# Corporate Presentation

September 2022

SpringWorks® THERAPEUTICS

# Forward-Looking Statements

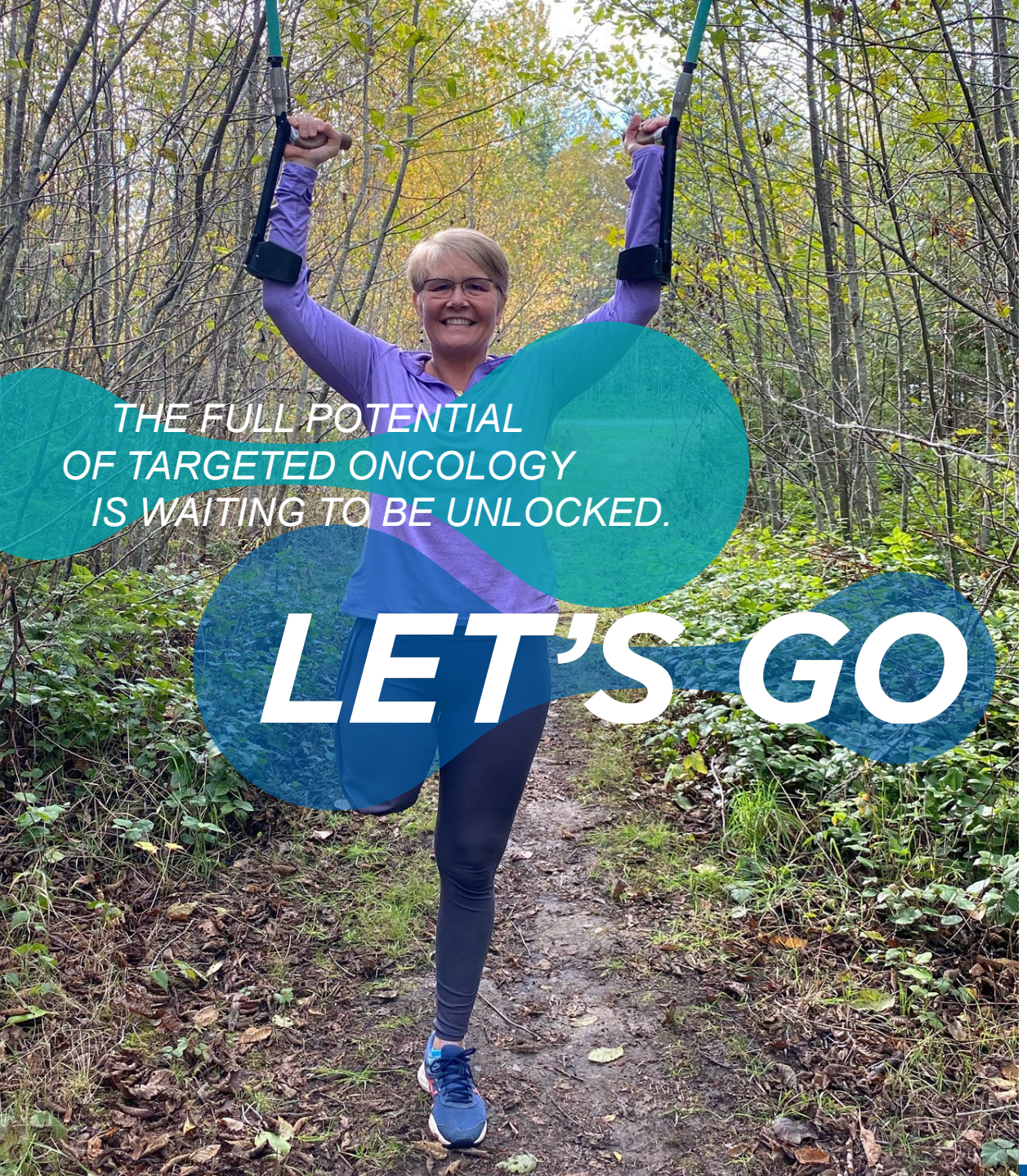
Note: Unless otherwise indicated, the information presented herein is as of September 2022 and made publicly available on September 21, 2022.

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

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

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

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




## 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 $69.7 million August 2022 ATM Offering (as described on page 73), (b) the $225 million private placement transaction announced on September 7, 2022, and (c) the $75 million 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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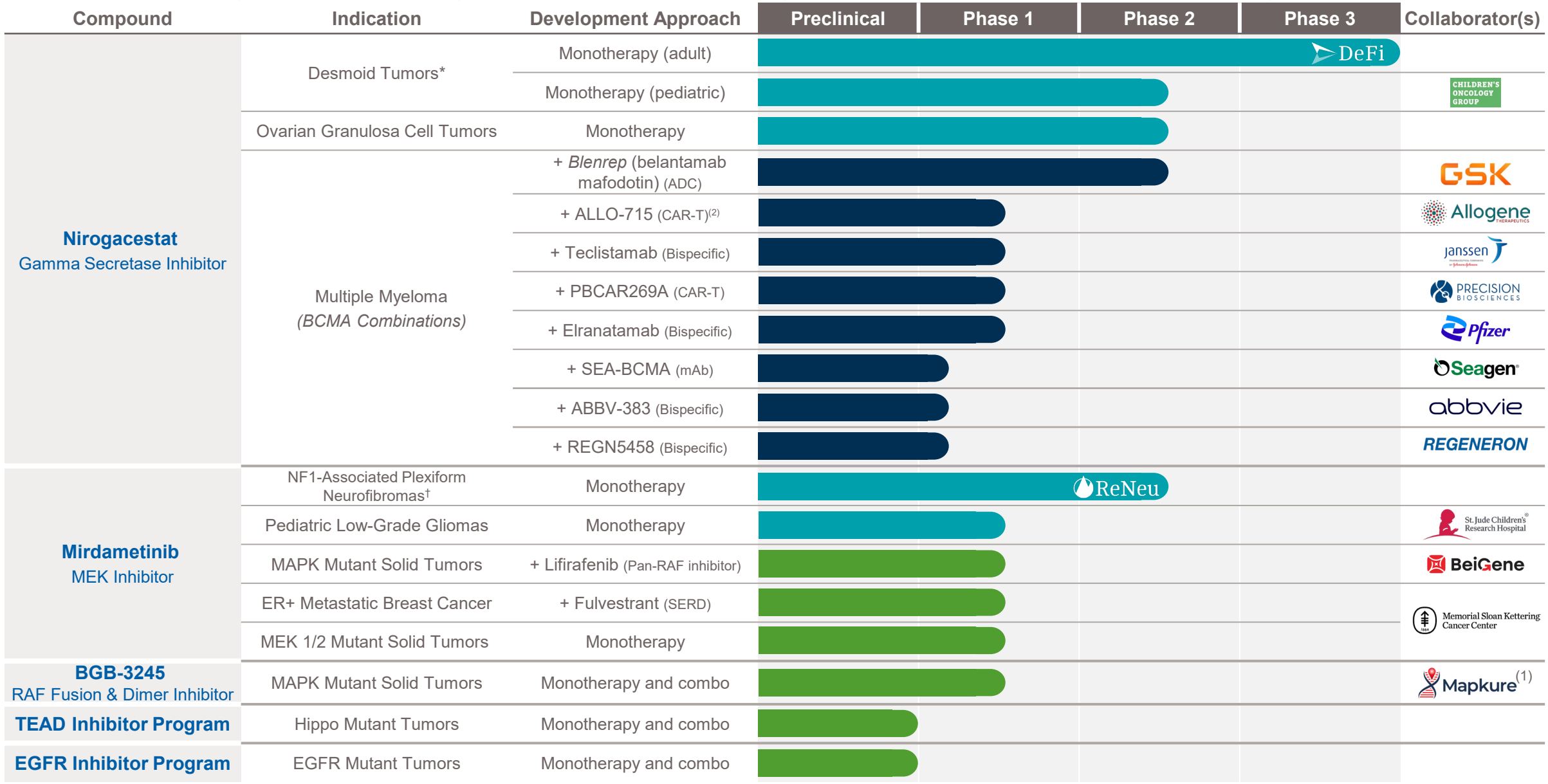
# Diversified Targeted Oncology Pipeline Spanning Solid Tumors and Hematological Cancers




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

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# Value-Driving Data Readouts and Program Updates Across the Pipeline

## 2022 Accomplishments

- ✓ Reported Phase 3 DeFi trial results at ESMO for nirogacestat in desmoid tumors
- ✓ Highlighted initial clinical data from Phase 1/2 nirogacestat combo trial with GSK (*Blenrep*) in MM
- ✓ Expanded global, non-exclusive collaboration with GSK for nirogacestat in combination with *Blenrep* across lines of therapy in MM
- ✓ Highlighted long-term follow-up data from Phase 2 trial of nirogacestat in progressing desmoid tumors
- ✓ Reported Phase 1b/2 initial clinical data for mirdametinib + lifirafenib in RAS/RAF-mutant solid tumors
- ✓ Reported Phase 1 initial clinical data for BGB-3245 in RAF-mutant solid tumors
- ✓ Highlighted initial data from Phase 1 trial sponsored by St. Jude for mirdametinib in pLGG at the ISPNO Conference
- ✓ Supported initiation of sub-studies combining nirogacestat, *Blenrep* and standard of care agents in collaboration with GSK
- ✓ Presented TEAD program preclinical data at AACR
- ✓ Completed further equity investment in MapKure to advance development of BGB-3245

**NDA submission for nirogacestat planned for 2H22; to be submitted for review under the FDA's RTOR program**



Note: MM: multiple myeloma; pLGG: pediatric low-grade glioma.

# Nirogacestat

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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
- 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 Submission in Desmoid Tumors:** | **2H 2022** |
| **Clinical Trials Ongoing or On Track for 2022 Initiation:** | **11** |
| **BCMA Collaborations(2):** | **8** |
| **US Composition of Matter and Method of Use patent protection:** | **2039** |



(1) Orphan Drug, Fast Track and Breakthrough Therapy Designations received from FDA for desmoid tumors and Orphan Drug Designation received from European Commission for soft tissue sarcoma.
(2) No further enrollment expected in ongoing Phase 1 study with Allogene per study update disclosed in Allogene press release on 08/09/22.

# Nirogacestat

## Desmoid Tumors

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**Dana**
**Desmoid tumor patient**

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

## Disease Characteristics

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

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

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

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

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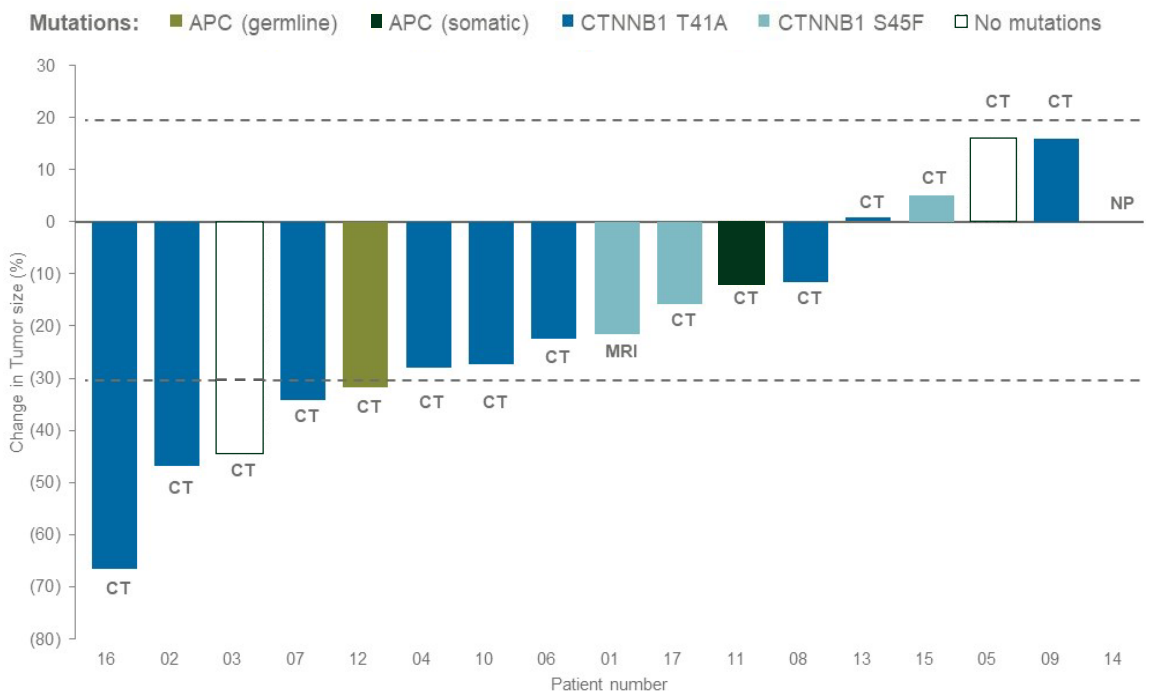
# Encouraging Phase 2 Data in Progressing Desmoid Tumors Were Published in 2017

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

## Clinical Responses by RECIST v1.1




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

Note: Per RECIST 16/17 patients were evaluable. One treatment cycle = 150 mg BID continuously for 21 days. Patient #1 had a missing baseline measurement (but had MRI). Patient #14 was not evaluable per protocol, withdrew from study after cycle 1 due to travel requirements.
Source: Kummar et al., *Journal of Clinical Oncology*, 2017.
(1) 71% had received chemotherapy, 65% NSAIDs, and 59% TKIs; 4/5 partial responses had previously failed imatinib or sorafenib.



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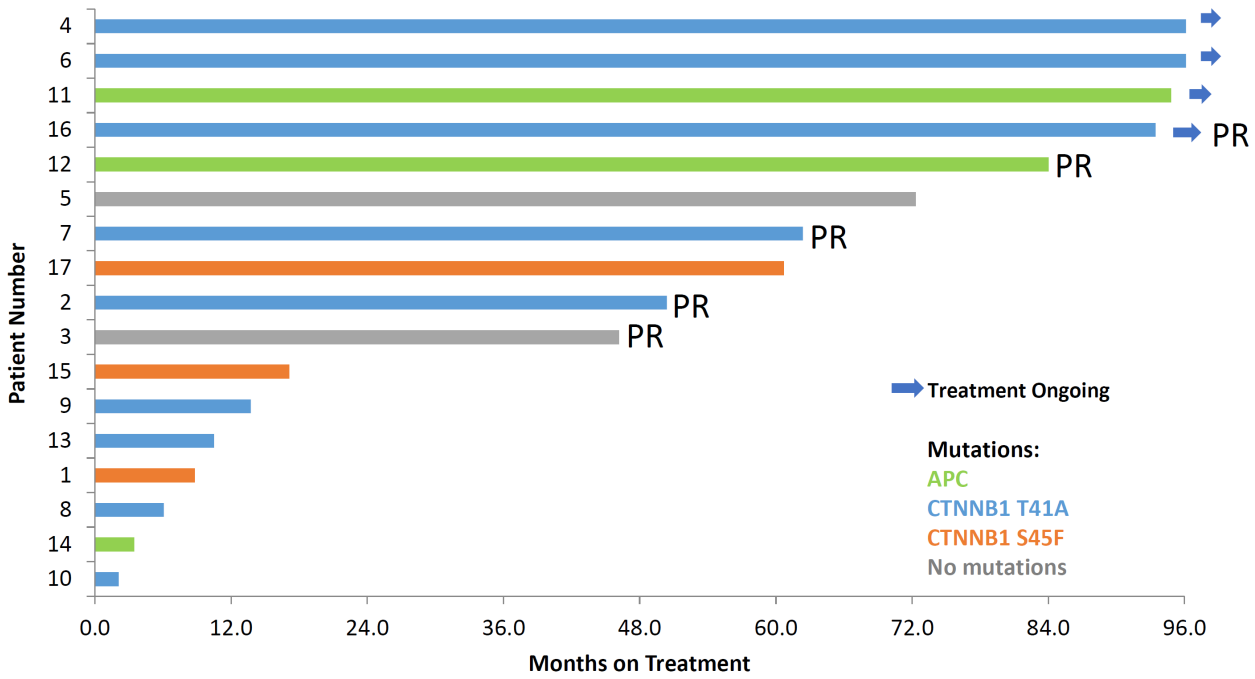
# Long-Term Safety and Efficacy Follow-Up Data from Phase 2 Trial Presented at ASCO 2022

PHASE 1 | PHASE 2 | PHASE 3

## Long-Term Progression Free Survival




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



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

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

DeFi

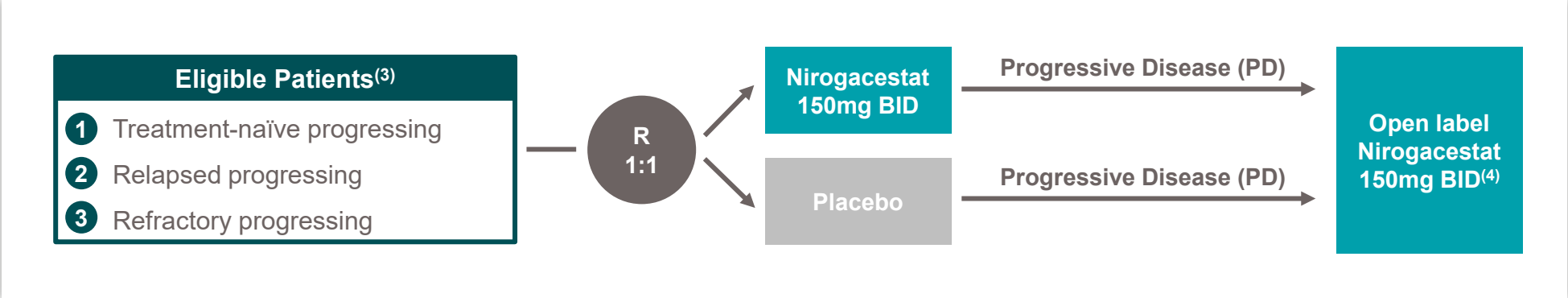
PHASE 1 | PHASE 2 | **PHASE 3**

## 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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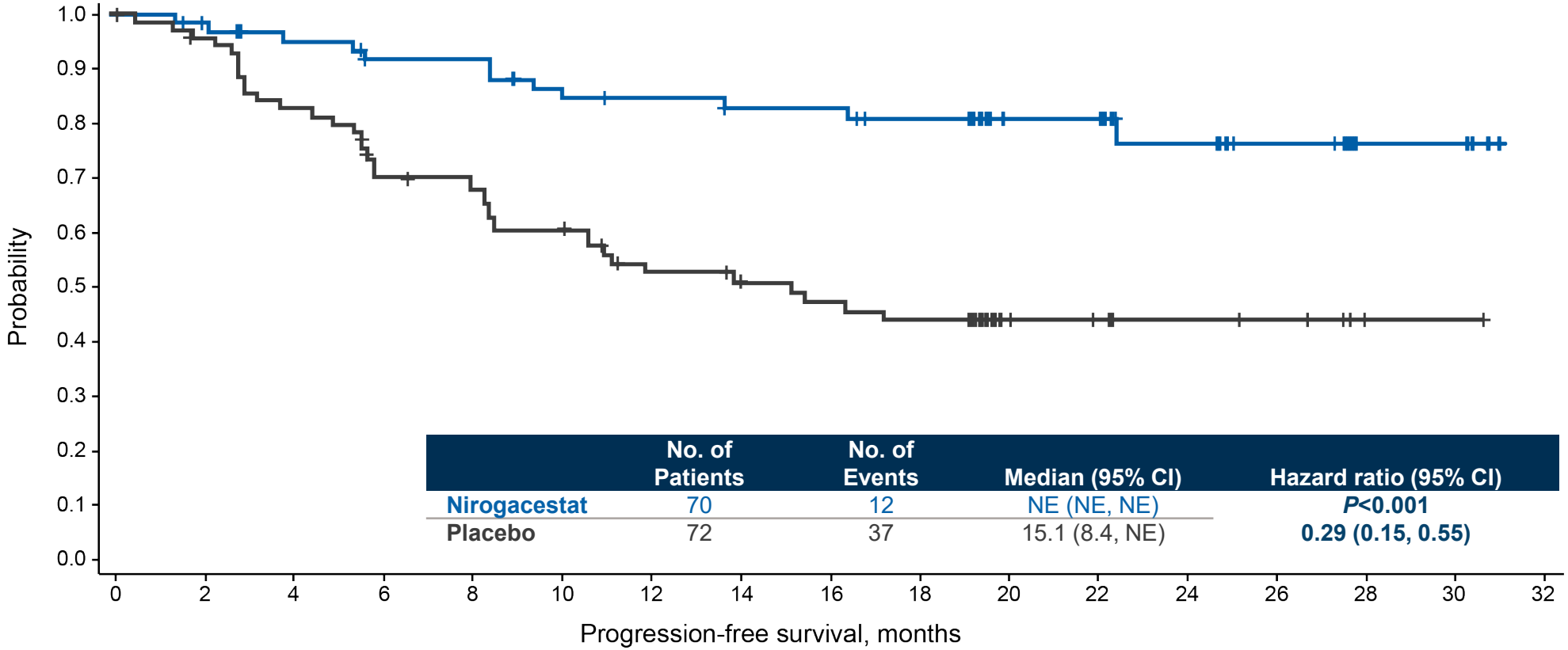
# Baseline Demographics and Characteristics

| 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) |
| Prior radiation therapy | 16 (23) | 16 (22) |
| Prior surgery | 31 (44) | 44 (61) |
| Patients with uncontrolled pain per BPI-SF API >4, n (%)[b] | 16 (23) | 14 (19) |

Source: Kasper et al., *ESMO,* 2022. 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 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)** |

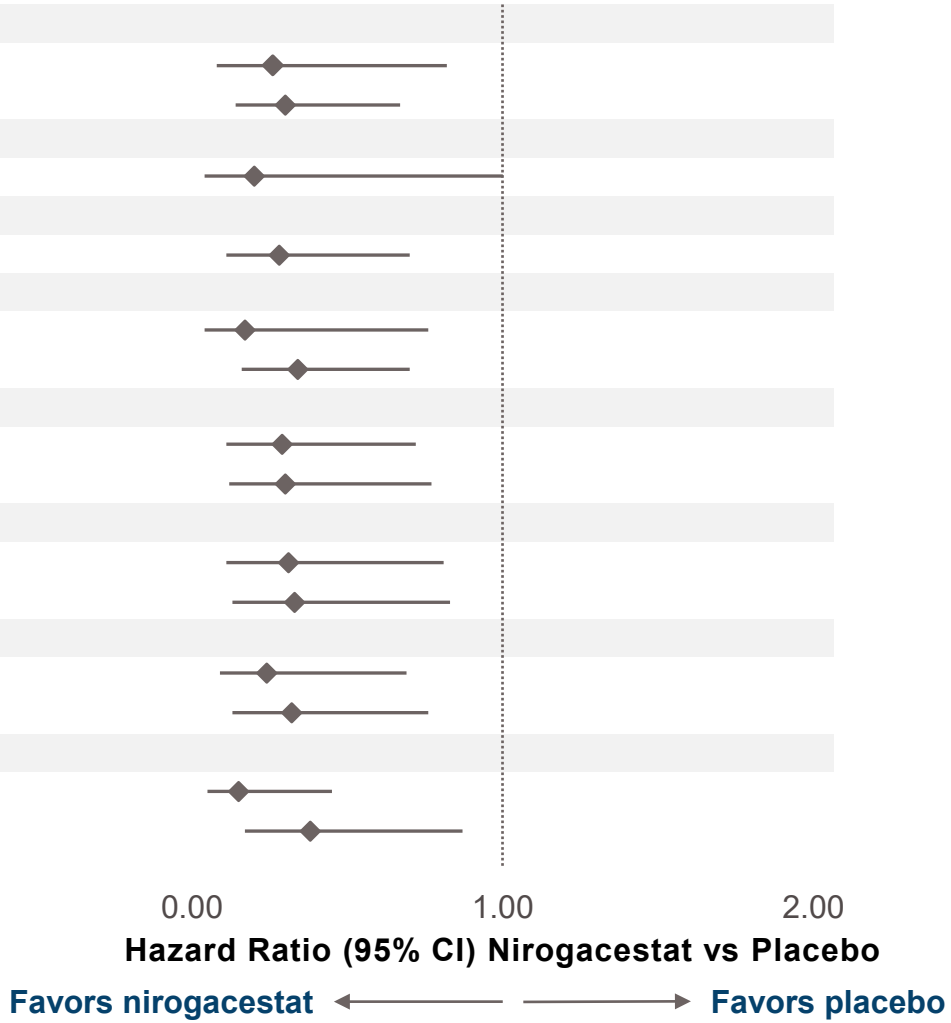
**No. of Participants at Risk:**

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **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

| | 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 |






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

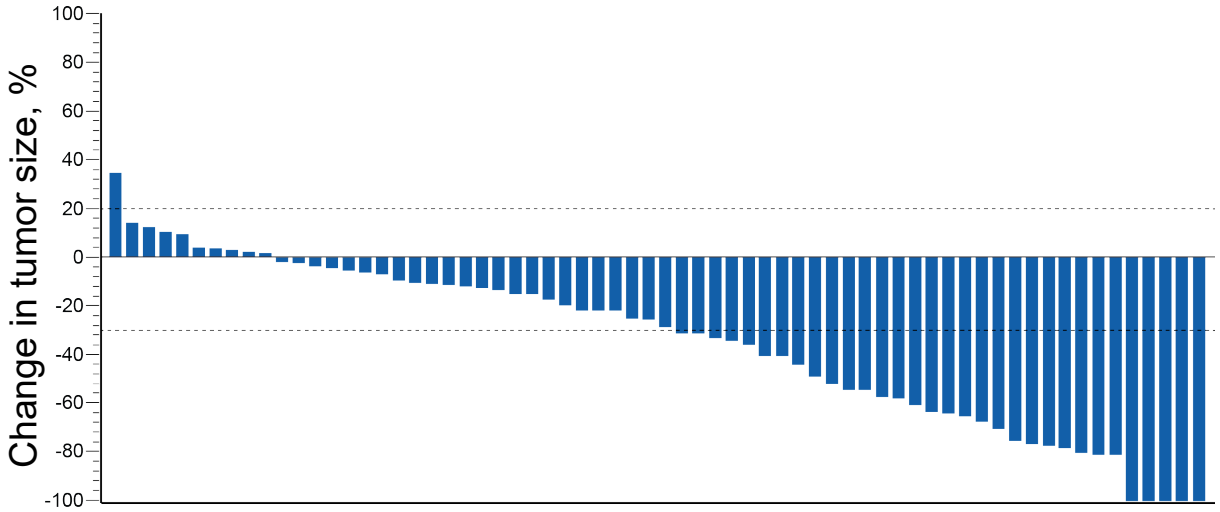
# Objective Response Rate by Blinded Independent Central Review

| | Nirogacestat (n=70) | Placebo (n=72) |
|---|---|---|
| **Objective response rate (CR+PR), n (%)**<br>95% CI<br>Two-sided *P* value | **29 (41)**<br>**(30.2, 54.5)**<br>**<0.001** | **6 (8)**<br>**(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) |

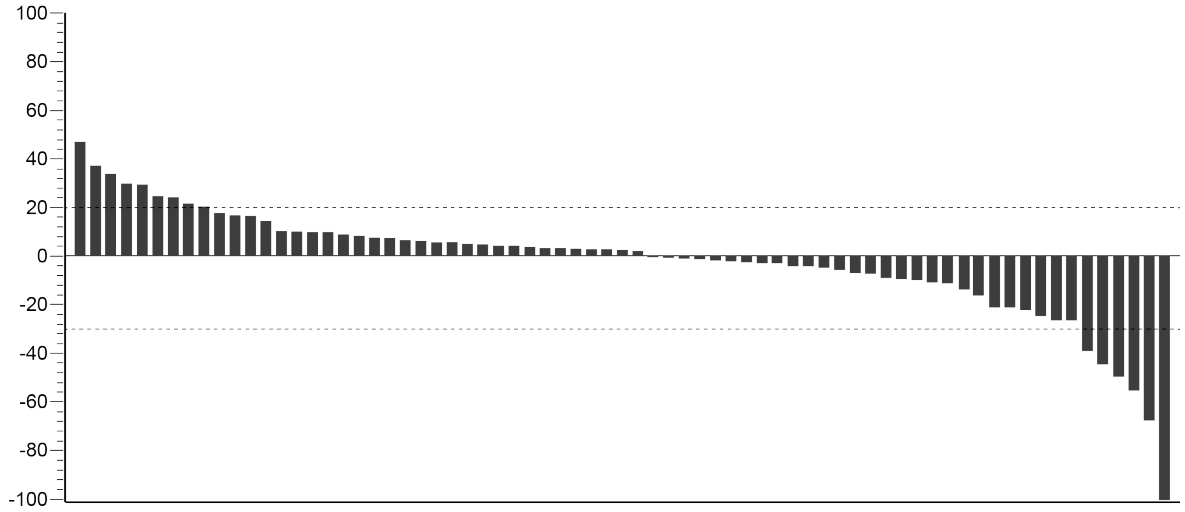
Source: Kasper et al., *ESMO,* 2022. Data as of the time of primary analysis (04/07/22).
a) Duration of objective response was defined as duration in months from the time CR or PR (which ever came first) was met until the date of progression, death, or censoring.
Note: CR, complete response; NE, not estimable; PR, partial response.

# Nirogacestat Treatment Resulted in Substantial Reductions in Tumor Size

## Nirogacestat




## Placebo




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

# 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 |
| | 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).
Note: Differences at Cycle 10 were statistically significant and clinically meaningful.
Note: 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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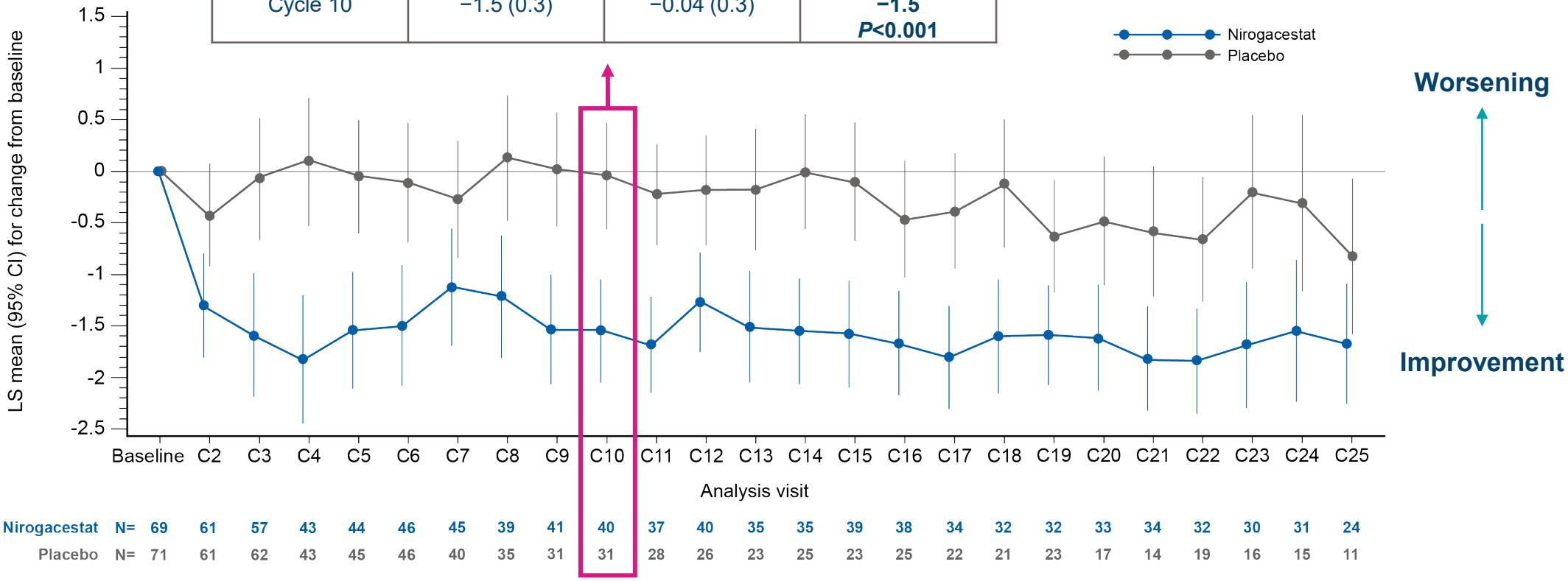
# Nirogacestat Significantly Reduced Pain Severity Compared with Placebo

| LS mean (SE) | Nirogacestat | Placebo | Difference |
|---|---|---|---|
| Cycle 10 | −1.5 (0.3) | −0.04 (0.3) | **−1.5**<br>***P*<0.001** |




**Nirogacestat demonstrated significant improvement on all key PROs at Cycle 10 compared to placebo; patients had early and sustained benefits – the majority of nirogacestat patients were still on treatment at the time of the primary analysis**

Source: Kasper et al., *ESMO*, 2022. Data as of the time of primary analysis (04/07/22).
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.
Note: LS, least squares.

# Nirogacestat Safety Profile

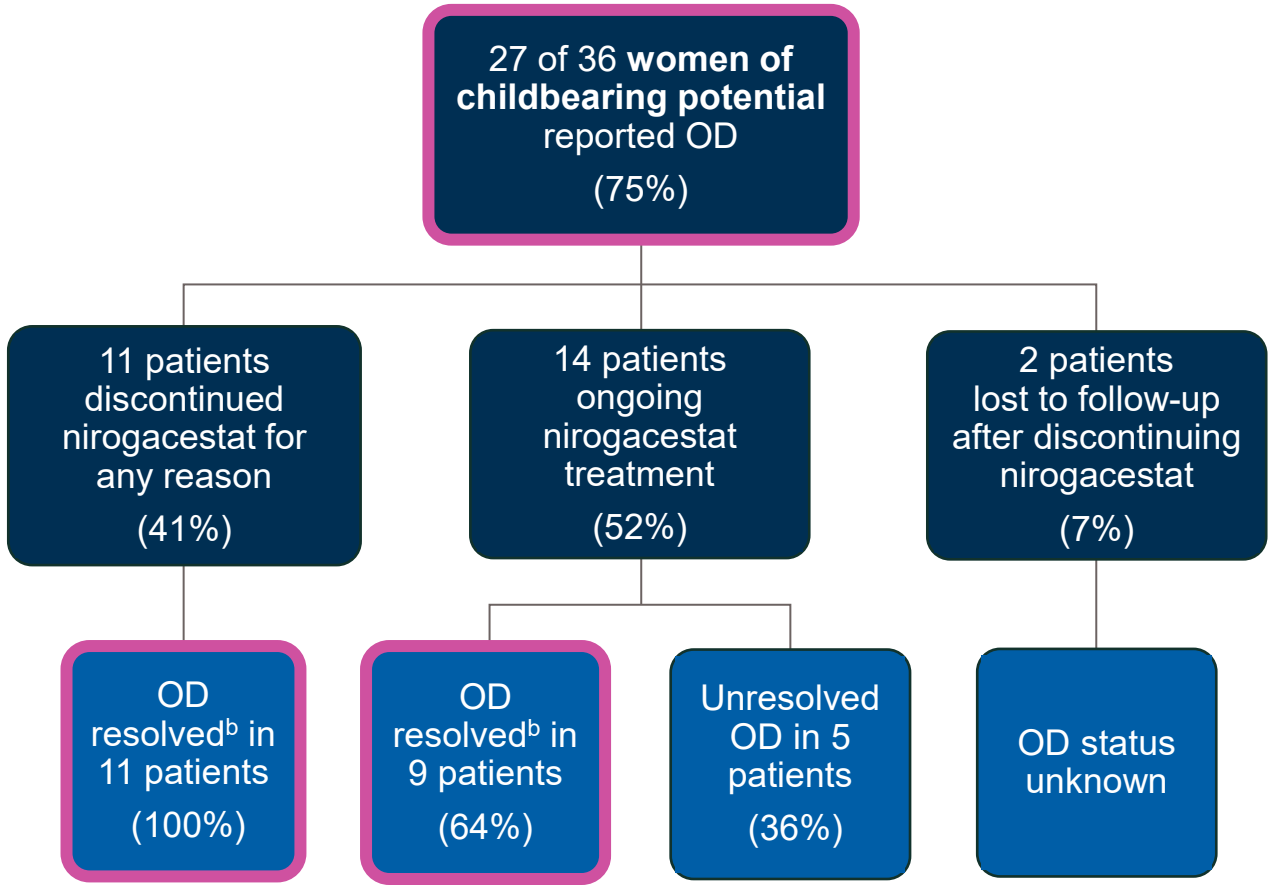
| Safety population, n (%) | Nirogacestat (n=69) | | Placebo (n=72) | |
|---|---|---|---|---|
| Duration of study drug exposure, median (range), months | 20.6 (0.3, 33.6) | | 11.4 (0.2, 32.5) | |
| Dose intensity, median (range), mg/d | 288.3 (169, 300) | | 300.0 (239, 300) | |
| | **Any Grade** | **Grade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




Source: Kasper et al., *ESMO,* 2022. Data as of the time of primary analysis (04/07/22).
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.
1) Thurston et al., *Obstet Gynecol Clin North Am.* 2011;38:489-501; 2) Mauri et al., *Front Endocrinol (Lausanne).* 2020;11:572388.

# Phase 3 DeFi Trial Summary

## 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**

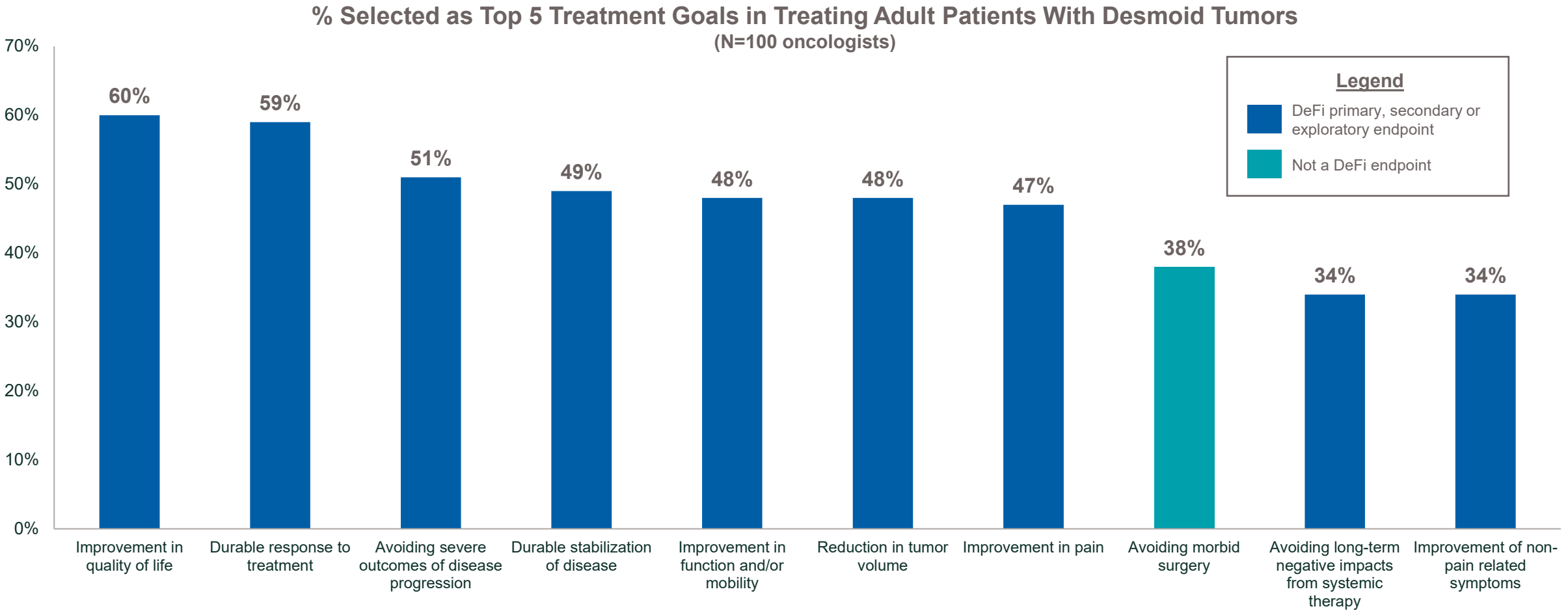
**74% of all OD events resolved(1)**

- 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.

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




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



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

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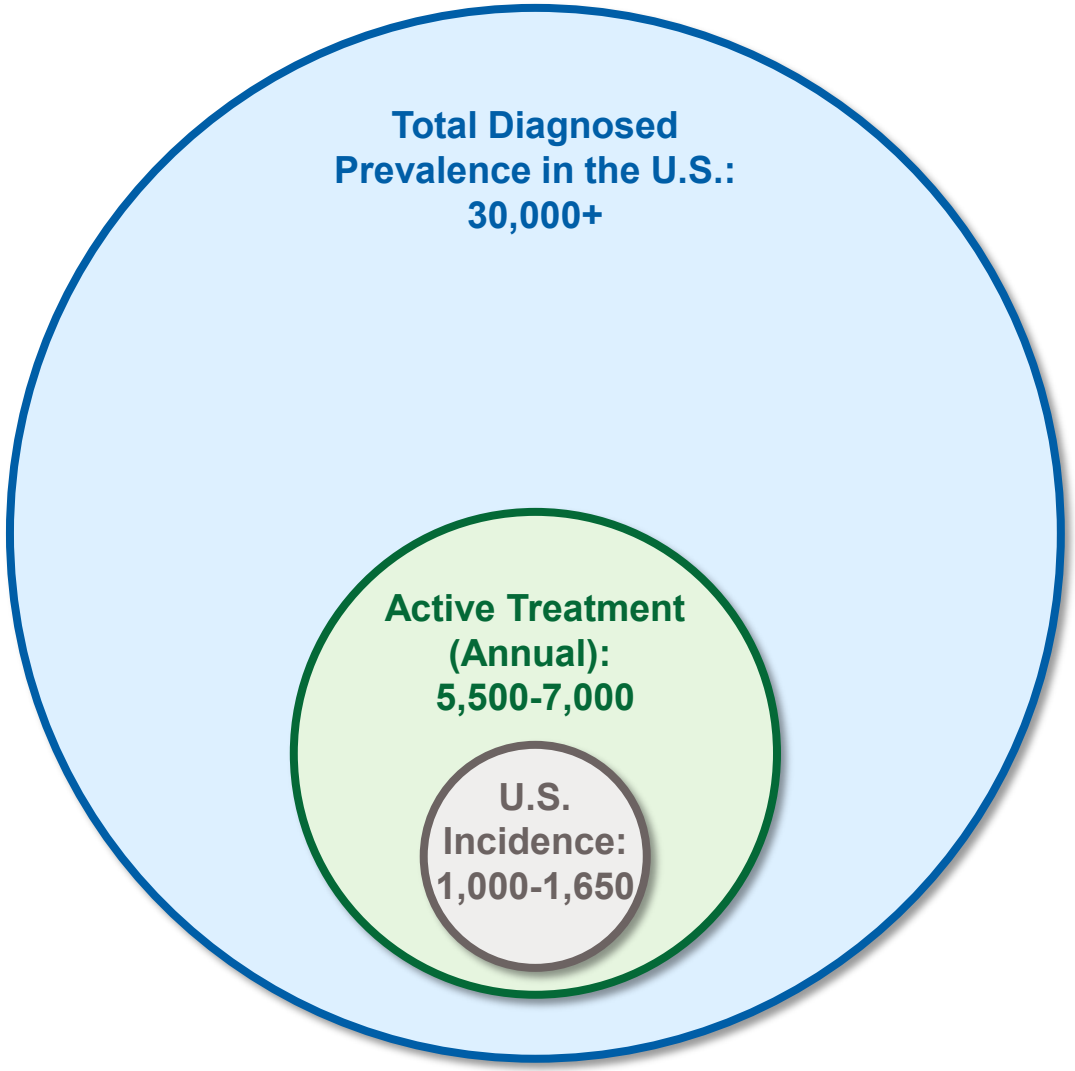
# Significant Unmet Need for Desmoid Tumor Patients




## 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.

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# Building Blocks to Support a Substantial Market Opportunity

## Large prevalent population due to high recurrence rates

**1,000 to 1,650 incident patients annually**

**Up to 77% post-surgical recurrence**
reported in the literature and confirmed in real-world data sets(1)

**Estimated prevalence 3-7x incidence(2)**
in a nationwide Danish epidemiology study

**5,500 to 7,000 US patients treated annually**

## High degree of physician awareness and engagement

**>70% of oncologists are aware of nirogacestat(3)**
in a survey of 100 US oncologists treating patients with desmoid tumors

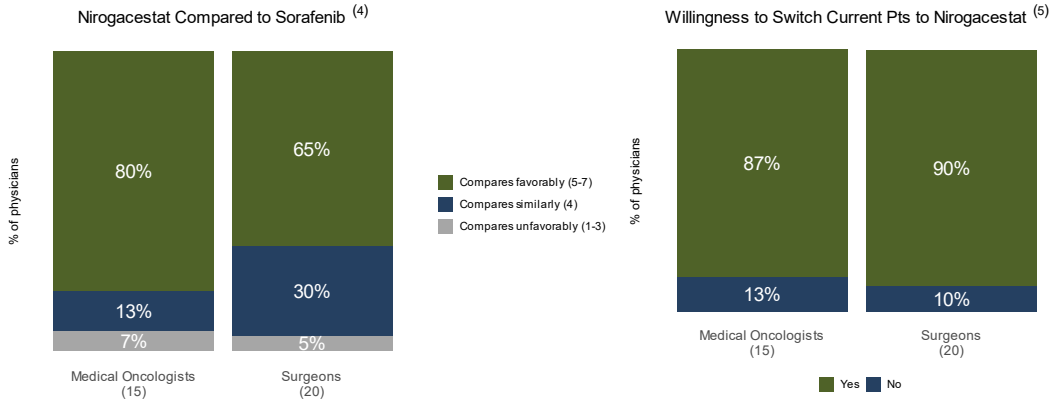
**More than 90% of U.S. DeFi sites were registered SARC centers**

**~65% were NCCN centers**

## Potential to be first and best in category

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

## Substantial enthusiasm for nirogacestat profile




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

# SpringWorks 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 submission in 2H22** under FDA's Real Time Oncology Review; **potential to be first FDA-approved therapy** in desmoid tumors

# Nirogacestat Clinical Activity Also Observed in Pediatric and Young Adult Desmoid Tumor Patients

**EXPANDED ACCESS PROGRAM**

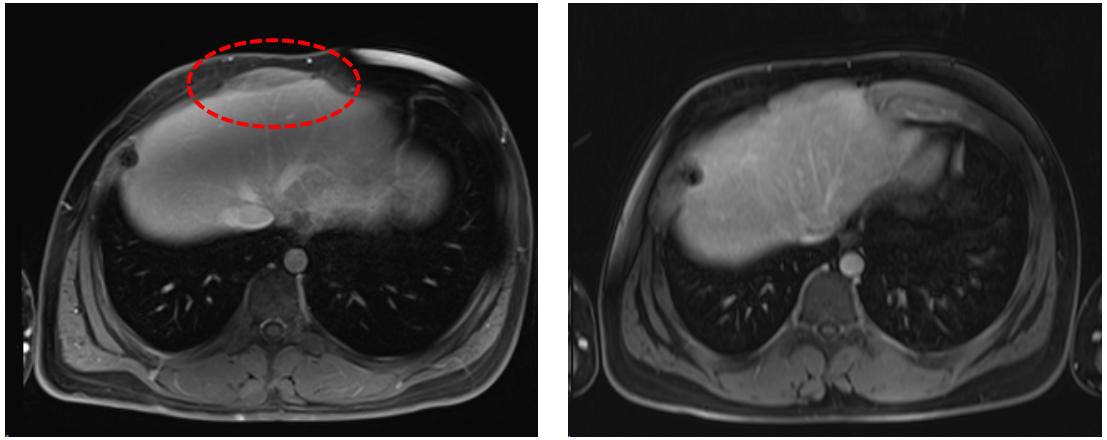
- Clinical benefit shown in four pediatric and young adult desmoid tumor patients who received nirogacestat (1 CR, 2 PR, and 1 SD)

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| **Age / Sex** | 17 yo male | 4 yo male | 19 yo female | 2.5 yo female |
| **APC Mutation** | No | Yes | Yes | Yes |
| **Prior Treatments** | ▪ Complete resection at 12 years old<br>▪ Sorafenib | ▪ Celecoxib | ▪ None | ▪ 8 prior lines incl. sorafenib, pazopanib, chemo, cryo |
| **Tumor Response** | CR | PR | SD | Initial PR; subsequent PD |
| **Duration of Benefit** | 18 months[1] | 17 months[1] | 10 months[1] | 6 months |

- **Nirogacestat was well tolerated; no grade 3 or 4 AEs**
  - 90 mg/m$^2$ per dose BID (max. 150 mg per dose BID)

## Patient 1: 17-year-old male with Complete Response

**Baseline MRI** | **After 9 months on nirogacestat**



- Prior treatments include complete resection at 12 years old (experienced recurrence) and sorafenib (intolerable AEs and PD after discontinuation)
- Tumor volume regressed by 15% on MRI within 6 months of starting nirogacestat; **tumor undetectable on imaging by 9 months**

**Announced collaboration with Children's Oncology Group in September 2020;**
**Patients being enrolled in single arm Phase 2 trial to evaluate nirogacestat in pediatric desmoid tumors**



Source: Takahashi et al., *Pediatr Blood Cancer*, 2020.
(1) Ongoing at time of publication.

# Nirogacestat

## Ovarian Granulosa Cell Tumors

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

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

## Disease Characteristics

- Ovarian granulosa cell tumors (OvGCT) are a rare ovarian cancer subtype that are usually slow-growing and have limited impact on mortality
- OvGCT are most commonly diagnosed in women during the perimenopausal / early postmenopausal period (median diagnosis age of 50 years)
- Patients typically present with severe abdominal pain, abdominal distension, and abnormal or postmenopausal bleeding alongside a large pelvic or abdominal mass(1)
- Recurrences can occur late, thereby requiring long-term surveillance and intervention to avoid bulky disease that is resistant to therapy

- OvGCT accounts for ~5% of all ovarian cancers(1)
- Estimated US incidence of 1,500-2,000 per year with a significant pool of prevalent patients of ~10,000-15,000(2,3)
- Prognosis for patients with advanced disease is poor, with a 10-year survival rate of approximately 25%(4)

- No currently approved therapies and limited treatment options
- Surgery is mainstay of treatment, but risk of recurrence is high for those with advanced disease(5)
- Systemic therapies (e.g., chemo, bevacizumab, paclitaxel and carboplatin) have shown limited benefit and tolerability

Sources: (1) Dridi et al., *Int J Surg Oncol*, 2018; (2) SEER; (3) Torre L. et al. *CA Cancer J Clin*, 2018; (4) Schumer S and Cannistra SA., *J Clin Oncol*. 2003. (5) Ayhan et al. *J Gynecol Oncol,* 2009.



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# Phase 2 Study of Nirogacestat in Recurrent Ovarian Granulosa Cell Tumors

PHASE 2

## Trial Summary

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

## Summary of Endpoints

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


**First site activated in June 2022**



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

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# Nirogacestat

## BCMA Combination Therapy Development in Multiple Myeloma

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

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

## Rationale and Development Strategy

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

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

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

Source: (1) Siegel et al., 2022; DRG market research.



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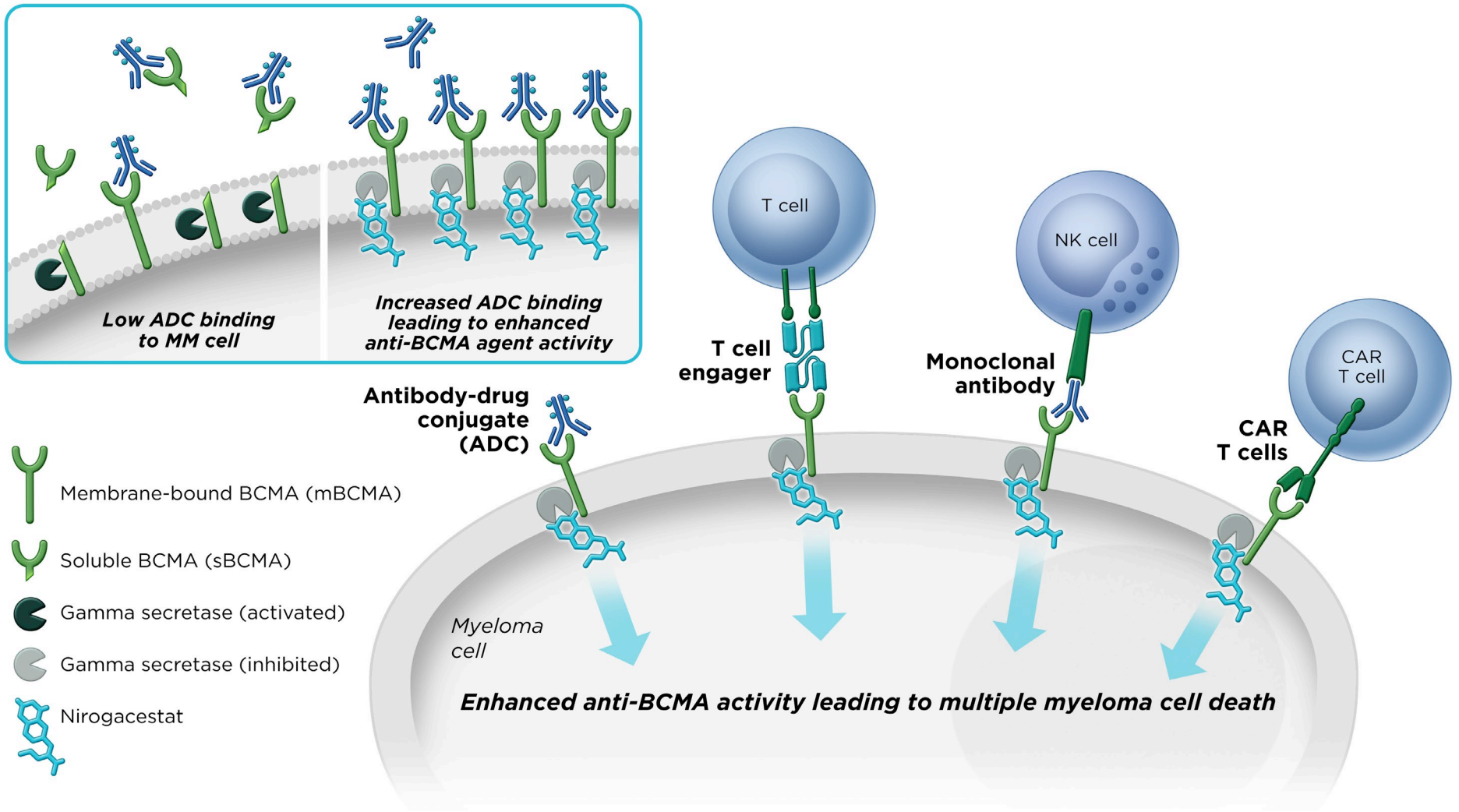
# SpringWorks is Leading the Mechanistic Understanding and Clinical Development of GSI + BCMA in Multiple Myeloma




Note: GSI: gamma secretase inhibitor.

# Eight Clinical Collaborations Covering All Key BCMA Therapeutic Modalities

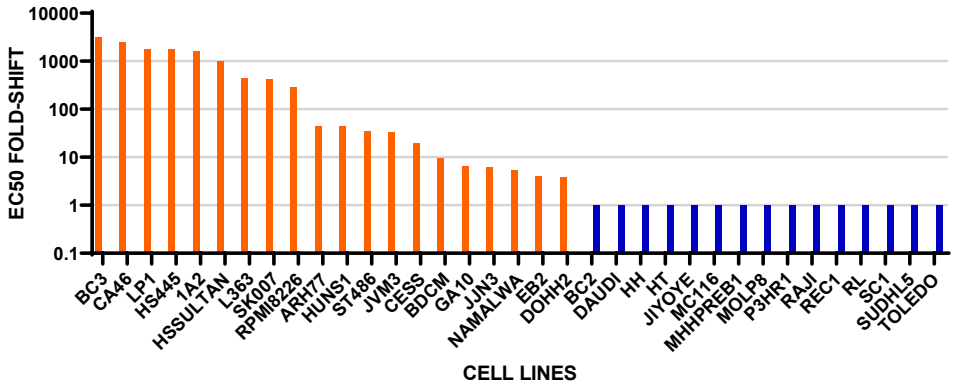
| Collaborator | Program | Modality | | | | Collaboration Signed | Current Status |
|---|---|---|---|---|---|---|---|
| | | ADC | Bispecific | CAR-T | mAb | | |
| GSK | *Blenrep* (belantamab mafodotin) | ✓ | | | | June 2019 | Randomized Phase 2 trial ongoing, various trials in combination with standard of care agents also ongoing |
| Allogene Therapeutics | ALLO-715 | | | ✓ | | January 2020 | Phase 1 dose escalation complete and awaiting long-term data analysis(1) |
| Janssen Pharmaceutical Companies of Johnson & Johnson | Teclistamab | | ✓ | | | September 2020 | Phase 1 trial ongoing |
| Precision Biosciences | PBCAR269A | | | ✓ | | September 2020 | Phase 1 trial ongoing |
| Pfizer | Elranatamab | | ✓ | | | October 2020 | Phase 1b/2 trial ongoing |
| Seagen | SEA-BCMA | | | | ✓ | June 2021 | Phase 1 trial planned |
| abbvie | ABBV-383 | | ✓ | | | December 2021 | Phase 1b trial planned |
| REGENERON | REGN5458 | | ✓ | | | April 2022 | Phase 1b trial planned |



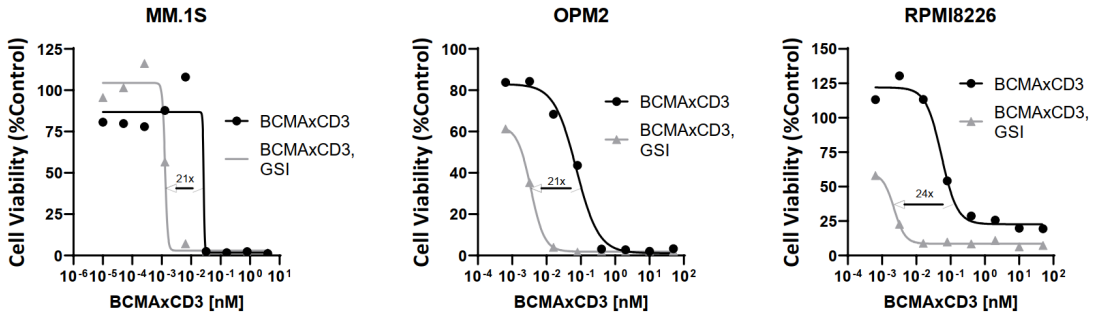
(1) No further enrollment expected; study update disclosed in Allogene press release on 08/09/22.

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

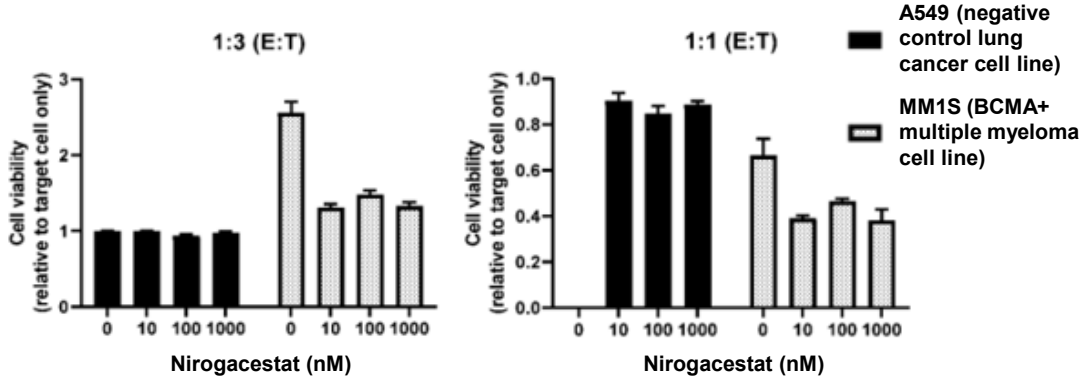
## BCMA ADC(1)



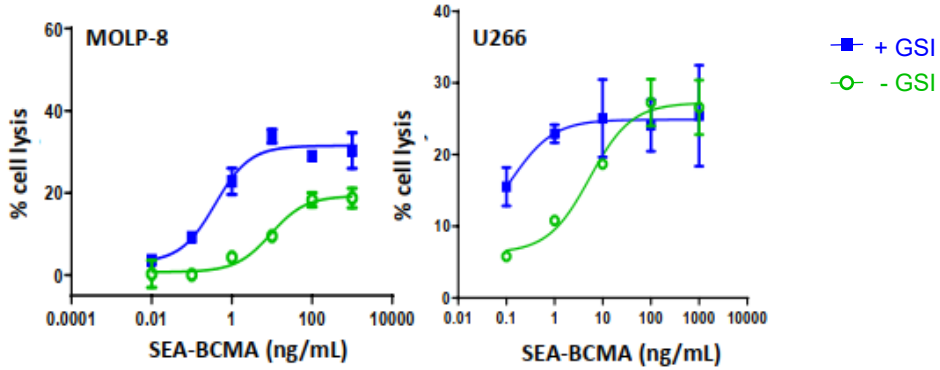

## BCMA-CD3 Bispecific(2)




## BCMA CAR-T(3)




## BCMA mAb(4)






Sources: (1) Eastman et al., *ASH*, 2019; (2) Karwacz et al., *AACR*, 2020; (3) Balakumaran, A. et al., "Combination therapies of chimeric antigen receptors targeting B-cell maturation antigen and gamma secretase inhibitors", World patent WO2021146604A1, July 2021; (4) Yu et al., *EHA*, 2021.

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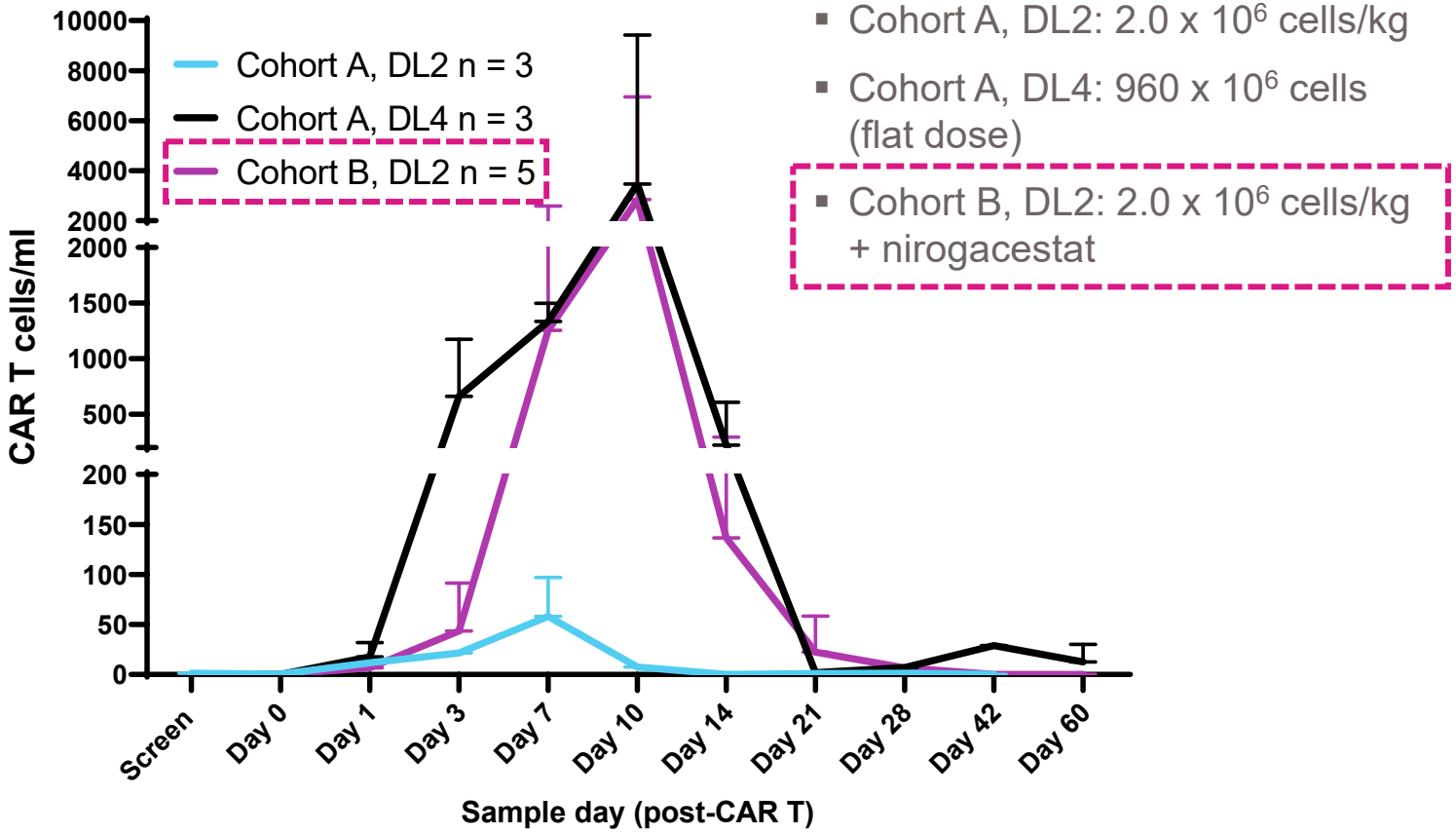
# Preliminary Clinical Data Demonstrate That Nirogacestat Treatment Can Lead to Profound Expansion of BCMA CAR-T Cells in Multiple Myeloma Patients

- Nirogacestat dosed from Day -3 to Day 60 and BCMA CAR-T cells dosed on Day 0 in relapsed/refractory multiple myeloma patients
- Study designed in two cohorts
  - Cohort A: CAR-T cells only
  - Cohort B: CAR-T cells + nirogacestat



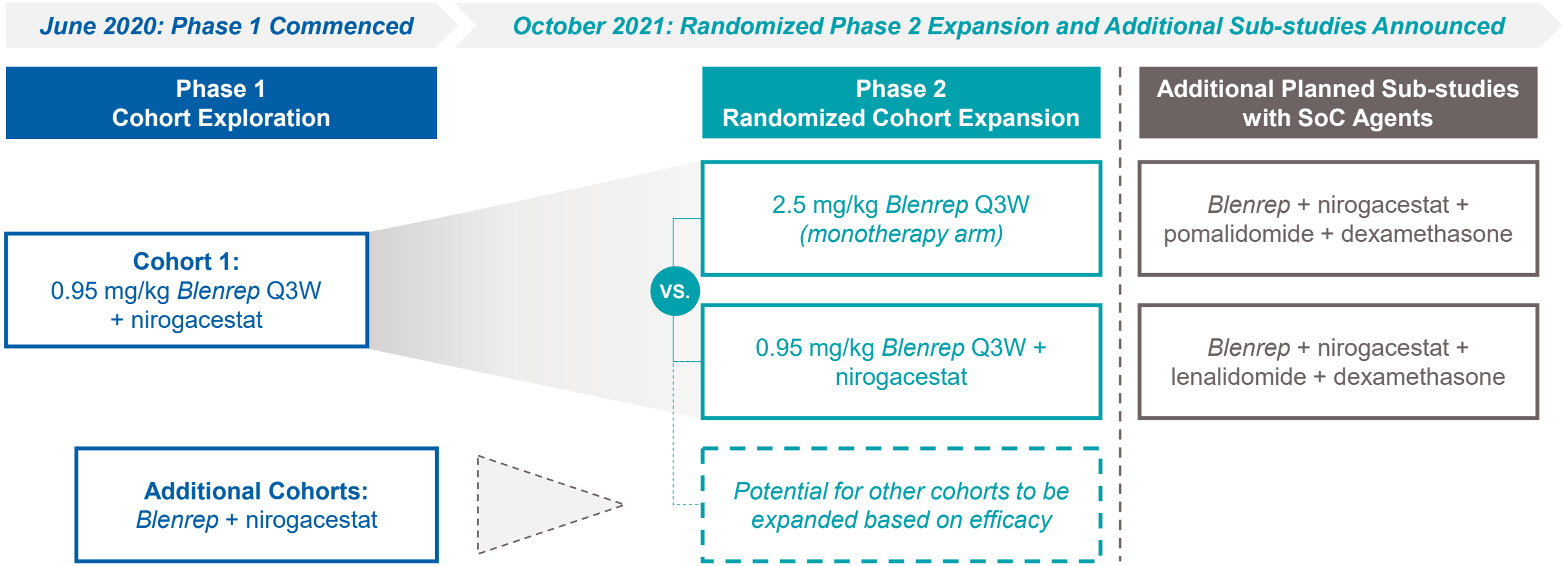

- Cohort A, DL2: 2.0 x $10^6$ cells/kg
- Cohort A, DL4: 960 x $10^6$ cells (flat dose)
- Cohort B, DL2: 2.0 x $10^6$ cells/kg + nirogacestat

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



Note: DL: dose level.
Source: Precision BioSciences investor materials (presented December 11, 2021); preliminary data from ongoing Precision-sponsored trial (NCT04171843).

# Initial Low-Dose *Blenrep* + Nirogacestat DREAMM-5 Cohort Has Advanced to Randomized Phase 2 Expansion Cohort – Additional Sub-Studies with SoC Agents Planned




**Based on encouraging preliminary data observed, first dose level advanced to randomized Ph2 expansion cohort vs. *Blenrep* monotherapy and additional sub-studies planned with SoC agents to potentially enable studies in earlier lines of MM**



Note: SoC = standard of care.

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

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

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

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

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

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



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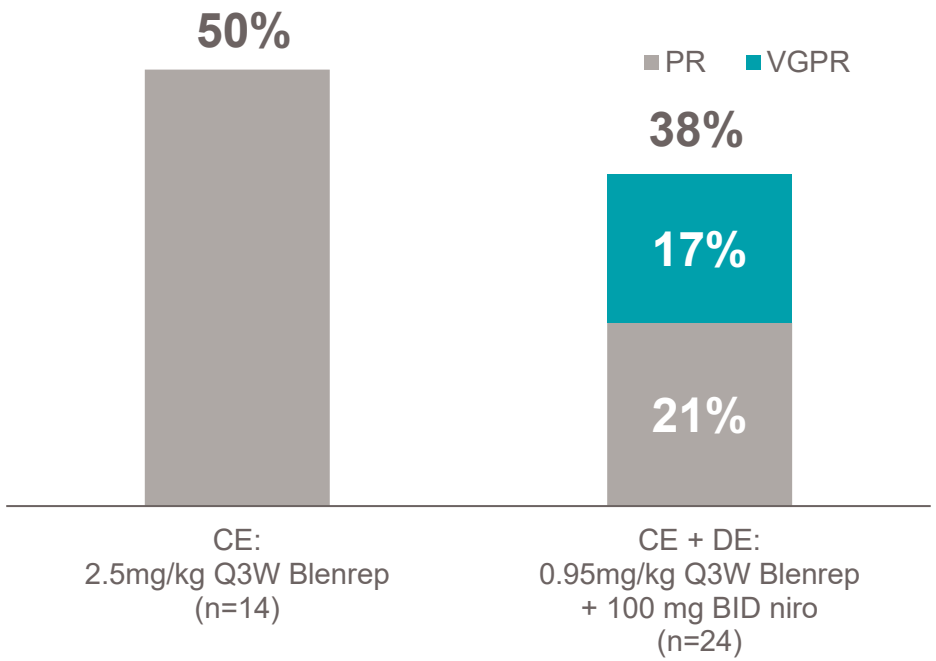
# Reduction in Ocular Adverse Events Observed with Combination Versus *Blenrep* Monotherapy at Interim Analysis

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

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

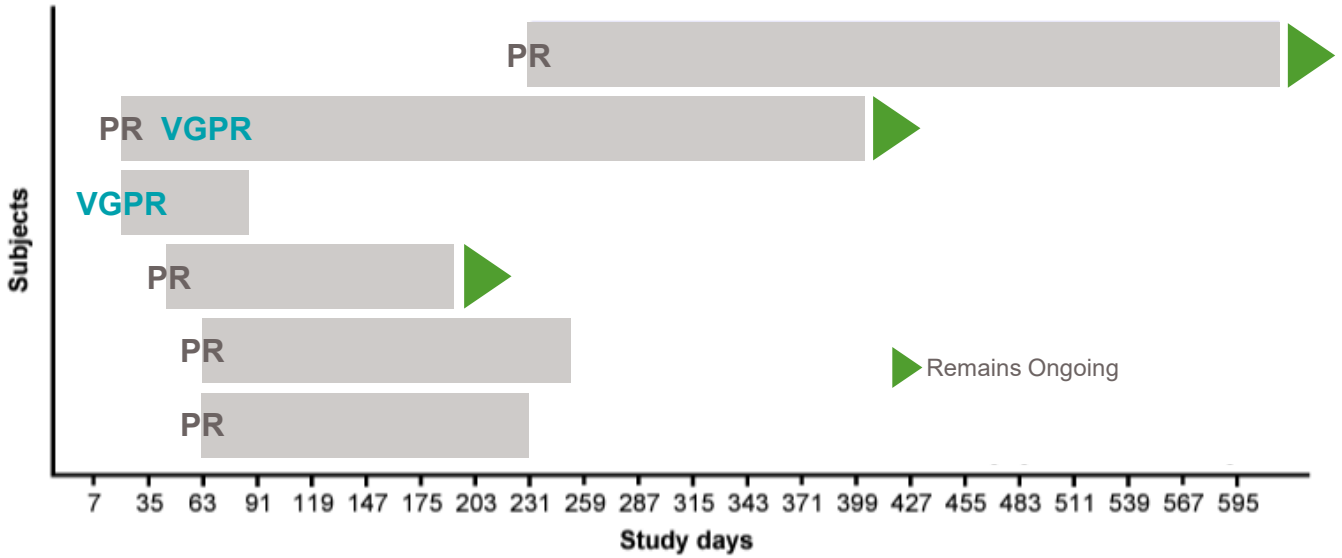
# Emerging Efficacy Profile of Low-dose *Blenrep* in Combination with Nirogacestat

## Objective Response Rate (ORR)




- Comparable efficacy with nirogacestat + low-dose *Blenrep* vs. monotherapy *Blenrep*

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




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

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



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

# Mirdametinib

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# Mirdametinib: Potent and Selective MEK Inhibitor With Differentiated Safety Profile

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

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



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

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

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

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

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

# Mirdametinib

NF1-PN

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**Kendall**
**NF1 Patient**

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

## Disease Characteristics

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

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

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

Source: Kim et al., 2017.

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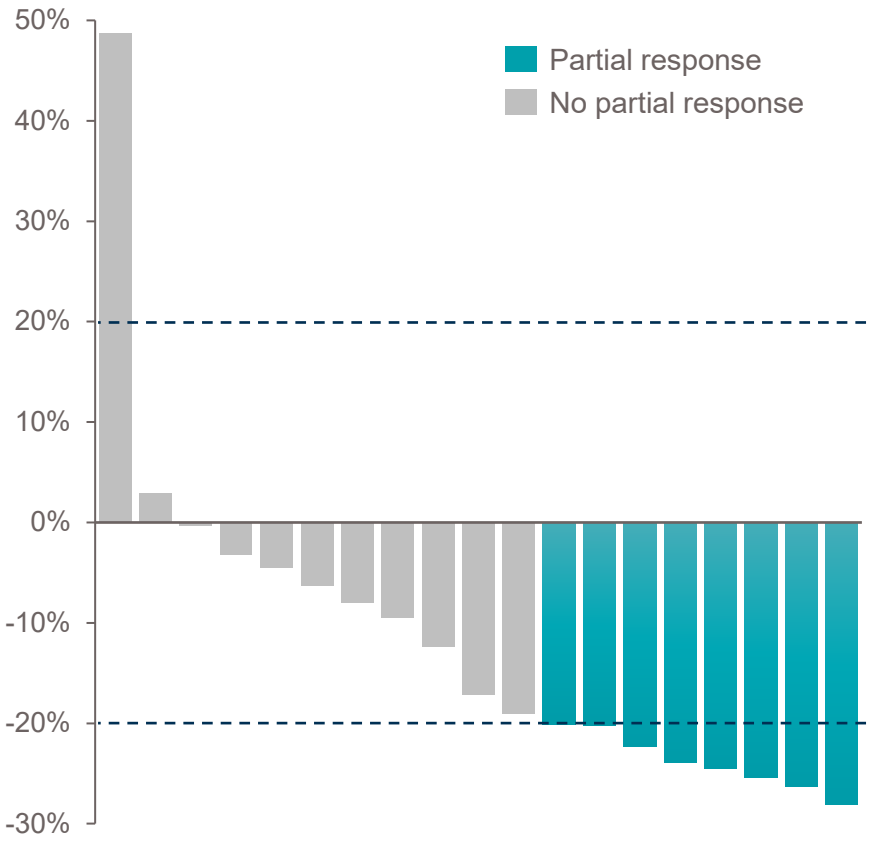
# ReNeu Trial Builds Upon Encouraging Phase 2 Results, Which Demonstrated Initial Clinical Activity, QoL Improvement for NF1-PN Patients and a Differentiated Safety Profile vs. Other MEK Inhibitors

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.

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

ReNeu

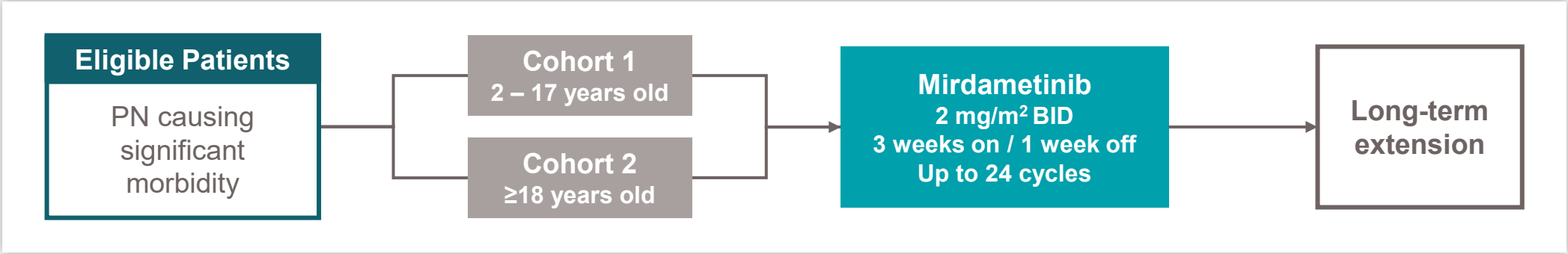
PHASE 2 | PHASE 2B

## Trial Summary

- Study fully enrolled with 114 patients in 2 cohorts (pediatric, adult participants) across ~50 sites in the US
- 2 mg/m$^2$ BID dosing with intermittent course (4-week cycles of 3 weeks on, 1 week off) for up to 24 cycles
  - Maximum dose of 4 mg BID
  - Treatment duration designed to evaluate longer-term benefit of mirdametinib in NF1-PN

## Study Endpoints

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




**Interim data from adult cohort presented at the CTF Scientific Conference in June 2021**



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

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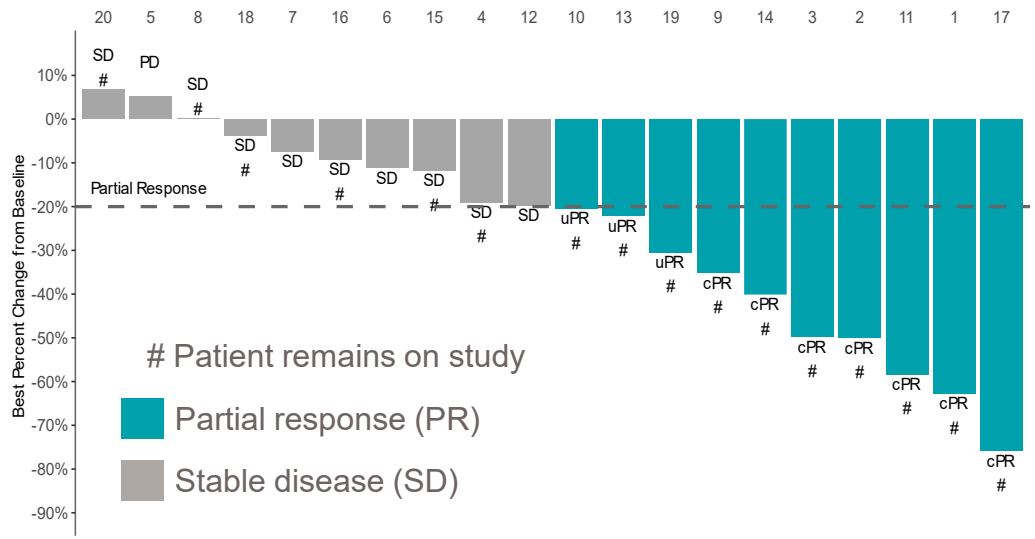
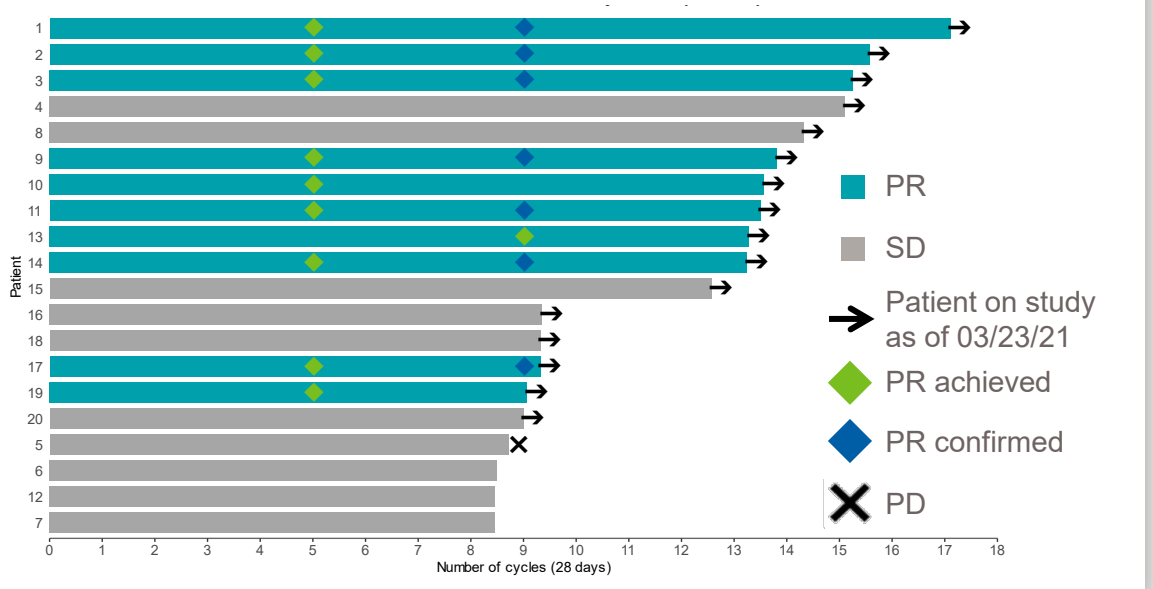
# Interim Data Update From ReNeu Trial Adult Stratum Presented at CTF in June 2021

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]

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.

# Mirdametinib

## Low-Grade Gliomas

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# Phase 1/2 Trial in Pediatric Low-Grade Glioma Provides Additional Expansion Opportunity for Mirdametinib

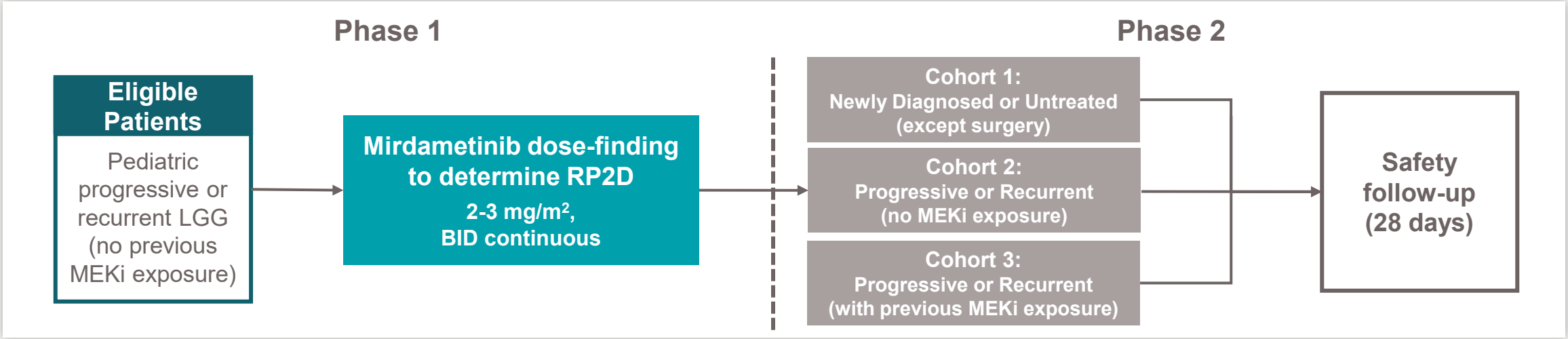
**PHASE 1/2**

## Trial Summary

- Open-label, multi-center study evaluating single agent mirdametinib, a brain penetrant MEK 1/2 inhibitor, in pediatric low-grade gliomas
- Recommended dose from Phase 1 dose-finding/dose-escalation study will be used (2-3 mg/m$^2$, BID continuous)

## Summary of Endpoints

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




**Favorable safety profile and blood-brain barrier penetration properties set the stage for a potential best-in-class profile for pediatric low-grade gliomas with initial data presented at ISPNO in June 2022**



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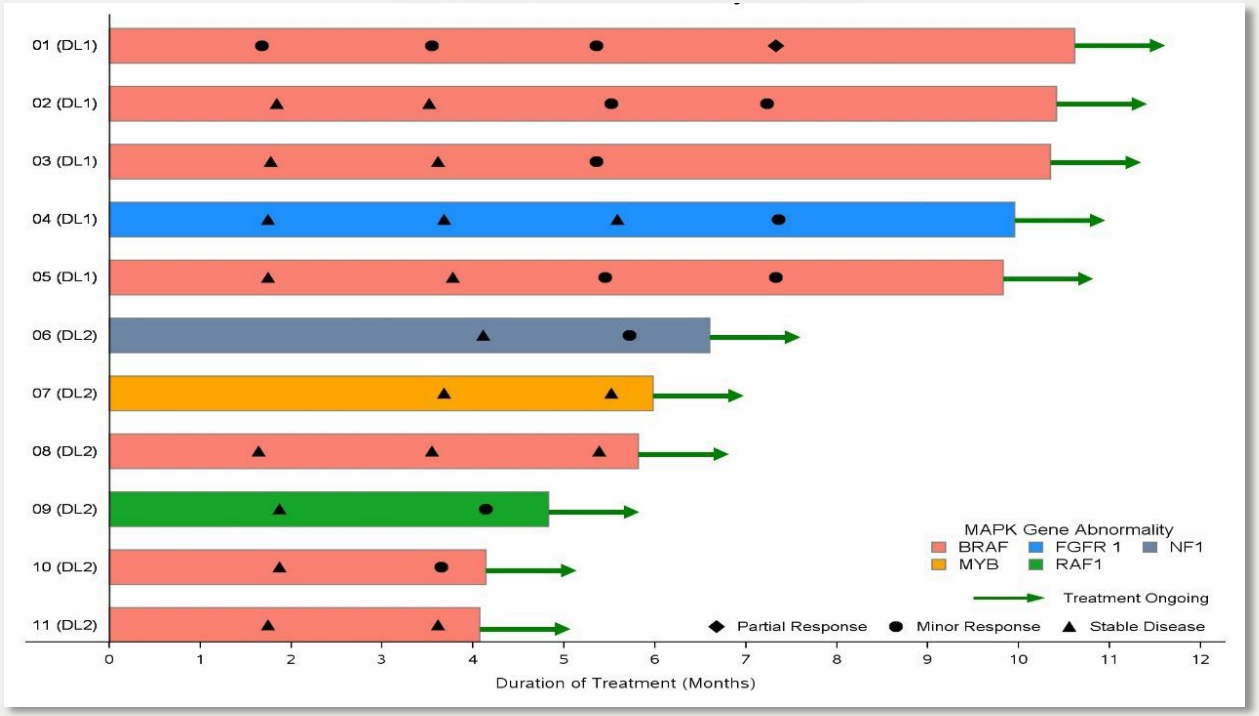
# Emerging Data Presented at ISPNO in June 2022 Show Promising Clinical Activity

**PHASE 1** | PHASE 2

- Data from first 11 patients treated across two initial dose levels during Phase 1 dose escalation, with all 11 patients treated remaining on study as of 05/01/22
  - 1 patient with partial response (decrease of 50-75%)
  - 7 patients with minor response (decrease of 25-50%)
  - 3 patients with stable disease (stable tumor size or decrease up to 25%)
- No DLTs observed
- Most common Grade 1/2 treatment-related AEs observed were elevated CPK, AST, acneiform rash and decreased neutrophil count
  - 2 treatment-related Grade 3 AEs reported: elevated CPK and decreased neutrophil count




**Once RP2D is determined, additional 10 patients will be enrolled into each expansion cohort**



Source: Vinitsky et al., *ISPNO* 2022.
Note: AE: adverse event; DLT: dose-limiting toxicity; ISPNO: International Symposium on Pediatric Neuro-Oncology; RP2D: recommended Phase 2 dose.

# Mirdametinib

## Additional Expansion Opportunities

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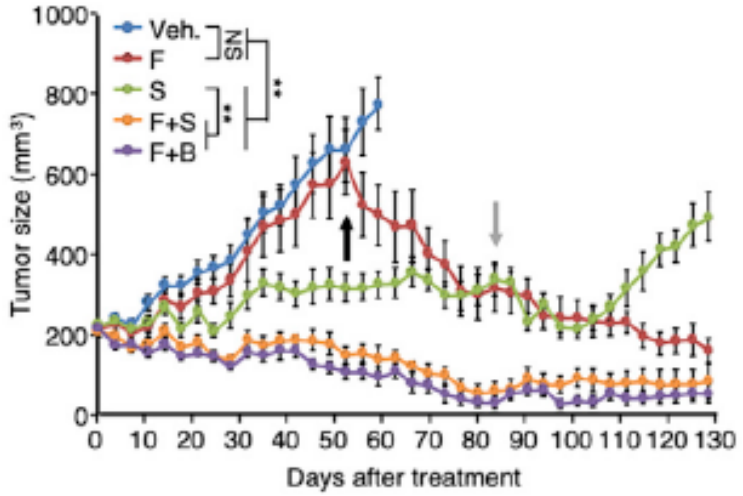
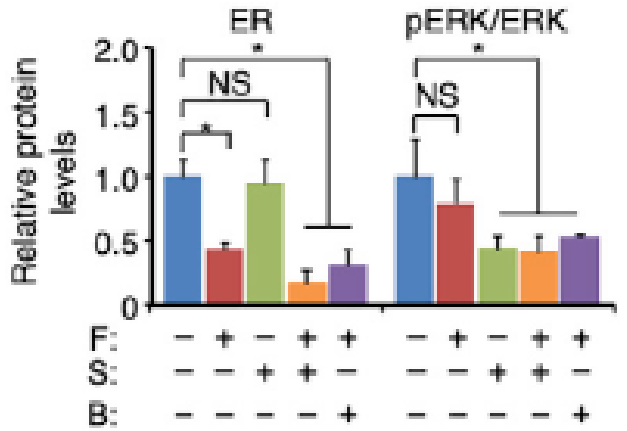
# Mirdametinib: MEK Inhibitors Can Potentially Address Endocrine Therapy Resistance Due to MAPK Mutations in ER+ Breast Cancer

- MAPK mutations in ER+ mBC cells can lead to fulvestrant resistance, which can be reversed with MEK inhibition[2]
- ~25% of ER+ mBC patients progress on endocrine therapy
- *NF1* deficiency has been shown to enhance ER transcriptional activity leading to hormone resistance[1]
  - Up to 15% of mBC harbor MAPK pathway mutations, including *NF1* LoF

## *NF1*-Deficient ER+ BC PDX: Durable Tumor Growth Inhibition with MEKi + Fulvestrant[2]




## MEKi + Fulvestrant Modulates ER and MAPK Signaling[2]




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

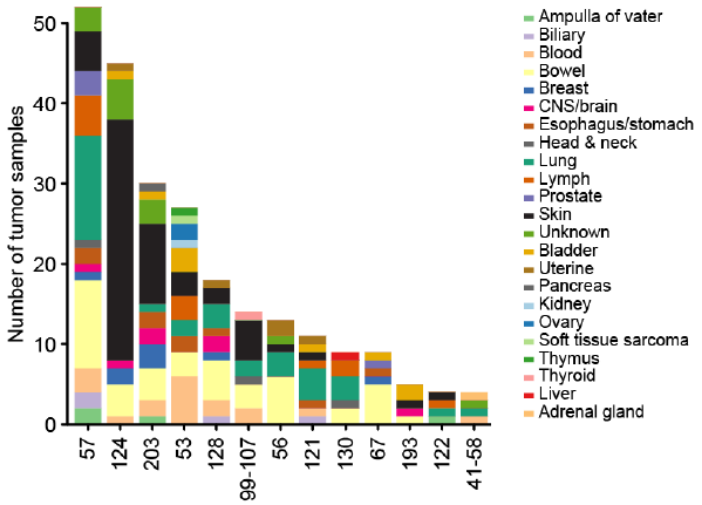


Note: B: buparlisib (PI3K inhibitor); F: fulvestrant; mBC: metastatic breast cancer; S: selumetinib (MEK inhibitor); SoC: standard of care; V: vehicle.
Sources: (1) Sokol et al., 2019; (2) Zheng et al., 2020.

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

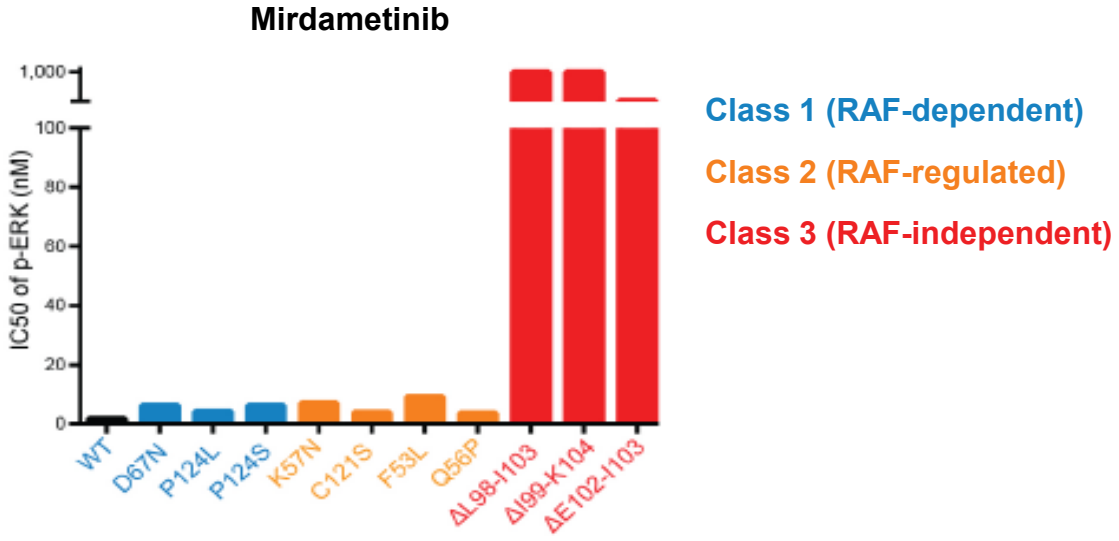
- Mirdametinib shows potent preclinical activity against Class 1 and Class 2 mutations in *MEK1* and *MEK2*[1]
- *MEK1* and *MEK2* have been validated as oncogenic targets with mutations present in ~2% of solid tumors[2]
- Clinical case reports with allosteric MEK inhibitors also support utility of mirdametinib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

## MEK 1/2 Mutants Occur Across Tumor Types[2]




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

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




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



Sources: (1) Gao et al., 2018; (2) Hanrahan et al., 2020.

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

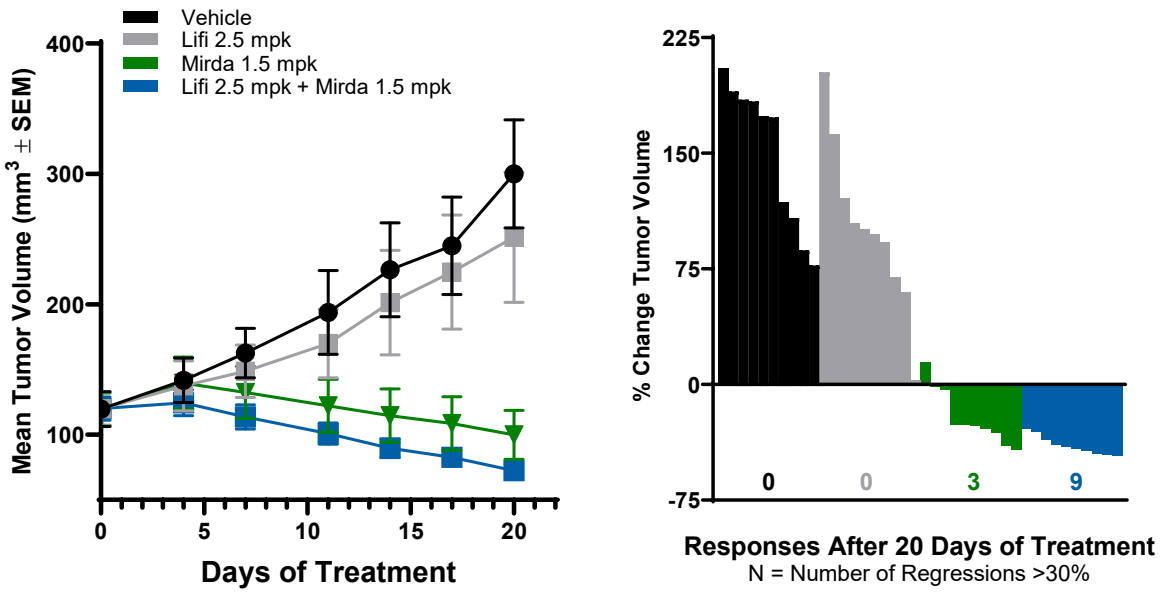
## Key Accomplishments from BeiGene Collaborations:

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

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

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

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




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



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

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

As of 11/05/21

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

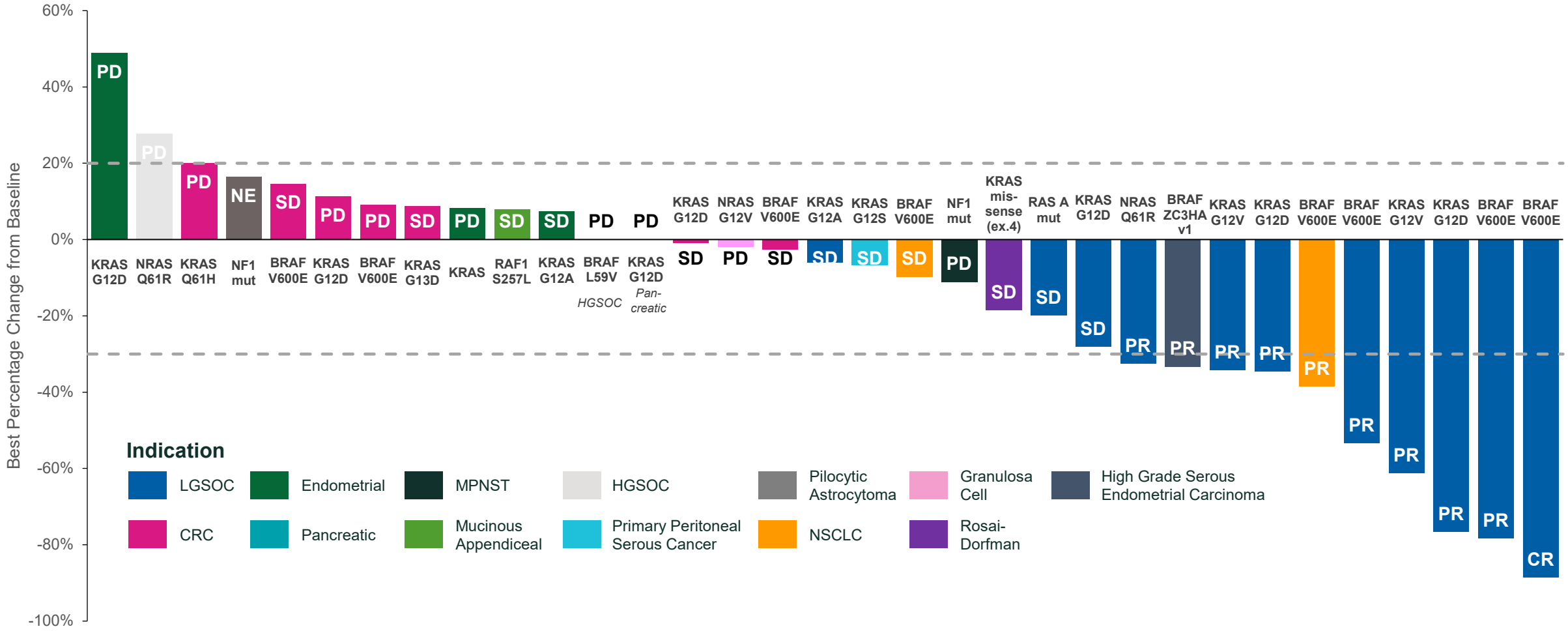
| Baseline Characteristics | Overall, n (%) |
|---|---|
| **Prior systemic cancer regimens** | |
| Median (Range) | 3 (1-9) |
| **ECOG status at entry** | |
| 0 | 24 (68.6) |
| 1 | 11 (31.4) |
| **Location of Tumor** | |
| Gynecological | 21 (60.0) |
| Gastrointestinal | 9 (25.7) |
| Lung | 2 (5.7) |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



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

# Mirdametinib + Lifirafenib: Clinical Efficacy Observed During Dose Escalation

As of 11/05/21




**10 objective responses observed in 33 evaluable patients**

CR: complete response; CRC: colorectal cancer; HGSOC: high-grade serous ovarian carcinoma; LGSOC: low-grade serous ovarian carcinoma; MPNST: malignant peripheral nerve sheath tumor; PD: progressive disease; PR: partial response; SD: stable disease.

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



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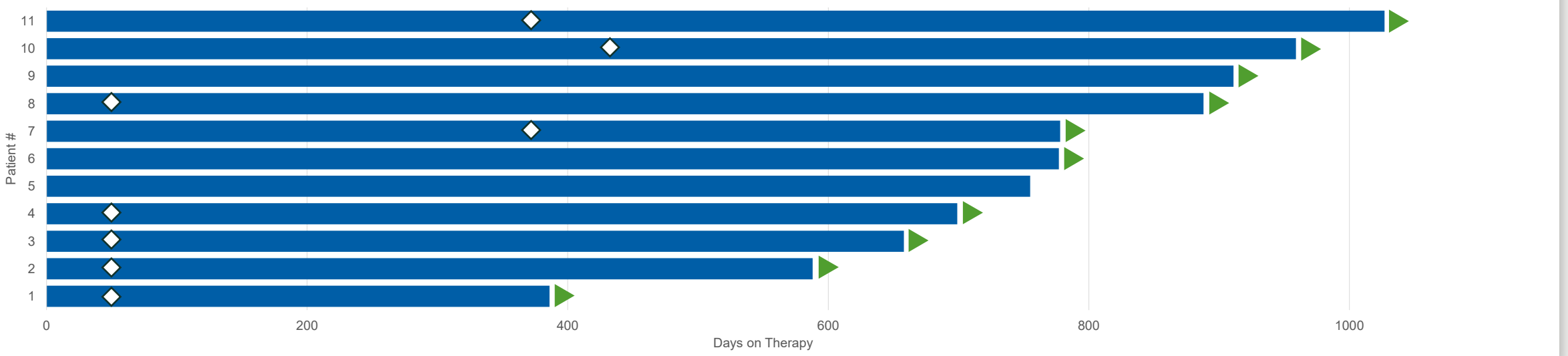
# LGSOC Patients Demonstrate Potential for Long Term Responses and Tolerability

Enrollment data as of 05/11/22

## Duration of Treatment in LGSOC Patients




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

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



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

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

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

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

**All-cause adverse event profile aligns with relapsed/refractory cancer patients generally; related TEAEs have been manageable with few treatment discontinuation due to adverse events**



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

# BGB-3245

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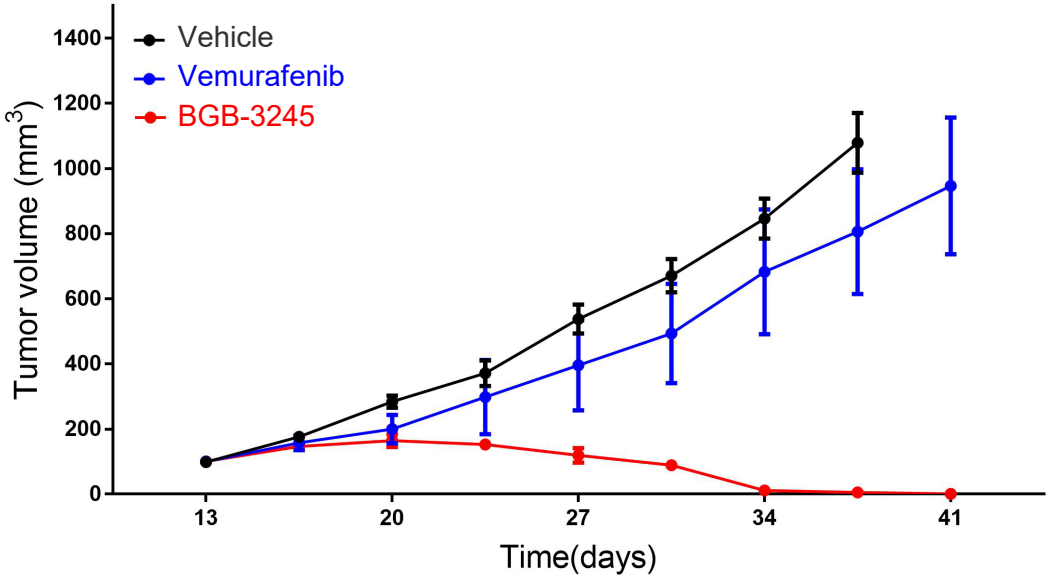
# BGB-3245: Preclinical Activity in BRAF Fusions and BRAF V600 Resistance Mutations Sets Up Multiple Monotherapy and Combination Therapy Development Avenues

**1** BGB-3245 is active in patient-derived xenografts driven by *BRAF* fusions and non-V600 mutations, where approved BRAF inhibitors do not work

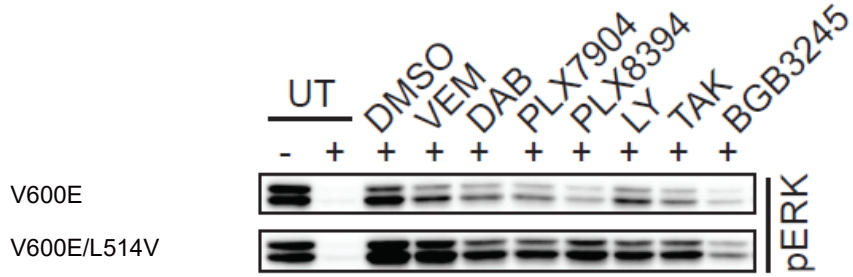
***BRAF* Fusion PDX: *In Vivo* Tumor Growth Inhibition[1]**




- Driver mutations and fusions potentially uniquely targetable by BGB-3245 could account for up to ~5% of all solid tumors[2,3]
- BGB-3245 also active preclinically against mutant *BRAF* monomers (e.g., V600)

**2** BGB-3245 is active against resistance mutations that arise in *BRAF* V600 patients treated with approved BRAF inhibitors

**pERK Activity in *BRAF* V600E/L514V Cell Line[4]**




- *BRAF* V600E/L514V is a dabrafenib resistance mutation[4]
- BGB-3245 showed strongest *in vitro* activity versus other first- and second-generation BRAF inhibitors tested



Sources: (1) Rosen presentation, Sixth International RASopathies Symposium: Precision Medicine – From Promise to Practice, 2019; (2) Dankner et al., *Oncogene*, 2018; (3) Ross et al., *IJC*, 2016; (4) Wang et al., *Cancer Discovery*, 2018.

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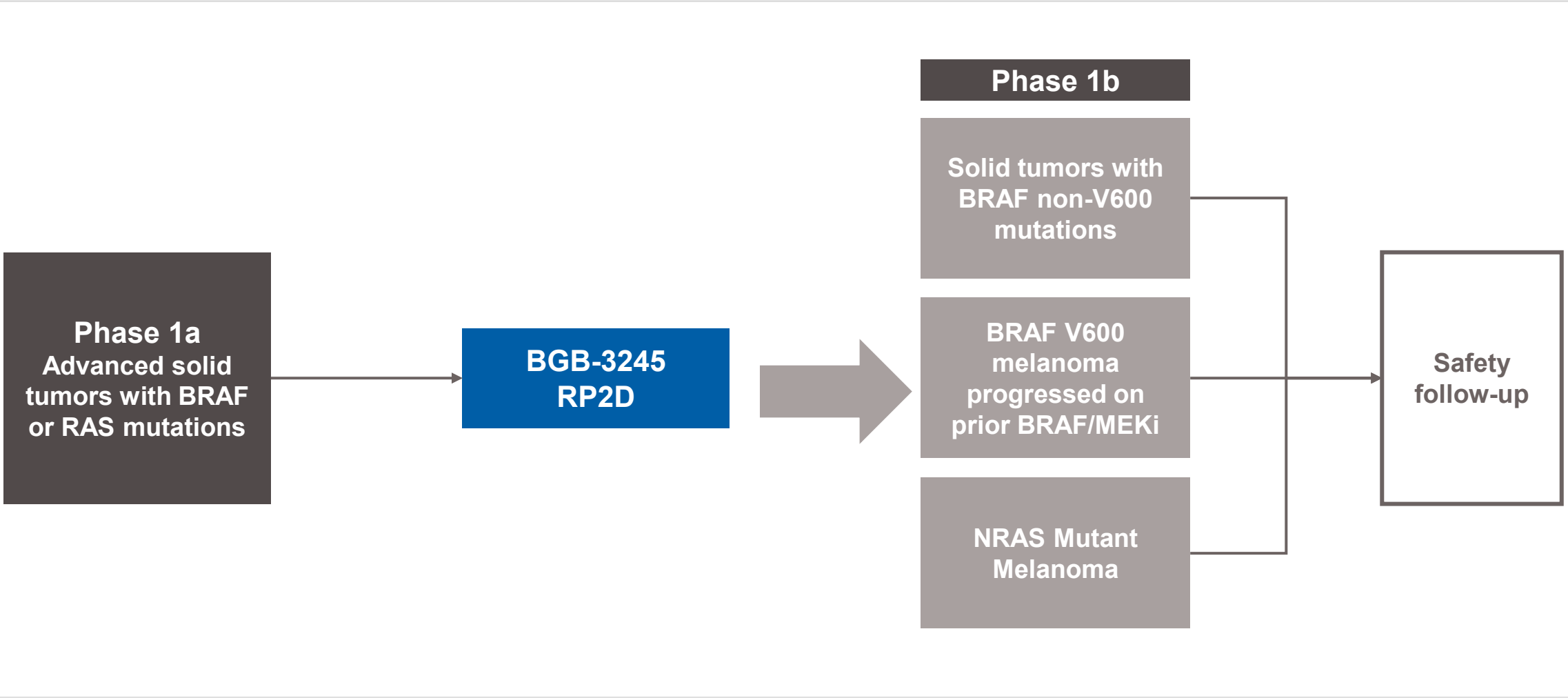
# BGB-3245 Monotherapy Phase 1a/1b Study Design




Note: RP2D: recommended Phase 2 dose.

# BGB-3245 Monotherapy Patient Characteristics in Dose Escalation

As of 02/26/22

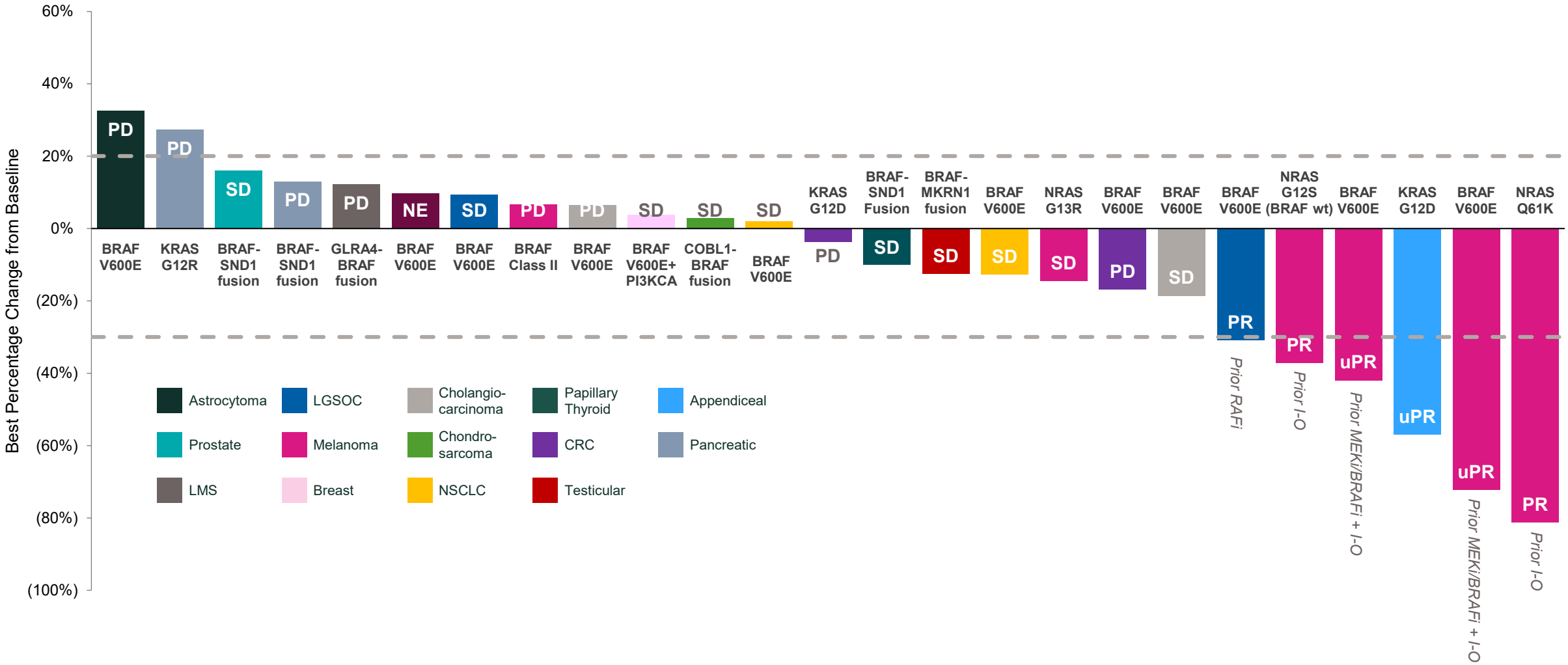
| Baseline Characteristics | Overall, n (%) |
|---|---|
| **Patients treated** | 38 (100) |
| Still on Treatment | 14 (36.8) |
| **Sex** | |
| Male | 22 (57.9) |
| Female | 16 (42.1) |
| **Age** | |
| Mean | 58.6 |
| Median (Range) | 57 (31-83) |
| **Cancer stage at entry** | |
| III/other | 5 (13.2)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

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

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

# BGB-3245: Early Clinical Efficacy Observed in Dose Escalation

As of 02/26/22




Note: CRC: colorectal cancer; IO: immuno-oncology; LMS: leiomyosarcoma; LGSOC: low-grade serous ovarian cancer; NSCLC: non-small cell lung cancer; PD: progressive disease; PR: partial response; SD: stable disease; TL: target lesion; uPR: unconfirmed partial response; wt: wildtype.

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



SpringWorks THERAPEUTICS

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

As of 01/10/22

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

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



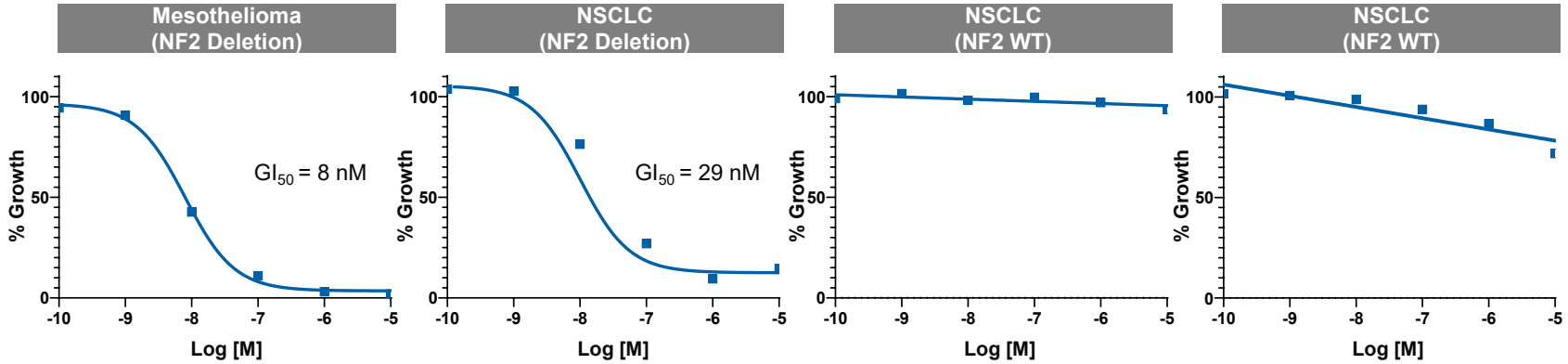
Note: TEAE: treatment-emergent adverse event.
Note: Data are preliminary, investigator assessed, and have not been centrally reviewed. Safety data as of 01/10/22.

# Preclinical Pipeline

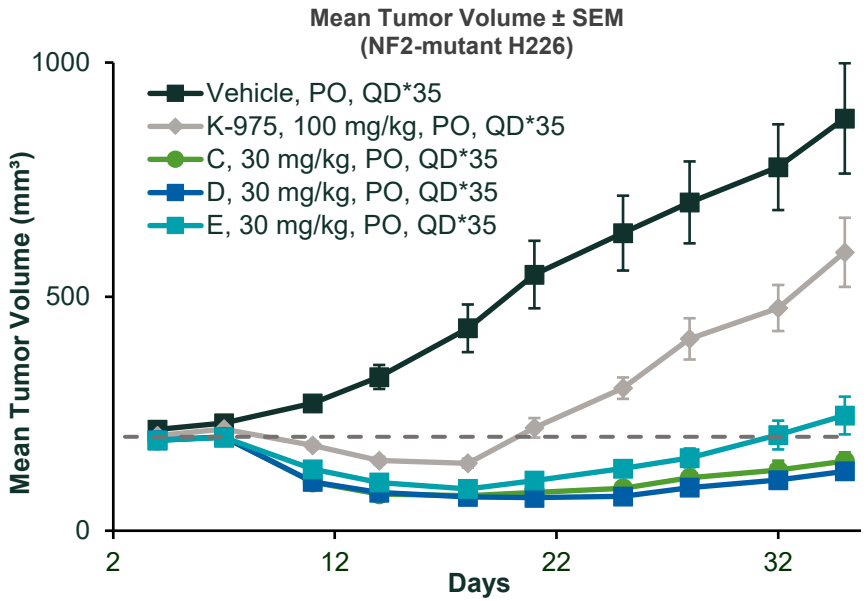
SpringWorks® THERAPEUTICS

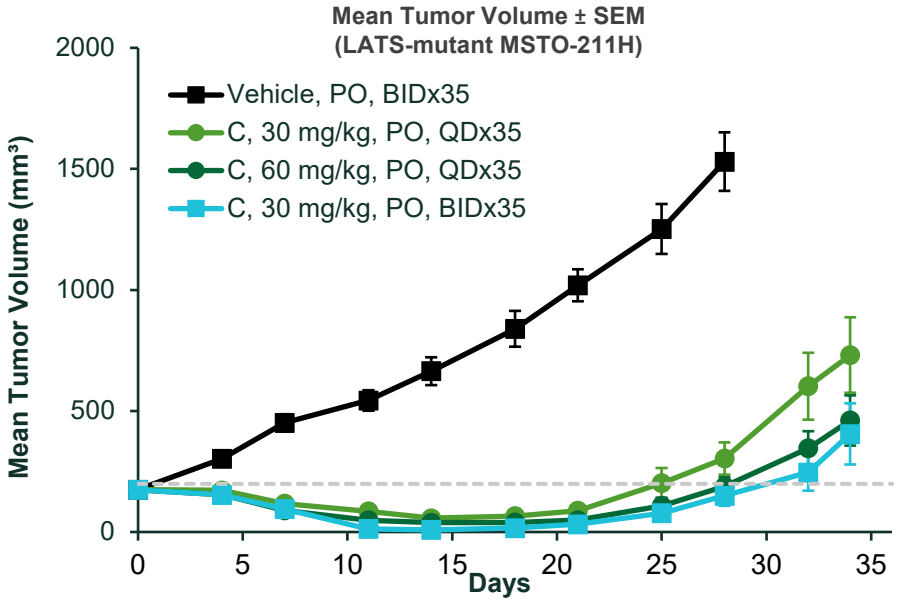
# TEAD Inhibitor: Program in Lead Optimization With Selectivity, Potency and In Vivo Tumor Growth Inhibition Demonstrated in Hippo-Driven Models

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




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






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

SpringWorks THERAPEUTICS

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

**Three EGFR Inhibitors**

*First program targeting C797S mutants*

*Two additional first-in-class approaches*

**EGFR Mutant Tumors**

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

# The SpringWorks Opportunity

# Well-Capitalized to Execute on Important Value-Driving Milestones

**$600M+**

**Cash, Cash Equivalents & Marketable Securities(1)**

**No Debt**

**NASDAQ: SWTX**

**62.4M**

**Common Shares Outstanding(2,3)**

(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 (i) the $69.7 million August 2022 ATM Offering (see definition below), (ii) the $225 million private placement transaction announced on September 7, 2022, and (iii) the $75 million 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.

(2) On August 15, 2022, the Company raised gross proceeds of $69.7 million through the closing of a sale of 2,247,500 basic common shares in an "at the market" (ATM) offering entered into on August 11, 2022 pursuant to the Company's pre-existing ATM facility (the "August 2022 ATM Offering"), with participation based on unsolicited interest received from an investment fund. The Company sold such shares at a purchase price per share of $31.00, a premium to the market price at the time of sale. After deducting commissions related to the ATM offering, net proceeds to the Company from the transaction were $67.9 million.

(3) Common shares ("Shares") outstanding for SpringWorks (the "Company") includes (i) 49,442,662 Shares as set forth in the Company's Quarterly Report for the quarter ending June 30, 2022 on Form 10-Q, filed with the Securities and Exchange Commission (the "SEC") on August 4, 2022, (ii) 2,247,500 Shares issued in the August 2022 ATM Offering closing on August 15, 2022, (iii) 2,050,819 Shares issued and sold to Glaxo Group Limited in a private placement that closed on September 9, 2022 as set forth in the Issuer's Current Report on Form 8-K filed with the SEC on September 7, 2022, and (iv) 8,650,520 Shares sold and issued by the Company to certain accredited investors in a private placement that closed on September 9, 2022 as set forth in the Company's Current Report on Form 8-K filed with the SEC on September 8, 2022.



SpringWorks THERAPEUTICS

# Foundation in Place to Execute on Multiple Revenue Generating Opportunities by 2025

## 2022

- Positive results from DeFi trial in desmoid tumors
- First NDA submission expected
- Clinical PoC demonstrated in BCMA combination and vertical MAPK inhibition programs
- 19 total programs in development
- Robust balance sheet in place

## 2023

- First FDA approval expected
- Continue commercial infrastructure build-out to support first potential launch in desmoid tumors
- Advance nirogacestat as a potential cornerstone of BCMA combination therapy across modalities
- Execute across late and early-stage development programs

## 2025 Plan

- Serve patients with 2 approved products in up to 4 different indications
- Advance mature portfolio of late-stage clinical programs
- Expand portfolio of opportunities as a partner of choice to industry and academia
- Continue disciplined capital allocation across earlier-stage programs and business development opportunities

# Thank you

SpringWorks® THERAPEUTICS