

SpringWorks THERAPEUTICS

Corporate Presentation

January 2021

NASDAQ: SWTX

Forward-Looking Statements

This presentation may contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 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 and 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 ongoing DeFi and ReNeu clinical trials, (ii) the success and timing of our product development activities and initiating clinical trials, (iii) the success and timing of our collaboration partners’ ongoing and planned clinical trials, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners’ abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) 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.

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

SpringWorks Therapeutics is a Clinical-Stage Targeted Oncology Company

- **Two late-stage rare oncology programs** in potentially registrational trials, each supported by strong clinical data
- **Seven programs addressing large opportunities in genetically defined cancers** in collaboration with industry leaders
- Leveraging **strong development capabilities** and **shared-value partnerships** to enhance portfolio value and become a partner of choice
- Led by an **experienced management team** with deep expertise in drug development and commercialization
- Well-capitalized to execute **important value-driving milestones** across both standalone and partnered programs

Our ambition is to ignite the power of promising science to unleash new possibilities for patients

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Demonstrated Leadership Advancing Transformative Therapies

Leadership Team

Saqib Islam, J.D.
Chief Executive Officer

moderna
ALEXION

Jens Renstrup, M.D., MBA
Chief Medical Officer

ALEXION
gsk

Badreddin Edris, Ph.D.
Chief Operating Officer

OrbiMed Healthcare Fund Management
BAIN & COMPANY

Frank Perier, MBA
Chief Financial Officer

Forest Laboratories, Inc.
Bristol-Myers Squibb

Mary Smith, Ph.D.
Chief Development Officer

Bamboo therapeutics
United Therapeutics CORPORATION

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Chief Financial Officer,
Amplyx Pharmaceuticals

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Former Chief Medical Officer,
IDEAYA Biosciences

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Jeffrey Schwartz
Managing Director,
Bain Capital Life Sciences

Stephen Squinto, Ph.D.
Executive Partner,
OrbiMed

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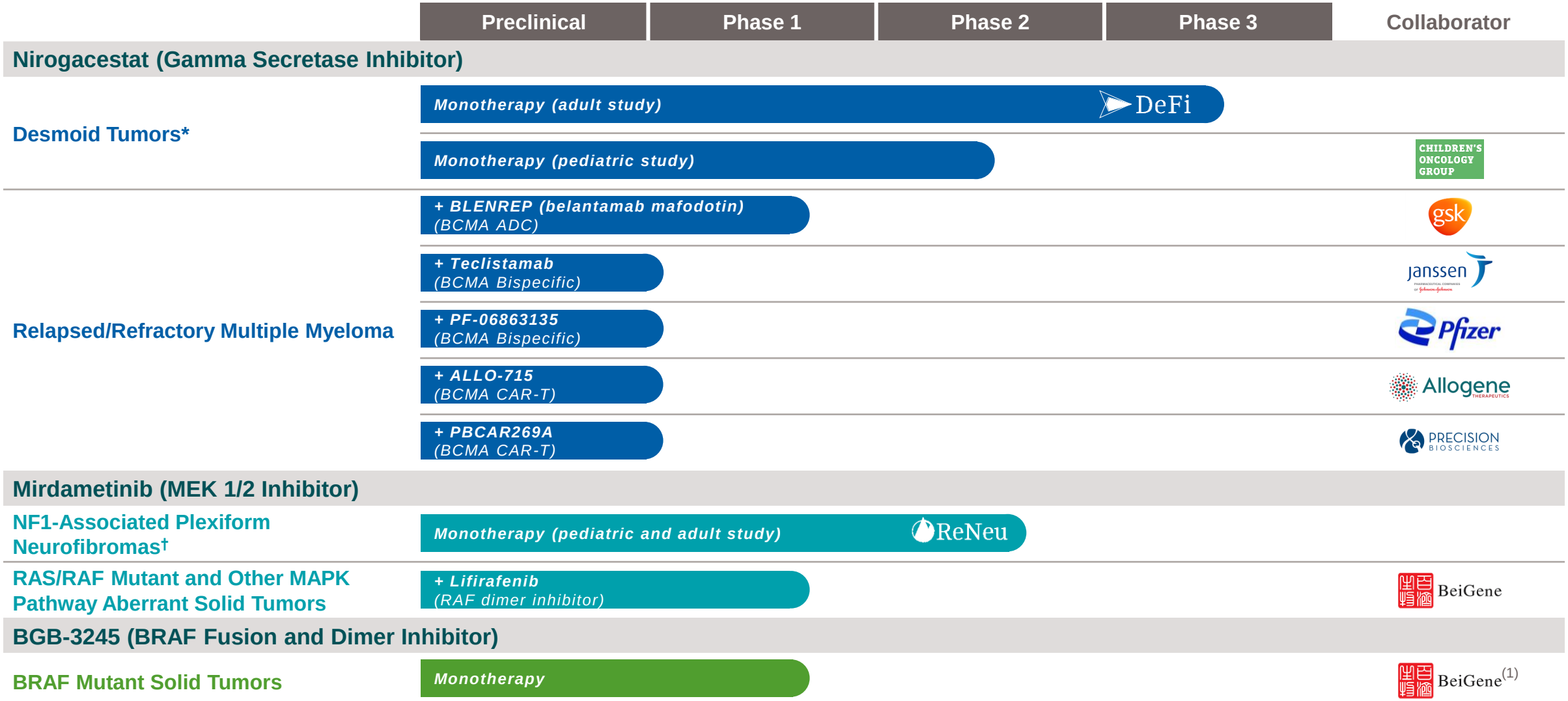
Advancing Diversified Clinical Pipeline of Targeted Oncology Programs



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.

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Pipeline Provides Multiple Opportunities for Value Creation Across Three Distinct Oncology Segments

1 Late-Stage Rare Oncology

Two registrational trials ongoing, each supported by strong Phase 2 data and with best-in-class potential

Nirogacestat
Desmoid Tumors
Phase 3 topline data: 2Q21-3Q21

Nirogacestat
Pediatric Desmoid Tumors
Phase 2 trial initiated: 3Q20

Mirdametinib
NF1-PN
Phase 2b trial update: 1Q21

2 BCMA Combinations in Multiple Myeloma

Advancing nirogacestat as a cornerstone of BCMA combination therapy across three modalities

Nirogacestat + BLENREP
BCMA ADC
Phase 1b initial clinical data: 2021

Nirogacestat + Teclistamab
BCMA-CD3 Bispecific
Phase 1 trial initiation: Early 2021

Nirogacestat + PF-06863135
BCMA-CD3 Bispecific
Phase 1b/2 trial initiation: 1H21

Nirogacestat + ALLO-715
BCMA Allogeneic CAR-T
Phase 1 trial initiation: 1Q21

Nirogacestat + PBCAR269A
BCMA Allogeneic CAR-T
Phase 1 trial initiation: 1H21

3 Biomarker-Defined Metastatic Solid Tumors

Precision oncology approach to highly prevalent cancers with near-term clinical POC readouts

Mirdametinib + Lifirafenib
RAS/RAF Mutant Solid Tumors
Phase 1b/2 initial clinical data: 2021

BGB-3245
RAF Mutant Solid Tumors
Phase 1 initial clinical data: 2021

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Successful Clinical and Operational Execution in 2020 Has Positioned SpringWorks for Multiple Important Data Readouts in 2021

	2020	2021
1 Late-Stage Rare Oncology	✓ Fully enrolled nirogacestat Ph3 DeFi trial ✓ Launched nirogacestat Ph2 trial with COG in pediatric desmoid tumors	❑ Mirdametinib Ph2b ReNeu trial update (*1Q21*) ❑ Nirogacestat Ph3 DeFi trial topline readout *(2Q21-3Q21)*
2 BCMA Combinations in Multiple Myeloma	✓ Signed 4 additional industry collaborations ✓ Achieved FPFD in GSK Ph1b combo trial ✓ Signed collaboration with Fred Hutchinson Cancer Research Center	❑ Initial Ph1b combo data with GSK *(2021)* ❑ Ph1 trial initiations for 4 BCMA combo studies *(1H21)*
3 Biomarker-Defined Metastatic Solid Tumors	✓ Achieved FPFD in BGB-3245 Ph1 trial ✓ Published AACR preclinical combination data from mirdametinib + lifirafenib	❑ Initial Ph1b/2 mirdametinib + lifirafenib data with BeiGene *(2021)* ❑ Initial Ph1 BGB-3245 data with BeiGene *(2021)*

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Late-Stage Rare Oncology

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Desmoid Tumors are Highly Morbid Soft Tissue Tumors that are Poorly Responsive to Surgical Interventions and Off-Label Therapies

Desmoid tumor patients present with significant morbidities

- Can manifest throughout the body including in the extremities, the head and neck region, intra-abdominally, and the thoracic region
- Patients can experience long-lasting pain due to nerve compression or tumor pressure, disfigurement, and restricted range-of-motion

No currently approved therapies and limited treatment options

- Post-surgical resection recurrence in up to 70%
- Off-label systemic therapies are poorly tolerated with inconsistent efficacy
- Physicians often adopt a watchful waiting approach

~1,000-1,500 newly incident patients per year in US

- Young patient population, with tumors more commonly diagnosed in the third and fourth decades of life
- ~5,500-7,000 patients actively receiving treatment in the US in any given year

Source: Penel et al., *European Journal of Cancer*, 2017; Tsagozis et al., *Annals of Medicine & Surgery*, 2017; SpringWorks market research.

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Nirogacestat: A New Paradigm for Patients With Desmoid Tumors

- Nirogacestat is an oral, selective gamma secretase inhibitor with over 10 years of clinical experience (approximately 300 subjects exposed)
- Clinical activity observed in Phase 1 and Phase 2 trials in desmoid tumors independent of prior lines of therapy and underlying mutation
- Generally well tolerated compound with evidence of being suitable for multi-year daily dosing
- Received Fast Track and Breakthrough Therapy Designations from FDA and Orphan Drug Designation from both FDA and European Commission
- US Composition of Matter and Method of Use patents provide protection to 2039

Phase 3 DeFi trial fully enrolled and topline data anticipated in 2Q-3Q 2021

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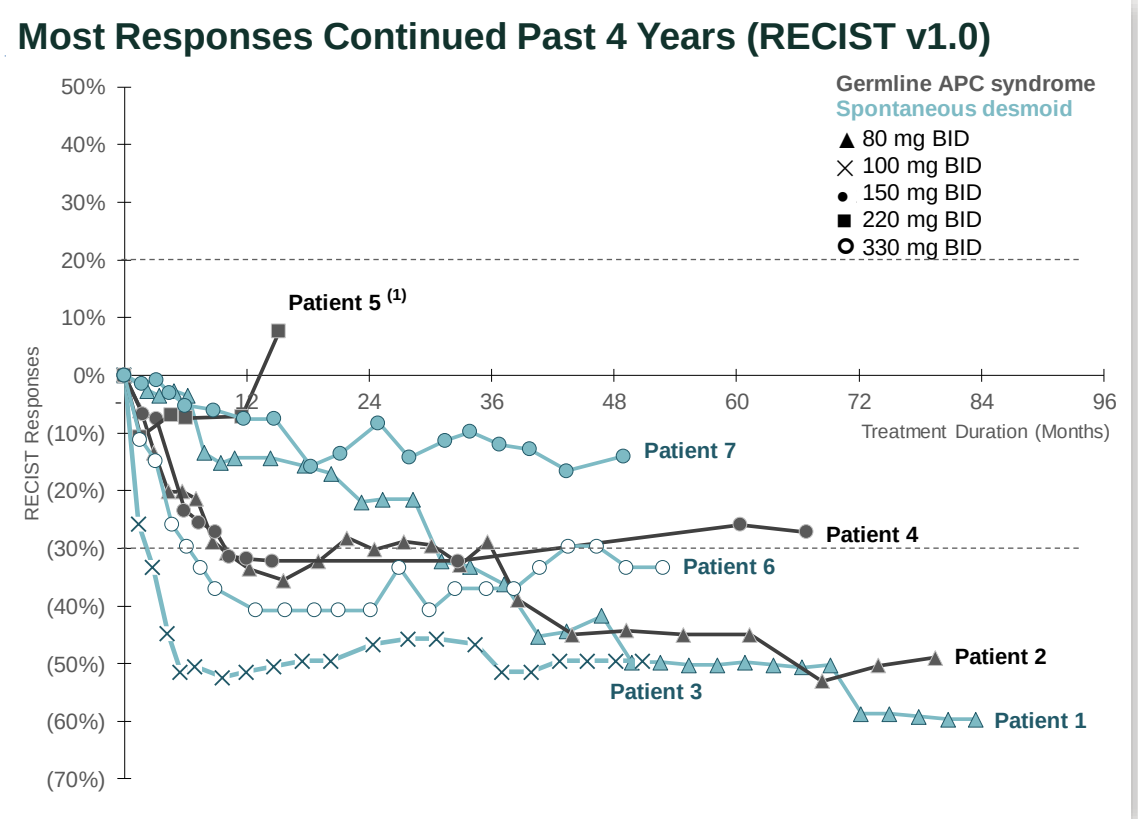
Initial Clinical Activity of Nirogacestat Observed in Desmoid Tumors

PHASE 1 | PHASE 2 | PHASE 3



- **All evaluable desmoid tumor patients in the study responded to nirogacestat treatment (1)**
  - Disease Control Rate (DCR): 100%
  - Objective Response Rate (ORR): 71.4% (5/7 evaluable desmoid patients)
  - Median PFS (mPFS): Not reached by publication date due to lack of tumor progression events
- **Median Duration of Treatment was 49.5 months at publication**
  - Of the 7 evaluable desmoid patients on study, none discontinued due to AEs (2)

Note: Disease control rate is percentage of patients experiencing objective response or stable disease on therapy as measured by RECIST v1.0.
Source: Villalobos, *Annals of Surgical Oncology*, 2018; Messersmith, *Clinical Cancer Research*, 2015.
(1) Per investigator "the only patient with clinical progression received PF-03084014 (220 mg BID) for 15.2 months and exhibited significant clinical improvement on therapy."
(2) Across the entire 64 patient Ph1 there were four discontinuations due to treatment-related AEs with a majority occurring during cycle 1.

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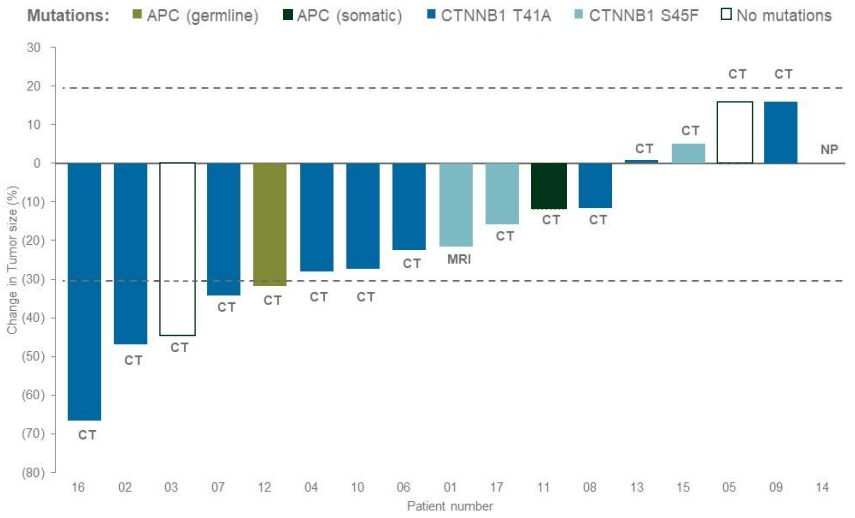
Encouraging Clinical Activity and Tolerability Observed in NCI-Conducted Phase 2 Trial in a Heavily Pre-Treated and Progressing Patient Population

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

Clinical Responses by RECIST v1.1



Durability and Tolerability with Long-Term Dosing

- **mPFS: Not reached by publication date due to lack of tumor progression events**
  - At time of enrollment, all patients had progressing tumors
  - Patients failed a median of 4 prior lines (1-9) of systemic therapy (1)
  - ORR of 29.4% (5/17) with no Progressive Disease

- **59% of patients remained on treatment >2 years and 71% of patients stayed on drug for >1 year**
  - Median Duration of Treatment was >25 months at publication, with 5 patients continuing as of January 2021 (treatment duration of 5+ years in these patients)
  - Well tolerated; only 1 discontinuation due to AE (2)

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.
(2) Discontinuation due to grade 2 urticaria not responsive to dose reduction. No grade 4 events, all grade 3 events related to hypophosphatemia, a known class effect easily reversible with oral supplements.

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Double-Blind, Placebo-Controlled Phase 3 DeFi Trial Is Fully Enrolled

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

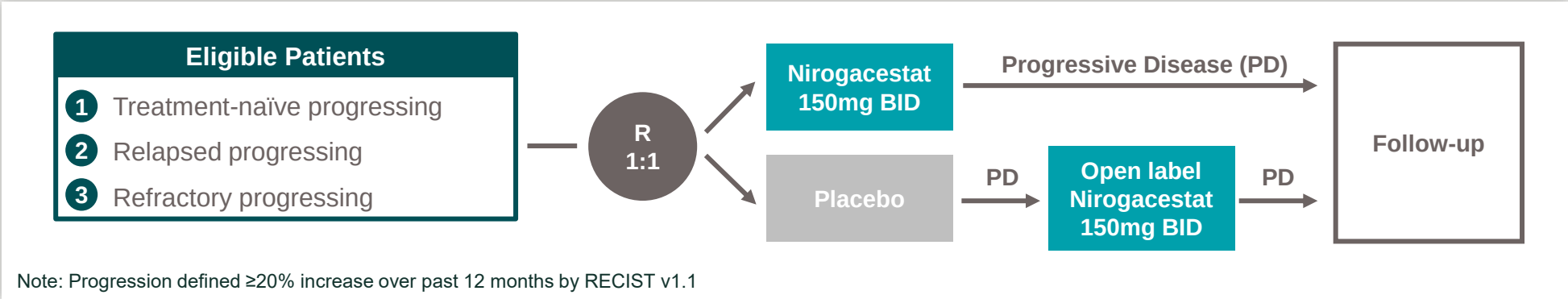
Trial Summary

- ~115 patients at ~50 sites in North America and Europe
- Open label extension for patients progressing on placebo
- 90% powered to show ~12 month PFS difference between nirogacestat and placebo (1)

Summary of Endpoints

DeFi

- Primary Endpoint: Progression-free survival
  - ~50% of placebo patients expected to progress by 8 months (2)
  - Study designed to enable a potential interim analysis
- Secondary: Safety and tolerability, ORR, duration of response, volumetric tumor change (MRI), patient-reported outcomes



Note: Progression defined ≥20% increase over past 12 months by RECIST v1.1

Full enrollment achieved in July 2020 and topline data expected 2Q – 3Q 2021

(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 in the nirogacestat group is 20 months and 8 months in the placebo group.
(2) Assumption based on placebo arm from sorafenib Ph3 trial presented at ASCO 2018.

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

EXPANDED ACCESS PROGRAM

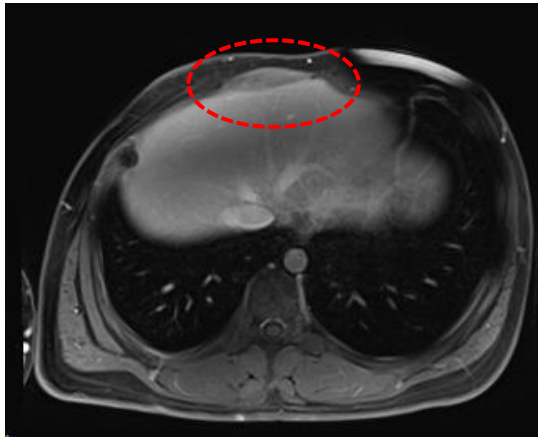
- **Clinical benefit shown in four pediatric and young adult desmoid tumor patients who received nirogacestat (1 CR, 2 PR, and 1 SD)**

	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 ▪ 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

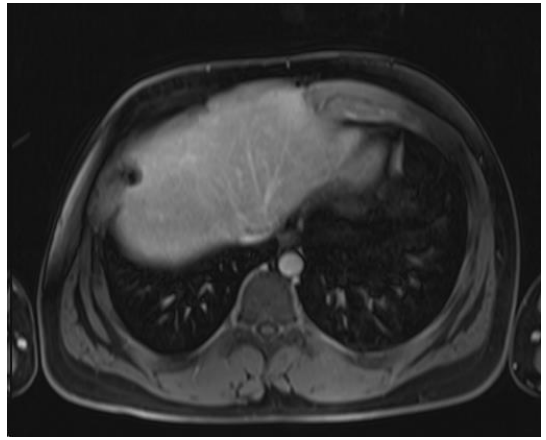
- **Nirogacestat was well tolerated; no grade 3 or 4 AEs**
  - 90 mg/m^2 per dose BID (max. 150 mg per dose BID)

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

Baseline MRI



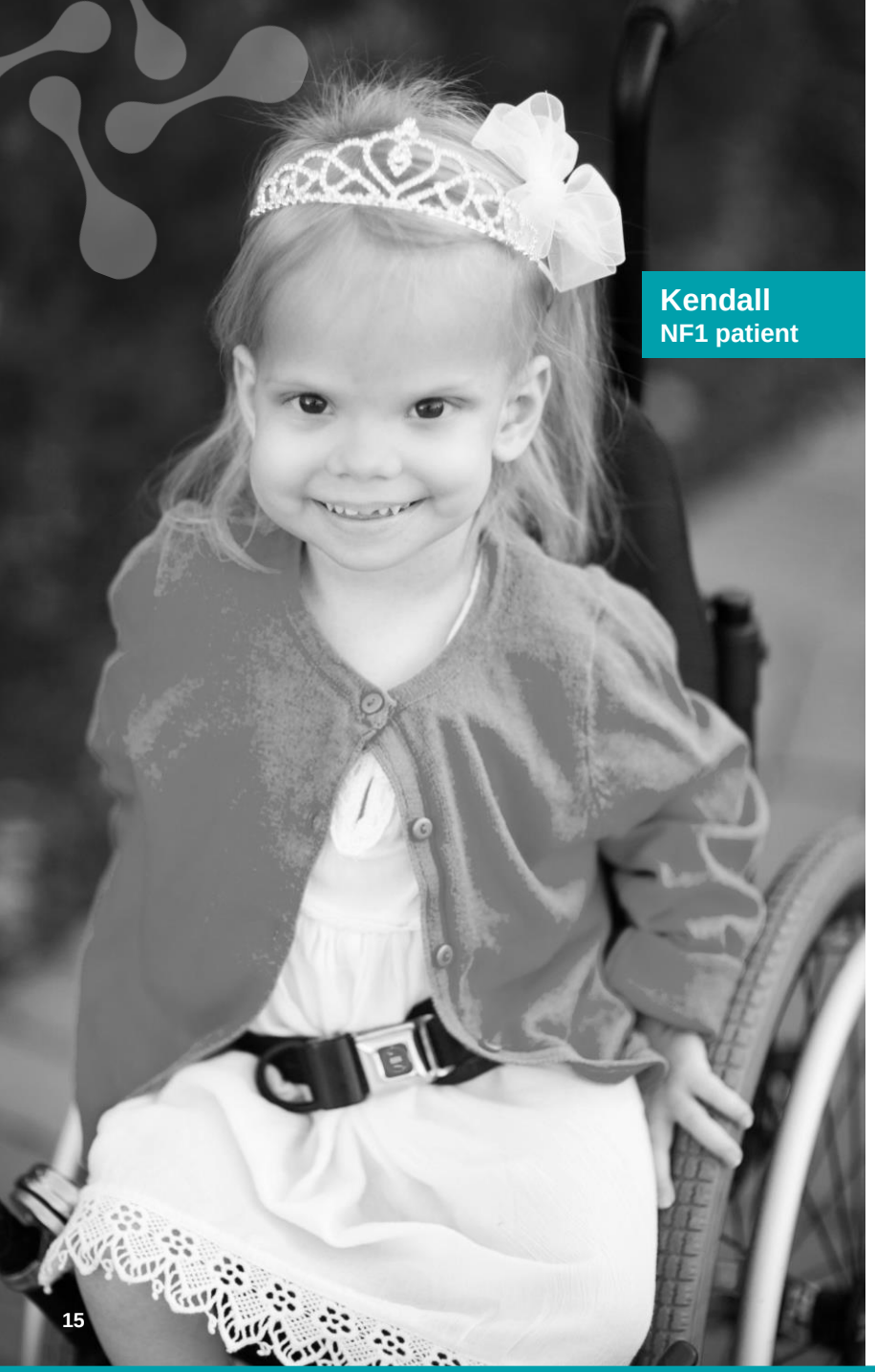
After 9 months on nirogacestat



- 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.



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

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

MEK inhibitors have emerged as 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

~100,000 NF1 patients in the United States

- ~30-50% lifetime risk of developing plexiform neurofibromas in NF1 population
- NF1-PN can malignantly transform into MPNST, a diagnosis that has a 12-month survival rate of under 50%

Source: Kim et al., *Sarcoma*, 2017.
MPNST = malignant peripheral nerve sheath tumor

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Mirdametinib: A Potentially Best-in-Class Therapy for Patients with NF1-PN

- Mirdametinib is an oral, small molecule MEK1/2 inhibitor with clinical validation and over 250 subjects exposed to date
- Encouraging safety and anti-tumor activity observed in Phase 2 investigator-initiated trial in adolescents and adults with NF1-PN
- Granted Orphan Drug Designation for NF1 by FDA and European Commission and Fast Track Designation for NF1-PN by FDA
- Compound potency, optimized dose/schedule, and lack of food effect may allow for a potentially differentiated profile compared to other MEK inhibitors

Phase 2b ReNeu trial is currently enrolling and update expected in 1Q 2021

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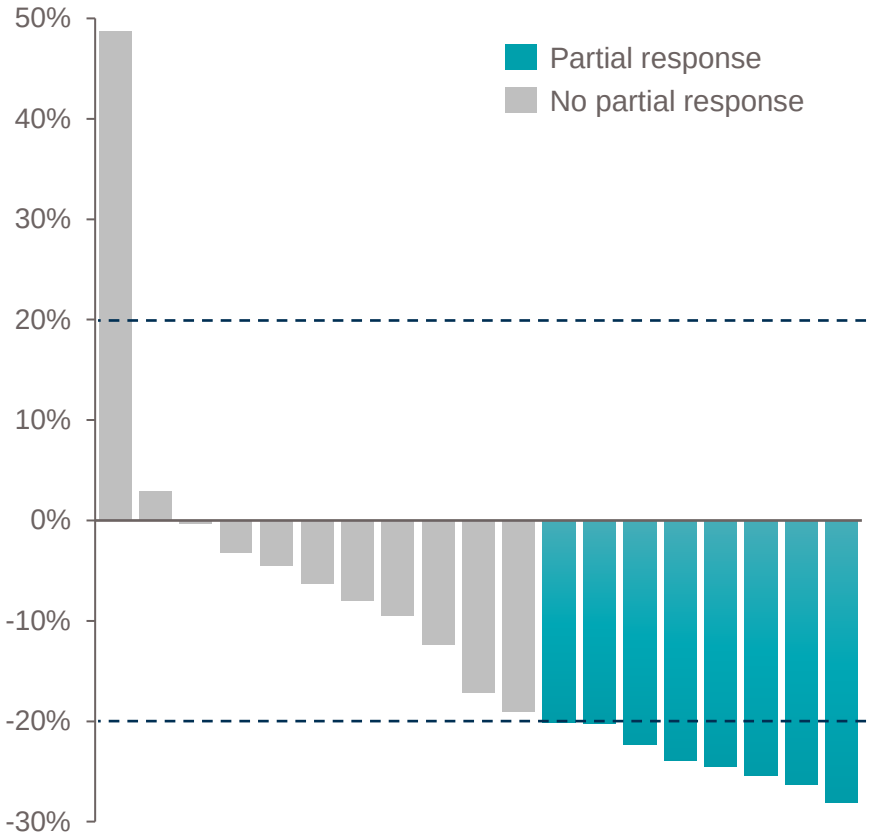
Mirdametinib: Encouraging Phase 2 Results with Potentially Differentiated Safety Profile vs. Other MEK Inhibitors

PHASE 2 | PHASE 2B

Maximum Tumor Volume Change from Baseline



Trial Design and Clinical Activity

NEUROFIBROMATOSIS CONSORTIUM

- 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.

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Potentially Registrational Pediatric and Adult Phase 2b ReNeu Trial in Progress

PHASE 2 | **PHASE 2B**

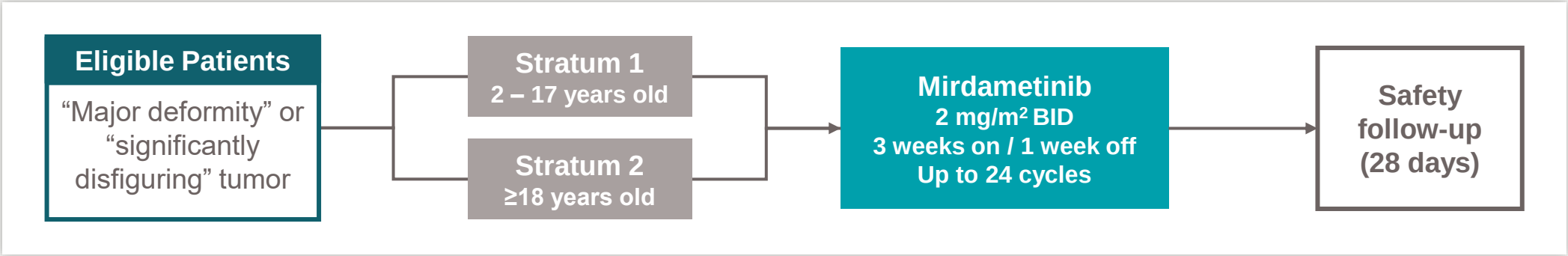
ReNeu

Trial Summary

- Enrolling ~100 patients in 2 strata (pediatrics, adults) across ~50 sites in North America
- 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

Summary of Endpoints

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



Expect to provide a trial update in 1Q 2021

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BCMA Combinations in Multiple Myeloma

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Nirogacestat in Multiple Myeloma: A Potentially Best-in-Class Potentiator of BCMA Therapies

Nirogacestat has the potential to be a cornerstone of BCMA combination therapy

- Significant unmet need in multiple myeloma (MM), with ~27,000 new patients in the relapsed/refractory setting in the US each year
- Gamma secretase directly cleaves membrane-bound BCMA, a clinically validated multiple myeloma target across modalities (ADC, CAR T, bispecific)
- Strong preclinical results and emerging clinical data support combining gamma secretase inhibitors with BCMA therapies
- Pursuing broad collaboration strategy with industry-leading BCMA developers to advance potentially best-in-class combinations using nirogacestat
- Entered into a sponsored research agreement with Fred Hutchinson Cancer Research Center to further evaluate nirogacestat as a BCMA potentiator in MM
- US Composition of Matter patents provide protection to 2039

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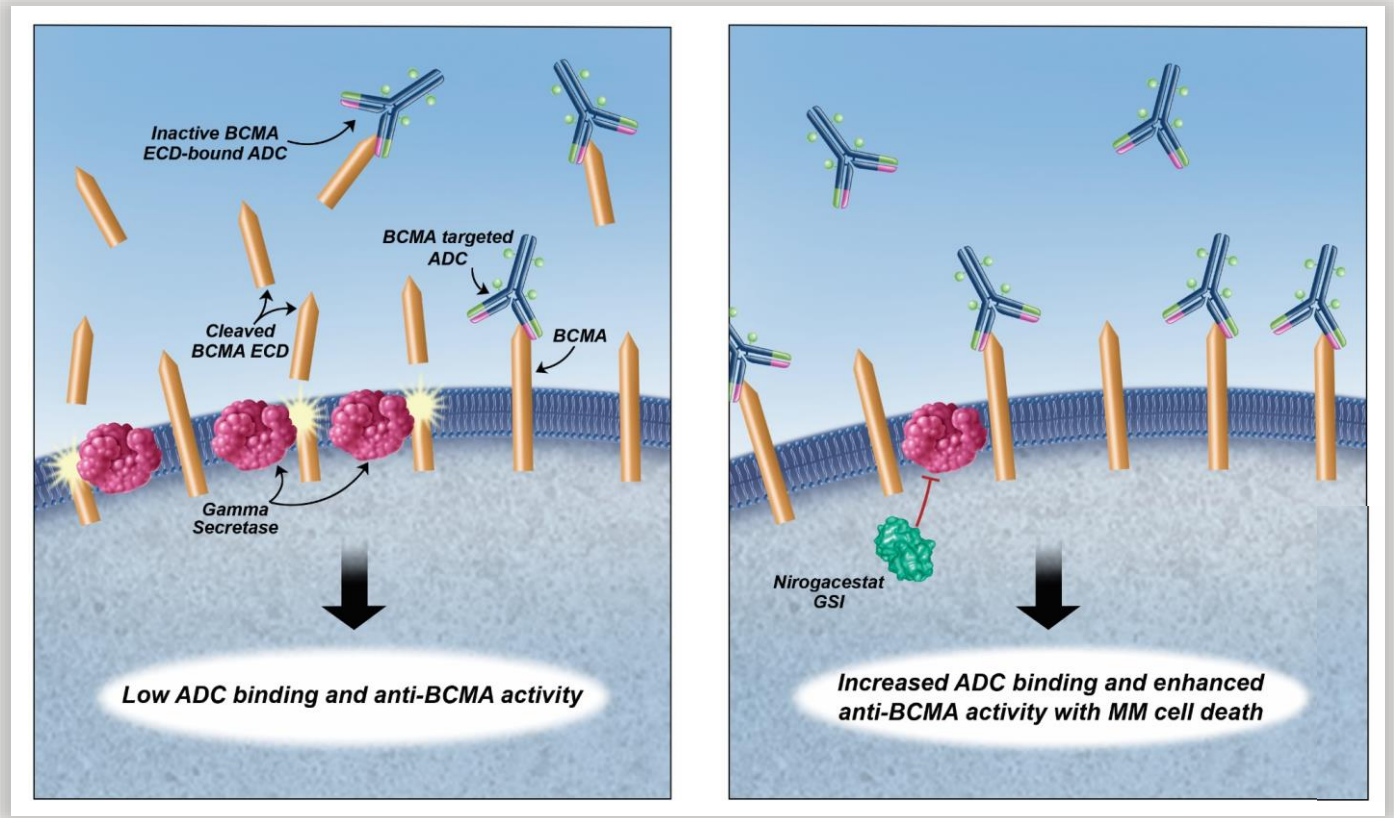
Gamma Secretase Inhibition is Emerging as a Clinically Validated Mechanism to Potentiate BCMA Therapies

- **Gamma secretase directly cleaves membrane-bound BCMA**
  - BCMA has emerged as a promising target in multiple myeloma across modalities
- **GSI can reduce cleavage of BCMA to improve activity of BCMA-directed therapies**
  - GSI can limit soluble BCMA levels, which can interfere with the activity of BCMA-directed therapies
  - GSI can dramatically increase levels of BCMA expression on the cell surface, including in patients that have failed prior BCMA-directed therapies
- **Preclinical and clinical data support combination approach**

MECHANISM OF ACTION OF NIROGACESTAT + BCMA THERAPY (ADC SHOWN)



Source: Cowan et al., Abstract #204 "Efficacy and Safety of Fully Human BCMA CAR T Cells in Combination with a Gamma Secretase Inhibitor to Increase BCMA Surface Expression in Patients with Relapsed or Refractory Multiple Myeloma", ASH 2019; Eastman et al., Abstract #4401 "Synergistic Activity of Belantamab Mafodotin (anti-BCMA immuno-conjugate) with Nirogacestat (PF-03084014, gamma-secretase inhibitor) in BCMA-Expressing Cancer Cell Lines", ASH 2019; Green et al., Abstract #1856 "Response to BCMA CAR-T Cells Correlates with Pretreatment Target Antigen Density and Is Improved By Small Molecule Inhibition of Gamma Secretase", ASH 2019; Laurent et al., *Nat. Comm.*, 2015; Pont et al., *Blood*, 2019.

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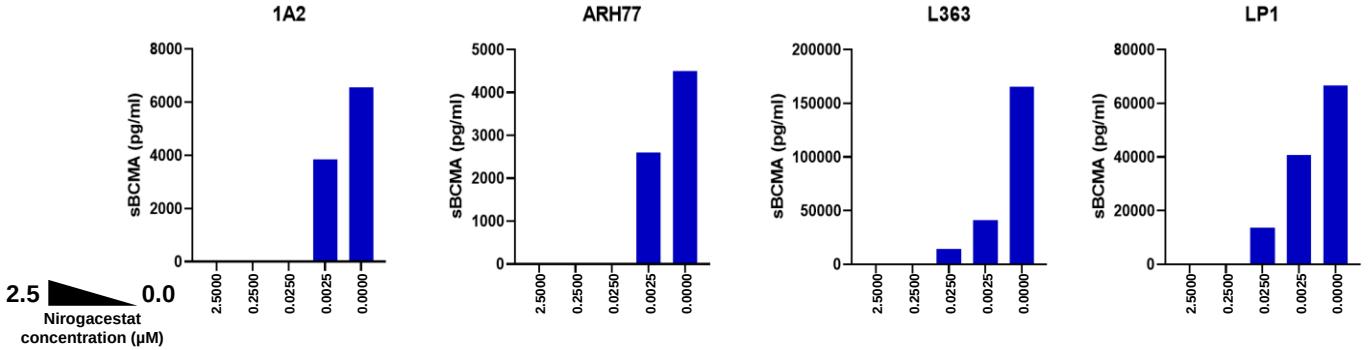
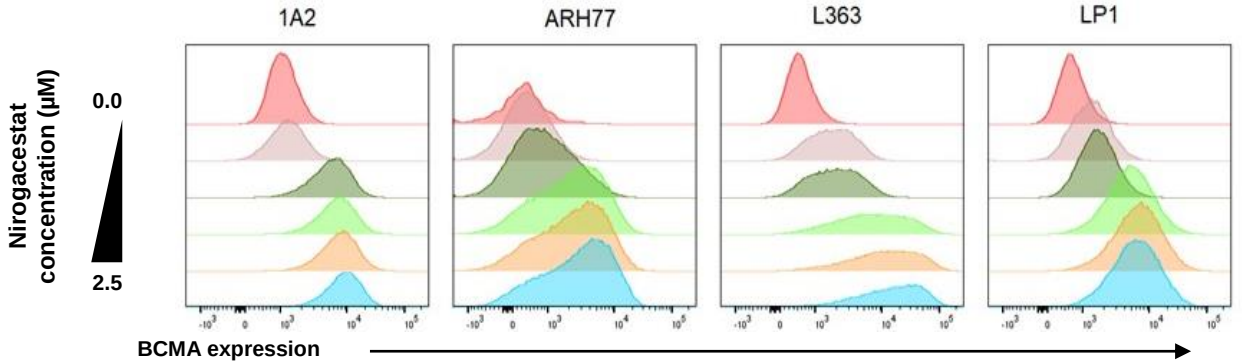
Nirogacestat Inhibited BCMA Shedding, Upregulated BCMA Expression, and Enhanced Activity of BCMA ADC Up to ~3,000-Fold

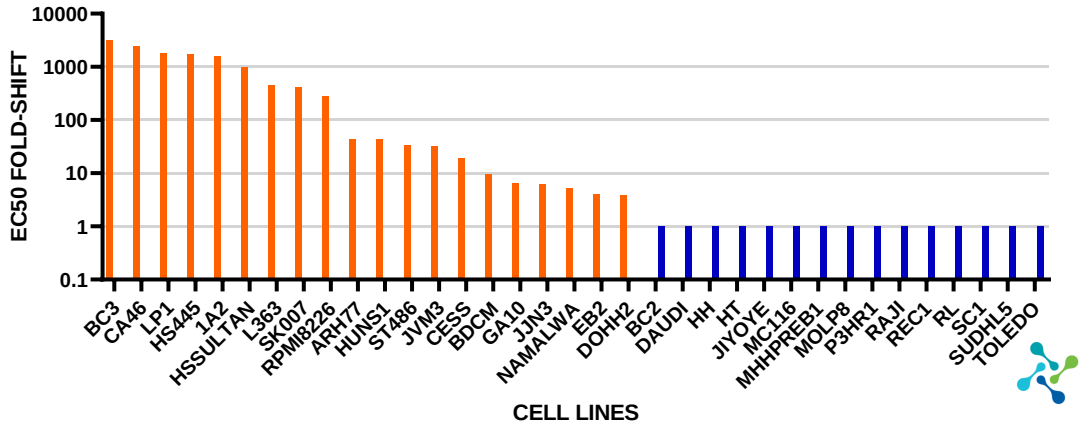
1 Nirogacestat inhibited cleavage of membrane-bound BCMA and shedding of soluble BCMA ECD



2 Nirogacestat rapidly and significantly upregulated BCMA cell surface expression levels



3 Nirogacestat enhanced multiple myeloma cell killing activity of BCMA ADC by up to ~3,000-fold



Note: ECD = extracellular domain; ADC = antibody-drug conjugate; MM = multiple myeloma.
Source: Eastman et al., Abstract #4401 “Synergistic Activity of Belantamab Mafodotin (anti-BCMA immuno-conjugate) with Nirogacestat (PF-03084014, gamma-secretase inhibitor) in BCMA-Expressing Cancer Cell Lines”, ASH 2019.

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Five Clinical Collaborations Signed Across BCMA-Targeted Modalities

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Nirogacestat (GSI)

+

Antibody-Drug Conjugate

BLENREP (belantamab mafodotin)

- BLENREP is first FDA approved BCMA-targeted therapy
- Clinical collaboration signed in June 2019
- Combination study initiated in June 2020 as part of GSK's DREAMM-5 trial
- Expect to report initial clinical data in 2021

Bispecific Antibodies

Teclistamab

- Clinical collaboration signed in September 2020
- Expected Janssen-sponsored Phase 1 trial initiation: early 2021

PF-06863135

- Clinical collaboration signed in October 2020
- Expected Pfizer-sponsored Phase 1b/2 trial initiation: 1H21

CAR T-Cell Therapies

ALLO-715

- Clinical collaboration signed in January 2020
- Expected Allogene-sponsored Phase 1 trial initiation: 1Q21

PBCAR269A

- Clinical collaboration signed in September 2020
- Expected Precision-sponsored Phase 1 trial initiation: 1H21

Biomarker-Defined Metastatic Solid Tumors

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Mirdametinib in *RAS/RAF* Mutant Solid Tumors: Advancing Potentially Best-in-Class MEK/RAF Dimer Inhibitor Combination in Collaboration with BeiGene

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+

BeiGene

Mirdametinib + Lifirafenib

MEKi + RAF dimer inhibitor

RAS/RAF Mutant and Other MAPK Pathway Aberrant Solid Tumors

- Significant area of unmet need in cancer patients with *RAS*/*RAF* mutations and other MAPK pathway aberrations (approximately 25% of solid tumors)
- Lifirafenib possesses potentially best-in-class profile among RAF dimer inhibitors
- Combination synergy demonstrated across preclinical models harboring a variety of *KRAS* and *NRAS* mutations
- Phase 1b/2 trial is ongoing in Australia and the US
- Focused investment until significant clinical validation achieved

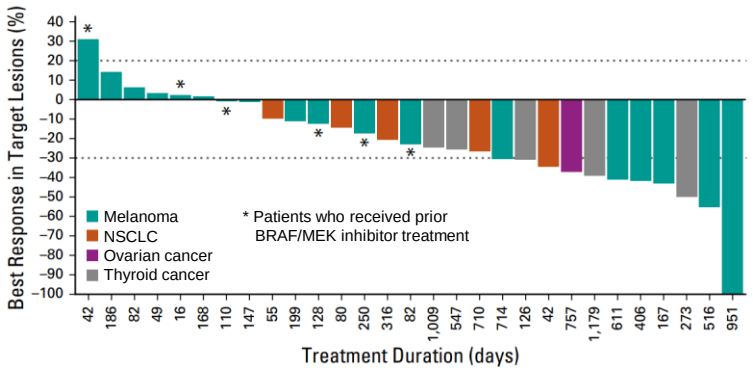
Expect to report initial clinical data in 2021

Mirdametinib + Lifirafenib: Encouraging Monotherapy Clinical Activity and Strong Preclinical Combination Data

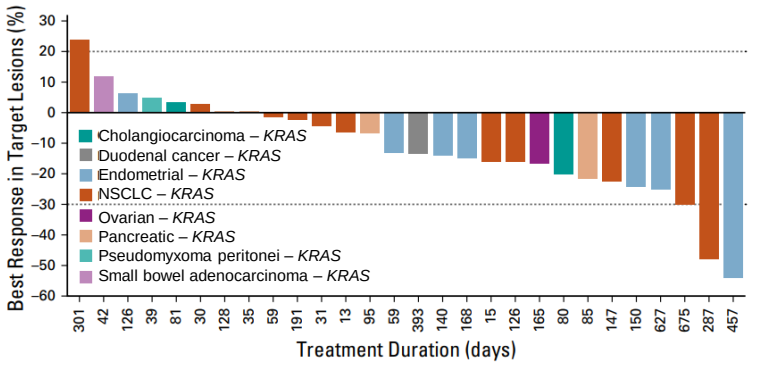
1 Lifirafenib monotherapy clinical activity in *BRAF* and *KRAS* mutant cancers

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

BRAF^{mut} Cancers: P1a/b Best Objective Response

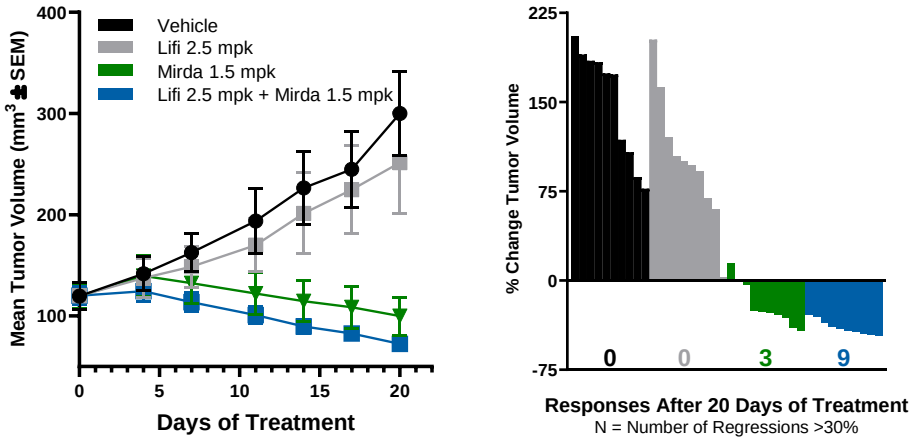


KRAS^{mut} Cancers (ex-CRC): P1a/b Best Objective Response



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)



Source: Desai et al., *J Clin Oncol,* 2020; Tang et al., *Mol Cancer Ther*, 2015; Yuan et al., *Molecular Oncology*, 2020; Yuan et al., Abstract #6415, AACR 2020 Virtual Annual Meeting II.

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BGB-3245: Potentially Differentiated Program for Currently Unaddressed *BRAF* Driver Mutations and Fusions

SpringWorks THERAPEUTICS

+

BeiGene

BGB-3245

Mutant BRAF monomer, dimer, and fusion inhibitor

***BRAF* Mutant Solid Tumors**

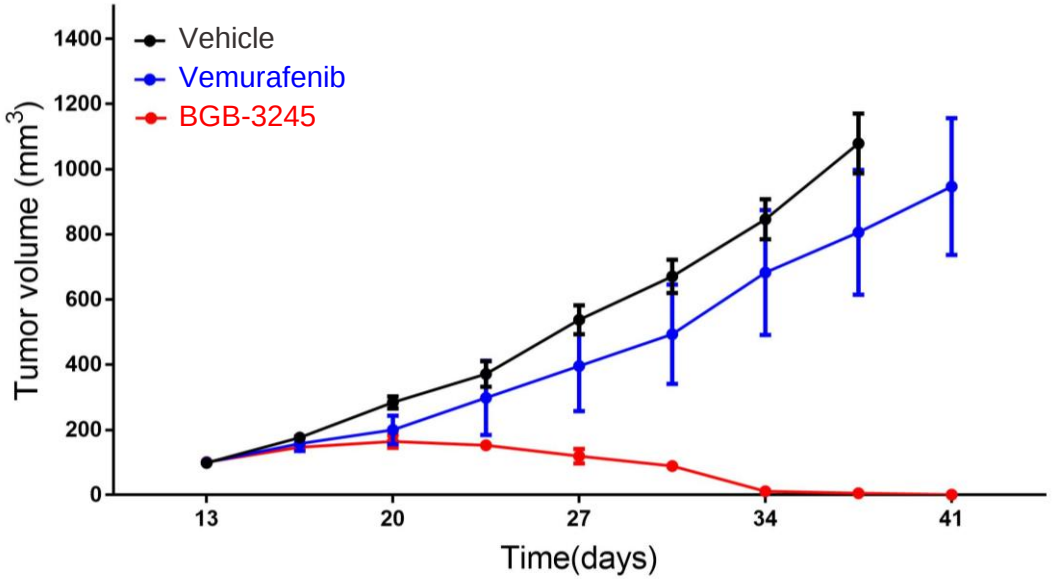
- MapKure is a joint venture between SpringWorks and BeiGene that is advancing BGB-3245, a novel BRAF inhibitor
- BGB-3245 could address *BRAF* alterations that currently lack targeted therapeutic options (non-V600 *BRAF* mutations and fusions)
- BGB-3245 has shown preclinical activity against resistance mutations to first generation *BRAF* V600 inhibitors
- Phase 1 trial initiated in 2020 and dose escalation ongoing in Australia and the US
- Industry-leading Scientific Advisory Board chaired by Dr. Neal Rosen of Memorial Sloan Kettering Cancer Center

Expect to report initial clinical data in 2021

BGB-3245 Has Demonstrated Encouraging Preclinical Activity

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

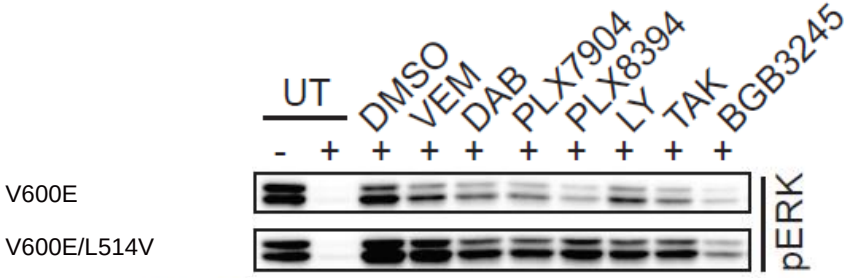
***BRAF* Fusion PDX: *In Vivo* Tumor Growth Inhibition**



- Driver mutations and fusions potentially uniquely targetable by BGB-3245 could account for up to ~5% of all solid tumors
- 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



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

Source: Rosen presentation, Sixth International RASopathies Symposium: Precision Medicine – From Promise to Practice, 2019; Dankner et al., *Oncogene*, 2018; Ross et al., *IJC*, 2016; Dimitriadis et al., *J Neurooncol*, 2013; Garnett et al., *Molecular Cell*, 2005; Siegel et al., *CA A Cancer J Clin*, 2019; Wang et al., *Cancer Discovery*, 2018.

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The SpringWorks Opportunity

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Multiple Milestones Anticipated Across Our Pipeline in 2021

	Indication	Program		Expected Milestone	Timing
Late-Stage Rare Oncology	Desmoid Tumors	Nirogacestat		Phase 3 DeFi topline data in adult desmoid tumor patients	2Q – 3Q 2021
	NF1-Associated Plexiform Neurofibromas	Mirdametinib		Phase 2b ReNeu trial update	1Q 2021
BCMA Combinations	Relapsed / Refractory Multiple Myeloma	Nirogacestat	+ BLENREP	Report initial Phase 1b data with GSK	2021
			+ Teclistamab	Phase 1 trial initiation with Janssen	Early 2021
			+ PF-06863135	Phase 1b/2 trial initiation with Pfizer	1H 2021
			+ ALLO-715	Phase 1 trial initiation with Allogene	1Q 2021
			+ PBCAR269A	Phase 1 trial initiation with Precision BioSciences	1H 2021
Biomarker-Defined Metastatic Solid Tumors	RAS/RAF Mutant and Other MAPK Pathway Aberrant Solid Tumors	Mirdametinib	+ Lifirafenib	Report initial Phase 1b/2 data with BeiGene	2021
	RAF Mutant Solid Tumors	BGB-3245		Report initial Phase 1 data	2021

Well Capitalized to Execute on Important Value-Driving Milestones

$566.6M

Cash, Cash Equivalents & Marketable Securities(1)

No Debt

NASDAQ: SWTX

48.8M

Common Shares Outstanding(2)

(1) As of November 30, 2020.
(2) Basic common shares outstanding as of November 12, 2020.

SpringWorks THERAPEUTICS

Strategic Priorities and Building Blocks for Substantial Value Recognition in 2021

- Execute **two ongoing potentially registrational trials** in rare oncology indications
- Develop nirogacestat as a **cornerstone of BCMA combinations**
- Continue disciplined investments in **high-value early pipeline programs**
- Drive **portfolio expansion** through additional in-licenses and clinical collaborations
- Expand capabilities and **scale the organization** with talented employees

10 programs in development

2 potentially registrational trials in progress

7 collaborations in large cancer indications

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Thank You

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