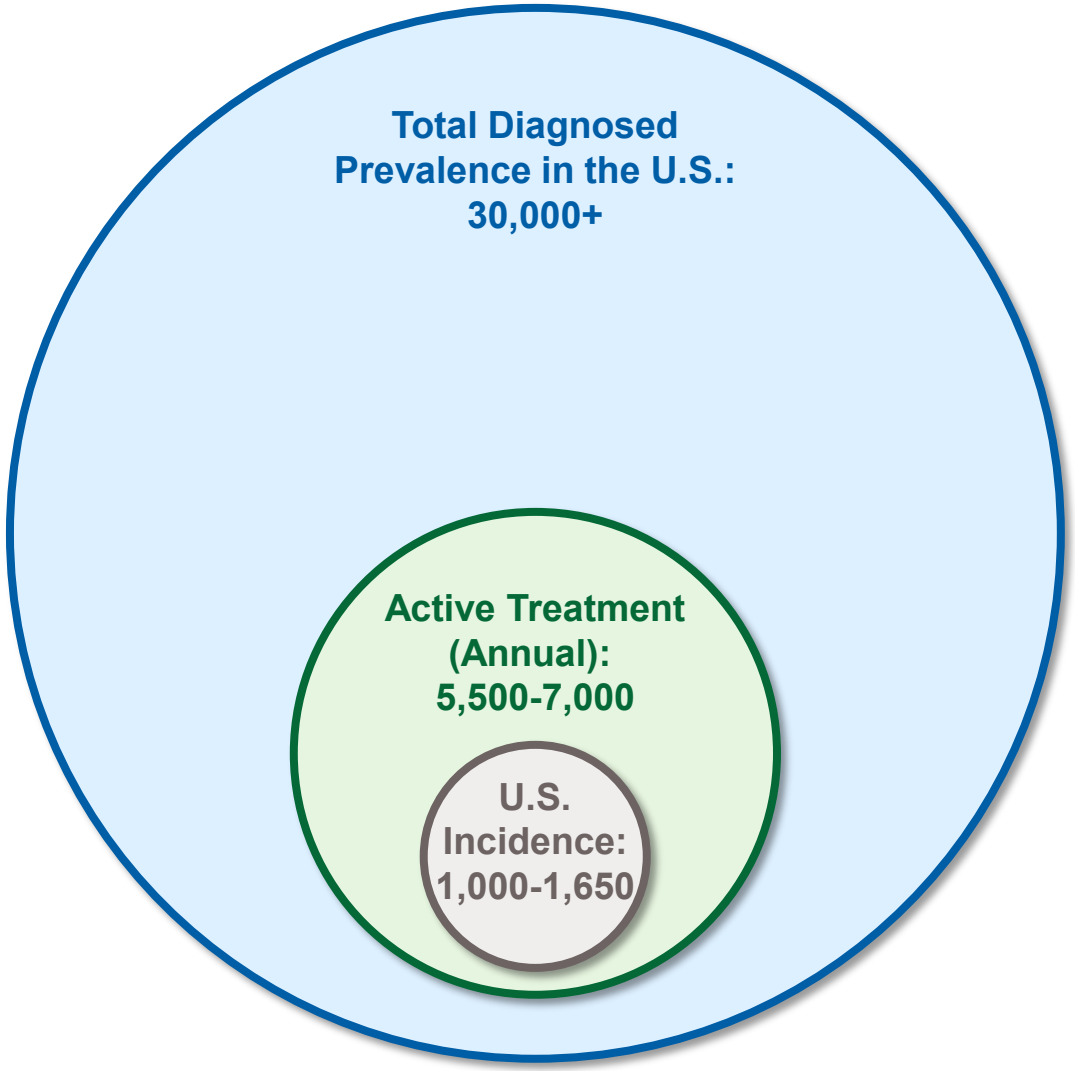
Significant Unmet Need for Desmoid Tumor Patients



Large Prevalent Population Seeking Active Treatment

- Incidence of 3 – 5 per million per year[1-3], 1,000 – 1,650 new diagnoses per year with ~35,000 patients living with desmoid tumors in the U.S.
- ~20 – 25% of total prevalent patients are under active treatment, yielding 5,500 – 7,000 patients per year[4]

Growth Drivers in Actively Treated Population with Limited Treatment Options

- Propensity to treat is high with over 90% of U.S. DT patients receiving an active intervention
- Off-label systemic therapies are often poorly tolerated with inconsistent efficacy
- Utilization of currently available therapies is fragmented due to treatment limitations
- Continued erosion of surgery with shift away from "cut-first" mentality due to high post-surgical recurrence rates up to 70%[5-6]
- Increased awareness leading to more "inactive" patients seeking treatment
- Opportunity for extended duration of therapy with nirogacestat

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.

SpringWorks is Excited By the Opportunity to Serve Desmoid Tumor Patients

- **Nirogacestat differentiated** based on evidence of efficacy, manageable tolerability, QoL improvement and oral convenience, which supports potential for extended duration of treatment
- **Large prevalent population** due to high recurrence rates and limited systemic treatment options
- **Awareness of nirogacestat is high** and significant clinical experience at SARC and NCCN centers
- **Launch activities rapidly advancing** to ensure successful preparation of market, organization and brand
- **Expected NDA filing in 2H22** under FDA's Real Time Oncology Review; **potential to be first FDA-approved therapy** in desmoid tumors

Q&A

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Thank You

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