

SpringWorks THERAPEUTICS

40th Annual Cowen Health Care Conference

Saqib Islam, Chief Executive Officer

March 3, 2020

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, statements regarding: (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 partner’s 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, and, (viii) our ability to meet any specific milestones set forth herein.

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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
- **Four 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 Business Officer

OrbiMed
Healthcare Fund Management

BAIN & COMPANY

Frank Perier, MBA
Chief Financial Officer

Forest Laboratories, Inc.

Bristol-Myers Squibb

Mary Smith, Ph.D.
Senior Vice President, Clinical Research and Development

Bamboo therapeutics

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SpringWorks Therapeutics,
Chief Executive Officer

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OrbiMed,
Executive Partner

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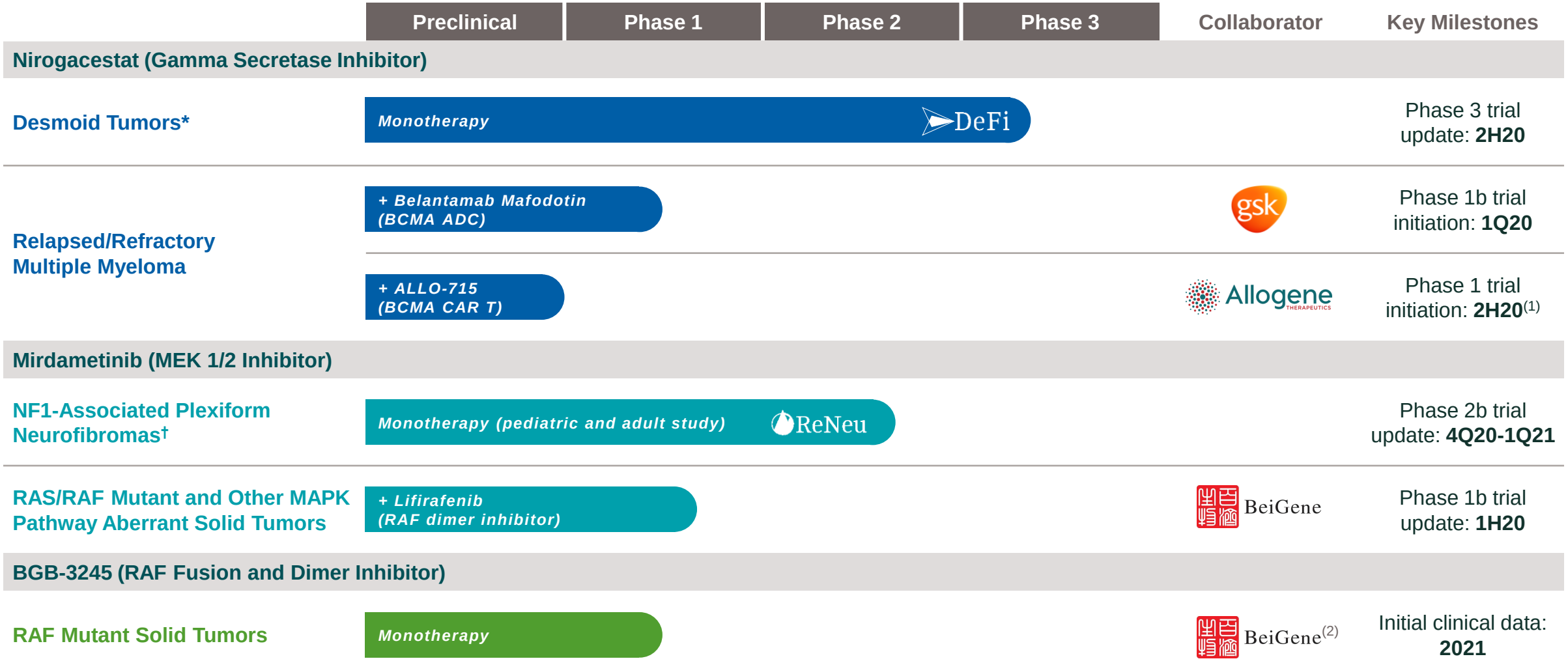
Advancing Diversified Pipeline of Targeted Oncology Programs as Standalone and Combination Therapies



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) Pending discussions with regulators.

(2) Being developed by MapKure, LLC, jointly owned by SpringWorks and BeiGene.

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Nirogacestat

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Nirogacestat: A New Paradigm for Patients With Desmoid Tumors

- Desmoid tumors are highly morbid soft tissue tumors with an estimated 5,500 to 7,000 patients actively receiving treatment in the US per year
- Nirogacestat is an oral, selective gamma secretase inhibitor with over 9 years of clinical experience (over 200 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 suitable for long term dosing
- Received Fast Track and Breakthrough Therapy Designations from FDA and Orphan Drug Designation from both FDA and European Commission

Phase 3 DeFi trial currently enrolling and update to be provided in 2H20

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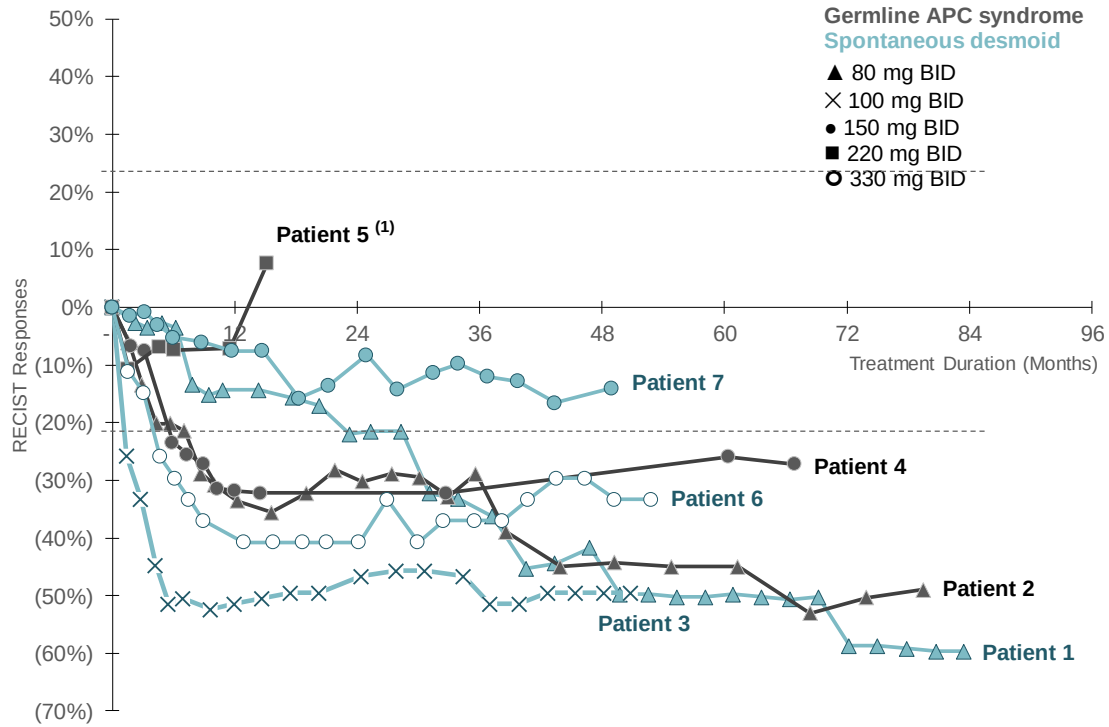
Initial Clinical Activity of Nirogacestat Observed in Desmoid Tumors

PHASE 1 | PHASE 2 | PHASE 3

Most Responses Continued Past 4 Years (RECIST v1.0)



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

All evaluable desmoid tumor patients in the study responded to nirogacestat treatment (1)

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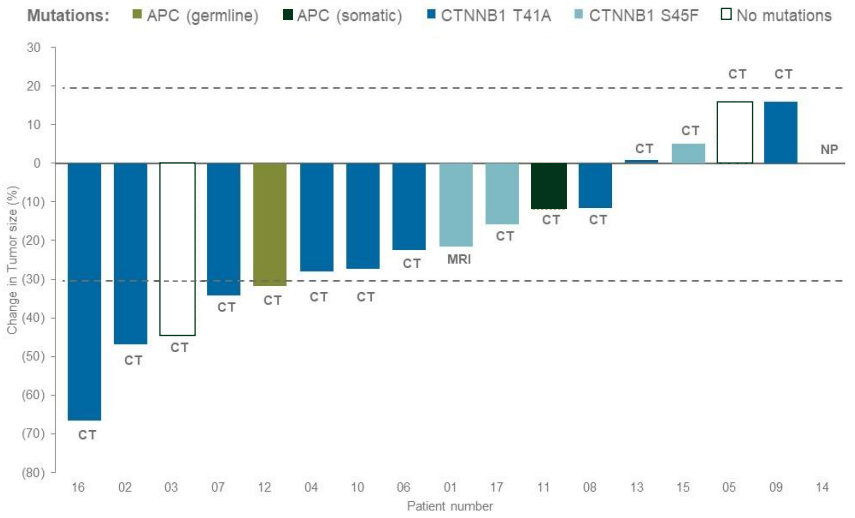
Encouraging Clinical Activity and Tolerability Observed in NCI-Conducted Phase 2 Trial in a Refractory and Heavily Pre-Treated Patient Population

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

Clinical Responses by RECIST v1.1



- **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

Durability and Tolerability with Long-Term Dosing

- **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 2020 (treatment duration of 55 to 65 months in these patients)
  - Well tolerated; only 1 discontinuation due to AE (2)

Shown to arrest tumor growth in a heavily pre-treated patient population (i.e., TKIs, chemo, surgery)

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 Trial (DeFi Trial) Has Commenced

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

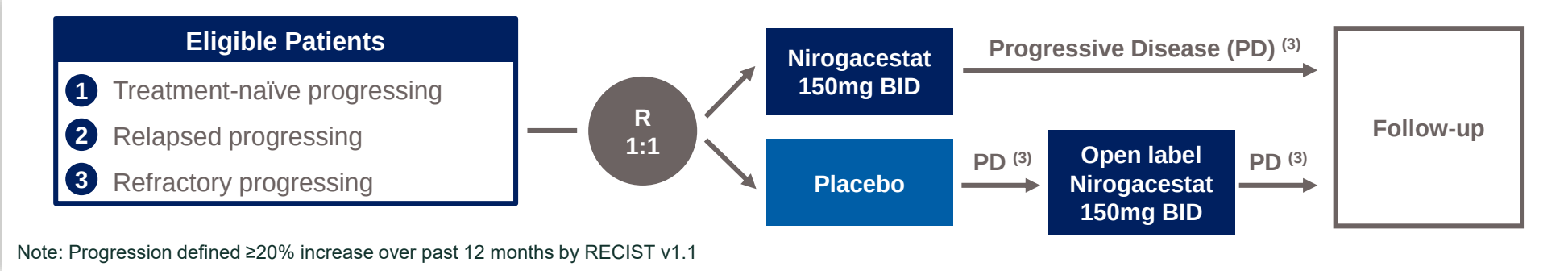
Trial Summary

- ~115 patients at ~60 sites in the US and EU
- 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 (PRO)



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

Key Event	Timing
Phase 3 Initiation	May 2019
Trial Update	2H20
Topline Data Readout	2Q21-3Q21

(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.
(3) As defined by RECIST v1.1.

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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, 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

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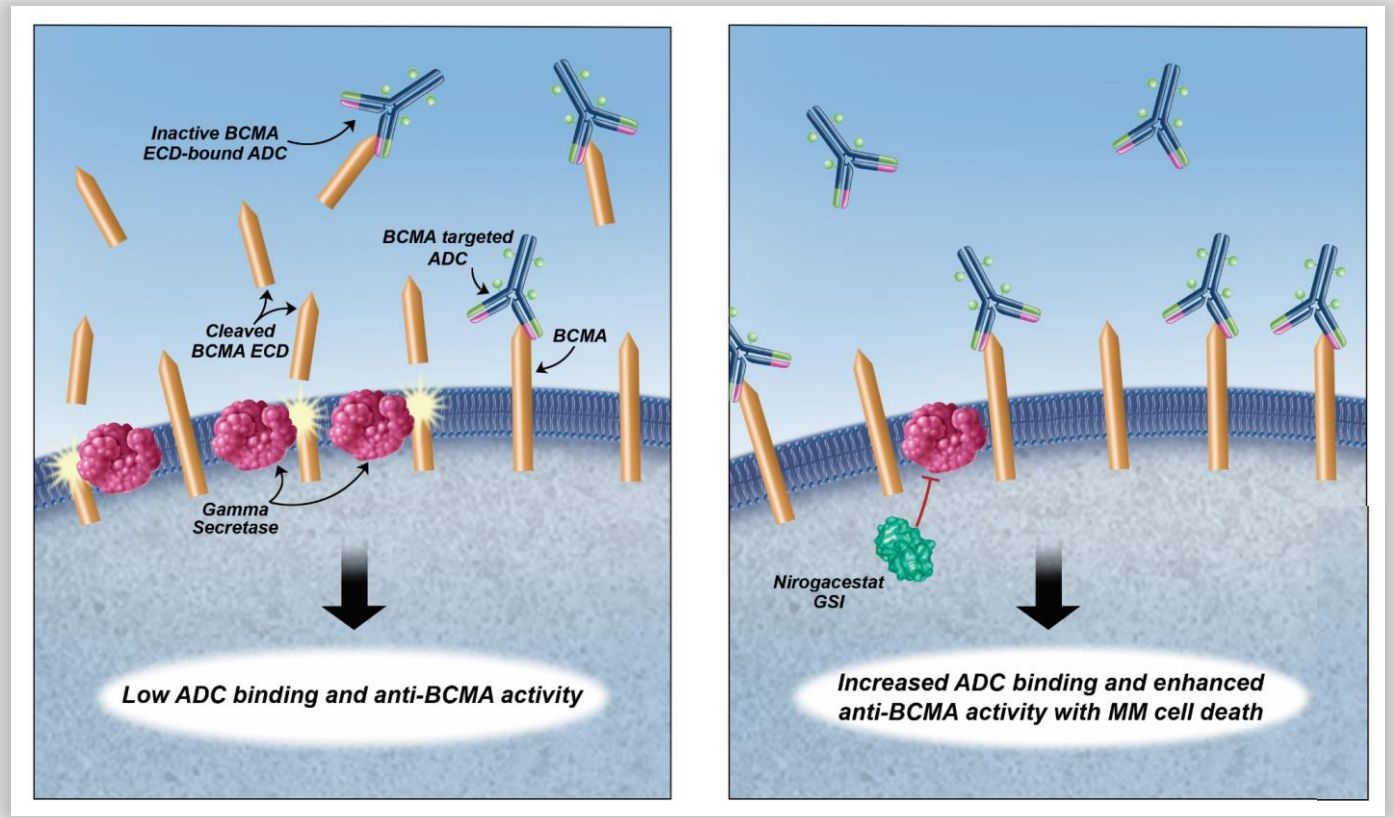
Gamma Secretase Inhibition is Emerging as a Clinically Validated Mechanism to Potentiate BCMA Therapies

- **BCMA has emerged as a promising target in multiple myeloma across modalities**
- **Gamma secretase directly cleaves membrane-bound BCMA**
  - **GSI can reduce shedding of BCMA** to improve activity of BCMA-directed therapies
  - **GSI can limit soluble BCMA levels**, which act as a 'sink' for BCMA-directed therapies
  - **GSI can upregulate surface BCMA expression**, 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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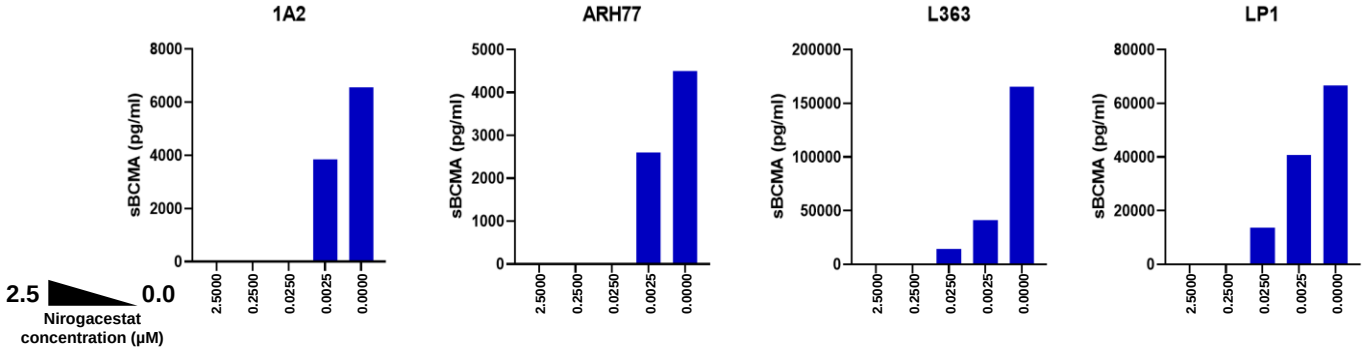
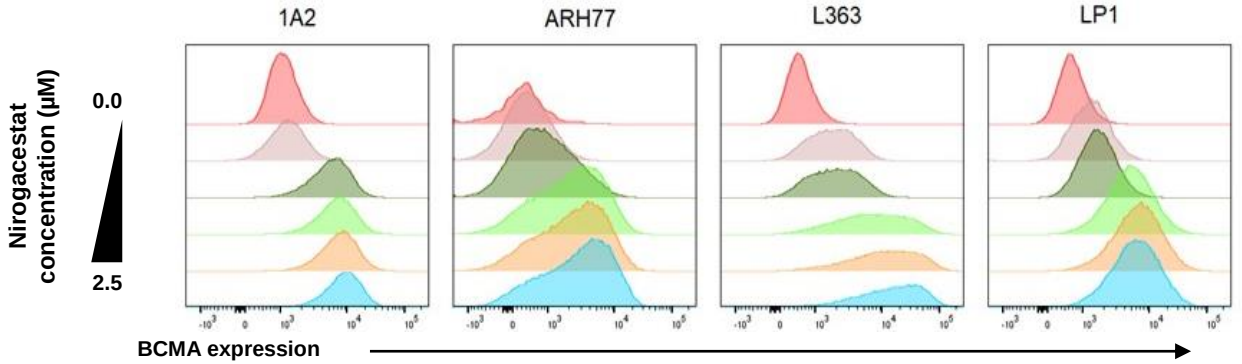
Nirogacestat Inhibited BCMA Shedding, Upregulated BCMA Expression, and Enhanced Activity of BCMA ADC Up to ~3,000-Fold

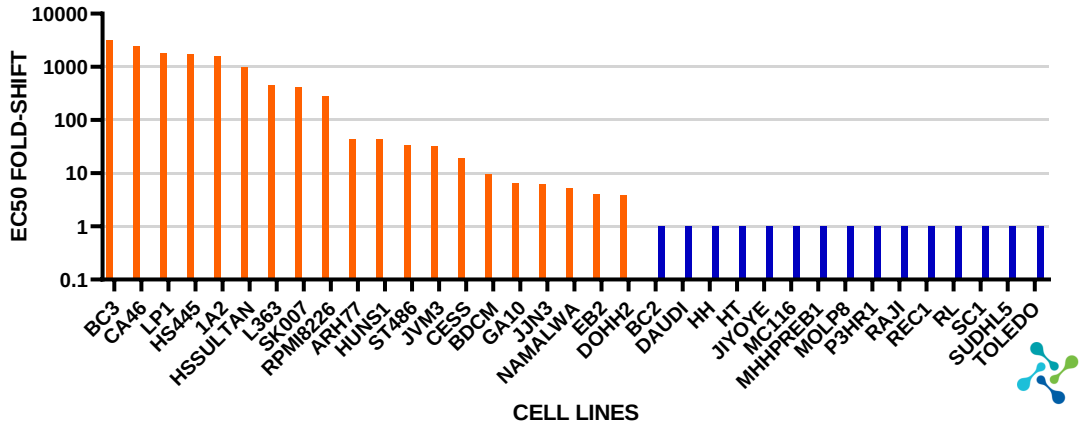
1 Nirogacestat inhibited cleavage of membrane-bound BCMA and shedding of soluble BCMA ECD



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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Two BCMA Collaborations Signed To Date with GSK and Allogene

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Nirogacestat + Belantamab Mafodotin

BCMA Antibody-Drug Conjugate (ADC)

- Clinical collaboration signed in June 2019 with first-in-class BCMA ADC
- Preclinical synergy demonstrated in data presented at ASH 2019
- Combination will be part of GSK's DREAMM-5 platform trial
- Nirogacestat sub-study to initiate 1Q20

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Nirogacestat + ALLO-715

BCMA Allogeneic CAR T Cell Therapy

- Clinical collaboration signed in January 2020 with first allogeneic BCMA CAR T cell therapy to enter the clinic
- Working with leaders in 'off-the-shelf' CAR T cell therapy field to further explore nirogacestat's potential benefit in multiple myeloma
- Combination clinical trial sponsored by Allogene expected to commence in 2H20(1)

Nirogacestat has the potential to become a cornerstone of BCMA combinations for the treatment of multiple myeloma

(1) Pending discussions with regulators.

Mirdametinib

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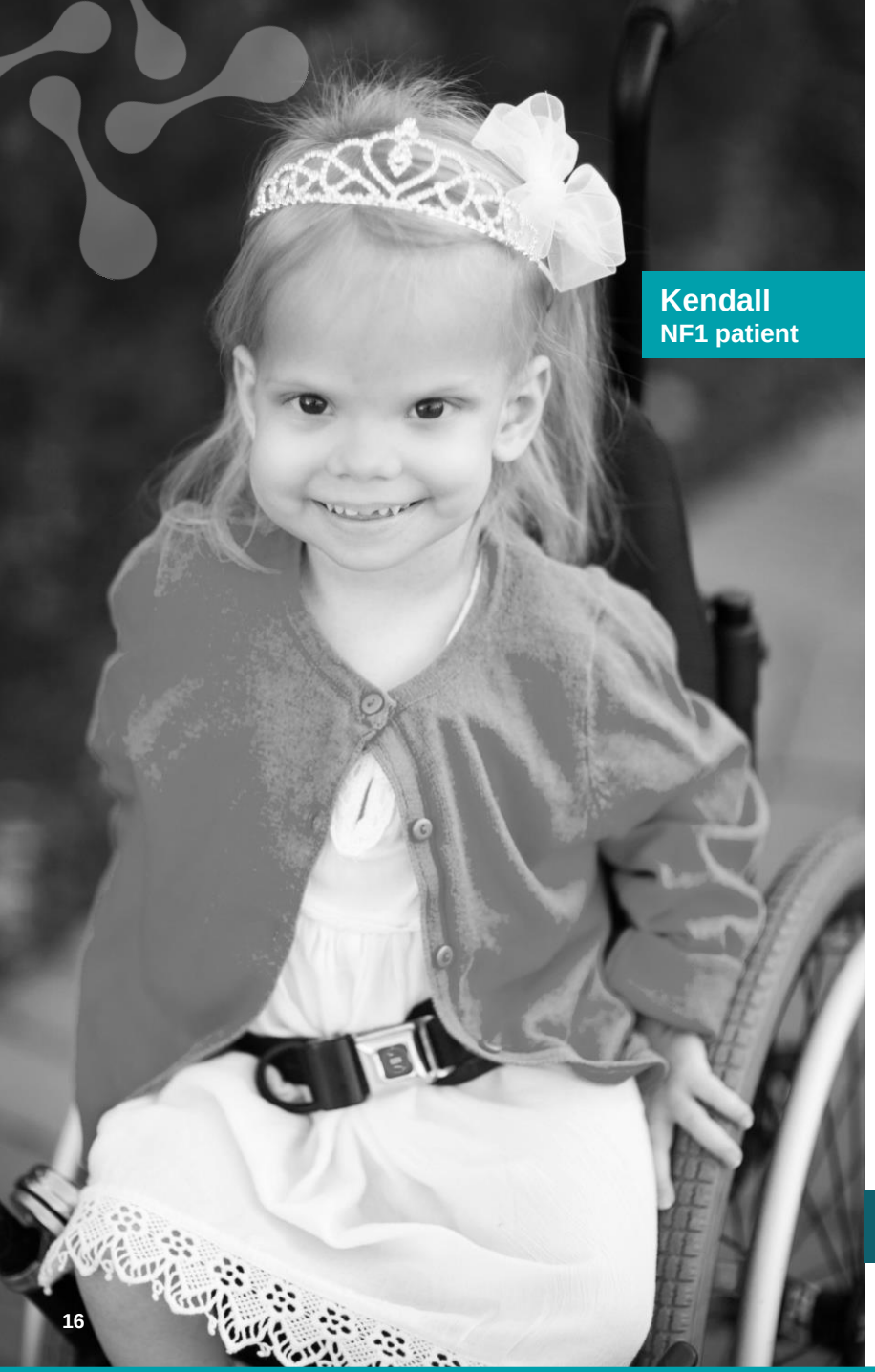

Mirdametinib: A Potentially Best-in-Class Therapy for Patients with NF1-PN

- ~100,000 patients in the US with NF1 – 30-50% lifetime risk of developing disfiguring peripheral nerve sheath tumors (plexiform neurofibromas)
- Mirdametinib is an oral, small molecule MEK1/2 inhibitor with clinical validation and over 200 subjects exposed to date
- Encouraging results from Phase 2 investigator-initiated trial in adolescents and adults with NF1-associated plexiform neurofibromas (NF1-PN)
- Granted Orphan Drug Designation by FDA and European Commission in NF1 and FDA Fast Track Designation in NF1-PN
- Compound potency and optimized dose/schedule may allow for a potentially differentiated profile versus other MEK inhibitors

Phase 2b ReNeu trial currently enrolling and update expected 4Q20-1Q21

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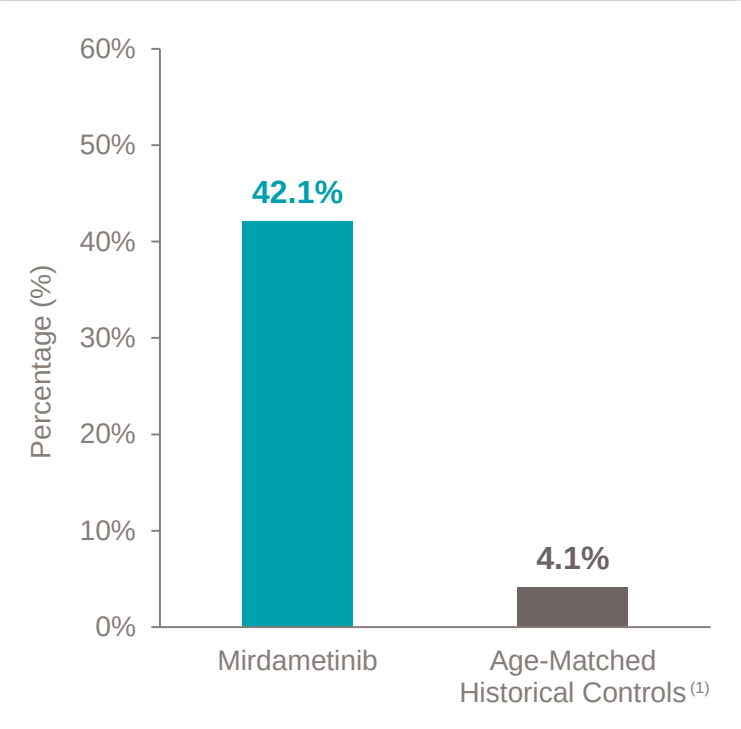
Mirdametinib: Encouraging Phase 2 Results with Potentially Differentiated Safety Profile vs. Other MEK Inhibitors

PHASE 2 | PHASE 2B

Objective Response Rate



NEUROFIBROMATOSIS CONSORTIUM

Trial Design and Clinical Activity

- 19 patients with inoperable and symptomatic or growing PNs, ages 16-39 years (median age: 24)
- 2 mg/m^2 (up 4 mg BID) intermittent dosing schedule (3 week on/1 week off)
- **8/19 (42%) responders, prospectively defined as ≥ 20% tumor reduction by course 12**

Tolerability

- 5 dose reductions, all due to Gr2 events: rash (2), nausea (1), fatigue (1) and pain (1)
- No Gr4 events; 7 treatment-emergent Gr3 events reported in 5 patients; only 2 events (pain in the same patient) were considered treatment-related by the investigator
- **Dose and schedule minimized historical class toxicities**

We believe that mirdametinib has the opportunity to demonstrate a more tolerable safety profile than other MEK inhibitors

Source: Weiss, Children's Tumor Foundation 2017 Annual Meeting Presentation.

(1) In Nguyen et al. 2012, 95 NF1-PN patients had the volumes of single PN lesions monitored over time. Of these patients, 69 were greater than 16 years of age at the time of the initial assessment (range: 16.1 to 62.6 years), representing a total of 146 NF1-PN lesions. The duration of follow-up between scans ranged from 1.05 to 4.10 years (average: 2.40 years). Of the 146 lesions monitored, 6 were documented to have had a volumetric decrease of ≥20% (4.1%).

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Potentially Registrational Pediatric and Adult Phase 2b ReNeu Trial Has Commenced

PHASE 2 | **PHASE 2B**

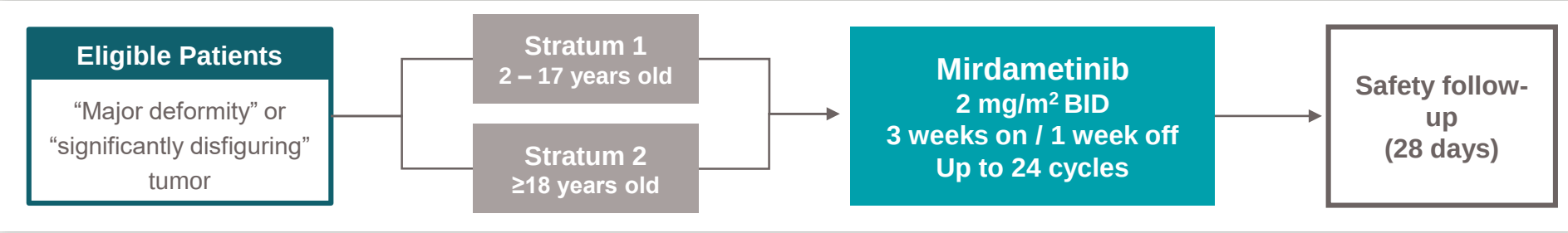
Trial Summary

- 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

Summary of Endpoints

ReNeu

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



Key Event	Timing
Phase 2b Initiation	October 2019
Trial Update	4Q20-1Q21

Treatment duration and trial populations designed to evaluate full potential of mirdametinib in NF1-PN

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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 and preclinical data supports combination with mirdametinib
- Phase 1b trial initiated in Australia in 2Q19 and US IND opened in 3Q19
- Update expected in 1H20 from dose-escalation portion of the trial
- Focused investment until significant clinical validation achieved

Phase 1b trial update expected in 1H20

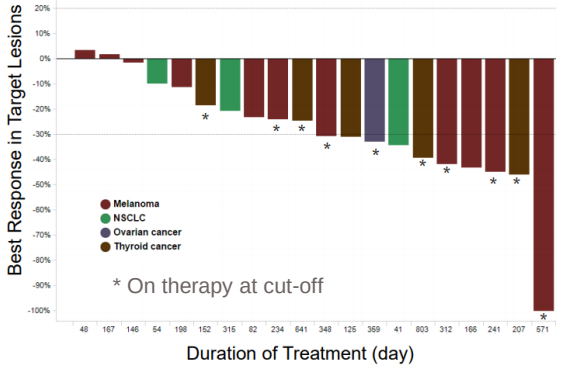
Mirdametinib + Lifirafenib: Encouraging Monotherapy Activity and Strong Preclinical Combination Data

1 Lifirafenib has demonstrated potent pharmacological activity against all RAF isoforms

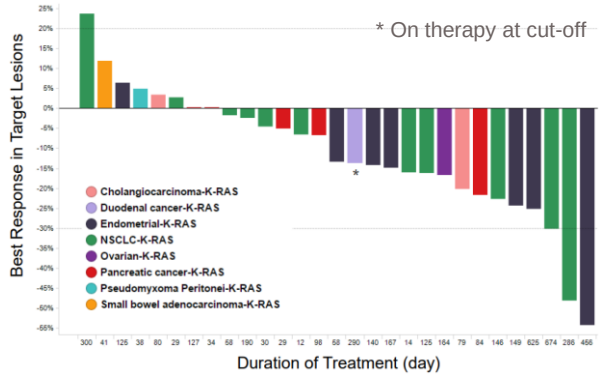
RAF isoforms	IC_{50} (nmol/L; mean ± SD)
$BRAF^{V600E}$	23 ± 5 nM
$BRAF^{WT}$	32 ± 8 nM
CRAF	7.0 ± 2.3 nM
ARAF	5.6 nM

2 Lifirafenib monotherapy clinical activity shown in *BRAF* and *KRAS* mutant cancers

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

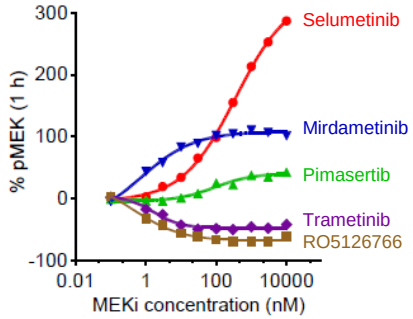


$KRAS^{mut}$ Cancers (ex-CRC): P1a/b Best Objective Response

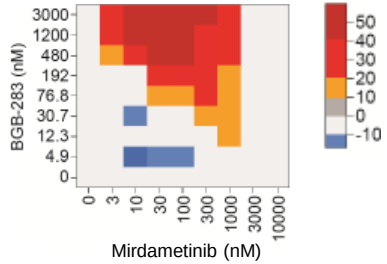


3 Compelling preclinical synergy demonstrated with mirdametinib and lifirafenib

MEKi Monotherapy



Mirdametinib + Lifirafenib



Source: Desai presentation, "A Phase IB study of RAF dimer inhibitor BGB-283 in patients with B-RAF or K-RAS/N-RAS mutated solid tumors," AACR 2017; Tang et al., Mol Cancer Ther, 2015; Yuan et al., Abstract #669: "BGB-283 effectively enhances MEK inhibitor induced tumor suppression in RAS mutant cancers", AACR 2015.

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BGB-3245

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

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BeiGene

BGB-3245

Mutant BRAF monomer, dimer, and fusion inhibitor

***BRAF* Mutant Solid Tumors**

- BGB-3245 is a novel BRAF inhibitor being advanced in collaboration with BeiGene through MapKure, a jointly owned entity
- 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 Australia in 1Q20 and US IND cleared
- Industry-leading Scientific Advisory Board chaired by Dr. Neal Rosen of Memorial Sloan Kettering Cancer Center

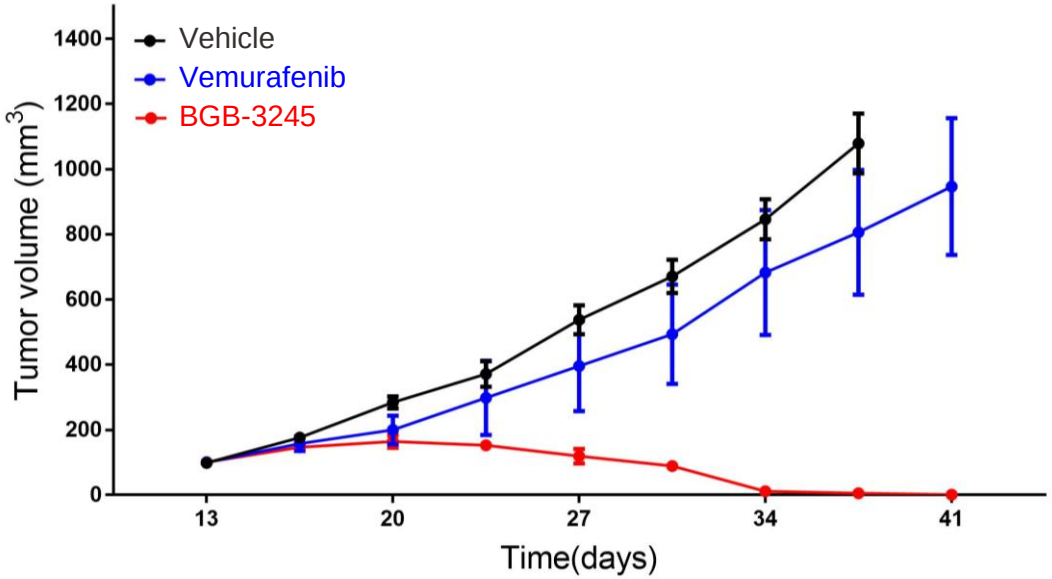
Phase 1 dose escalation and expansion trial in progress with initial clinical data expected in 2021

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

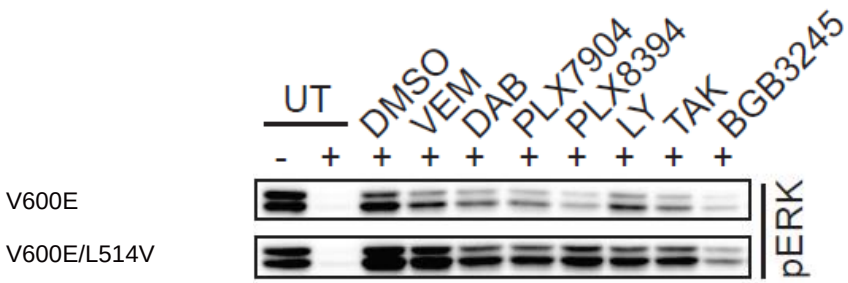


- Driver mutations and fusions potentially uniquely targetable by BGB-3245 could account for up to ~5% of all solid tumors
- BGB-3245 also active preclinically against mutant *BRAF* monomers (e.g., V600)

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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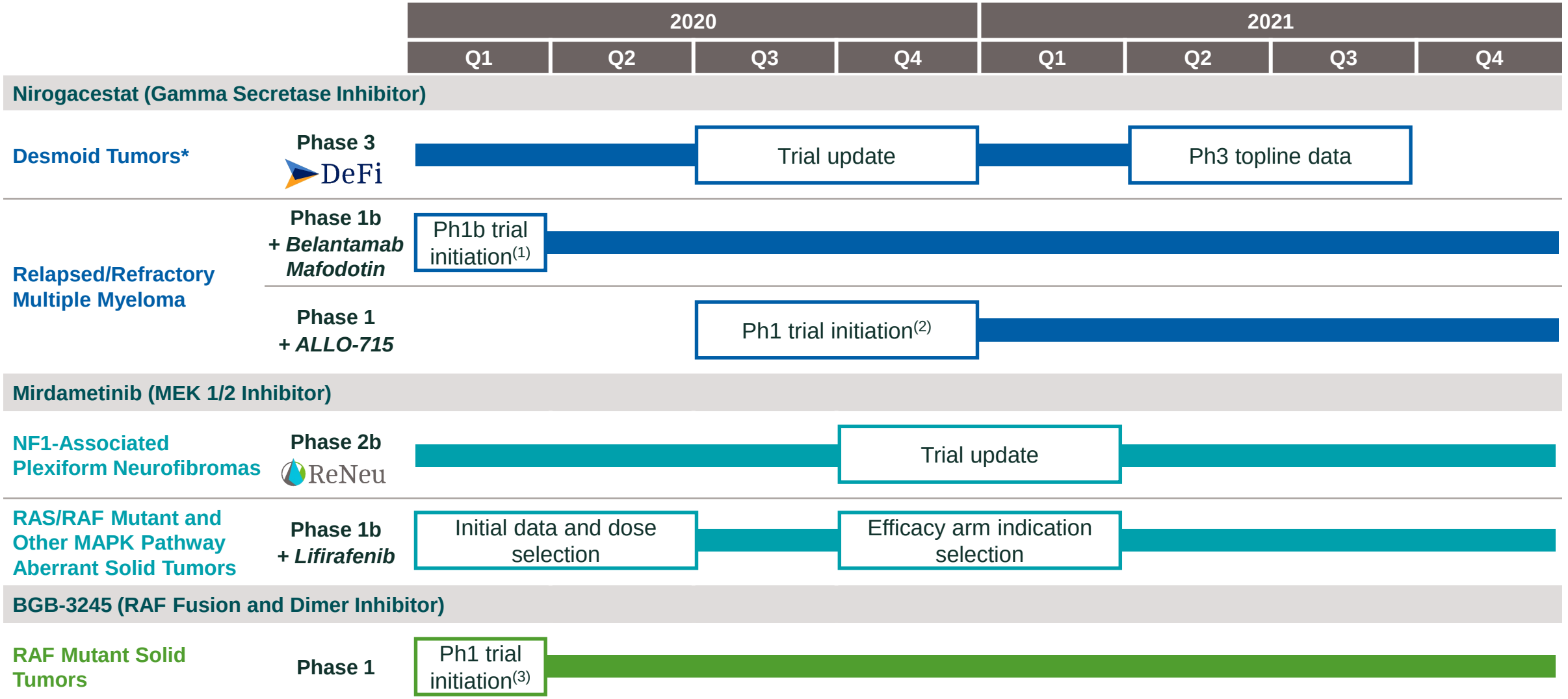
Pipeline is Rich in Anticipated Near-Term Catalysts



(1) Phase 1b clinical trial evaluating belantamab mafodotin in combination with nirogacestat in patients with relapsed or refractory multiple myeloma will be examined as a sub-study in GlaxoSmithKline's DREAMM-5 platform trial.
(2) Pending discussions with regulators.
(3) Program being developed by MapKure, LLC, jointly owned by SpringWorks and BeiGene.

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Well Capitalized to Execute on Important Value-Driving Milestones

$344M

Cash & Cash Equivalents

(as of 09/30/19)

No Debt

NASDAQ: SWTX

42.9M

Common Shares Outstanding(1)

Current cash position expected to fund operations through 2022, supporting completion of six ongoing and planned clinical trials

(1) Basic common shares outstanding as of December 31, 2019.

SpringWorks THERAPEUTICS

Strategic Priorities and Building Blocks for Substantial Value Recognition in 2020

- 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

6 programs in the clinic by **end of 2020**

2 potentially registrational trials in progress

4 collaborations in large cancer indications

SpringWorks THERAPEUTICS

Thank You

40th Annual Cowen and Company Health Care Conference

March 3, 2020

SpringWorks THERAPEUTICS