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# COMPANY PRESENTATION

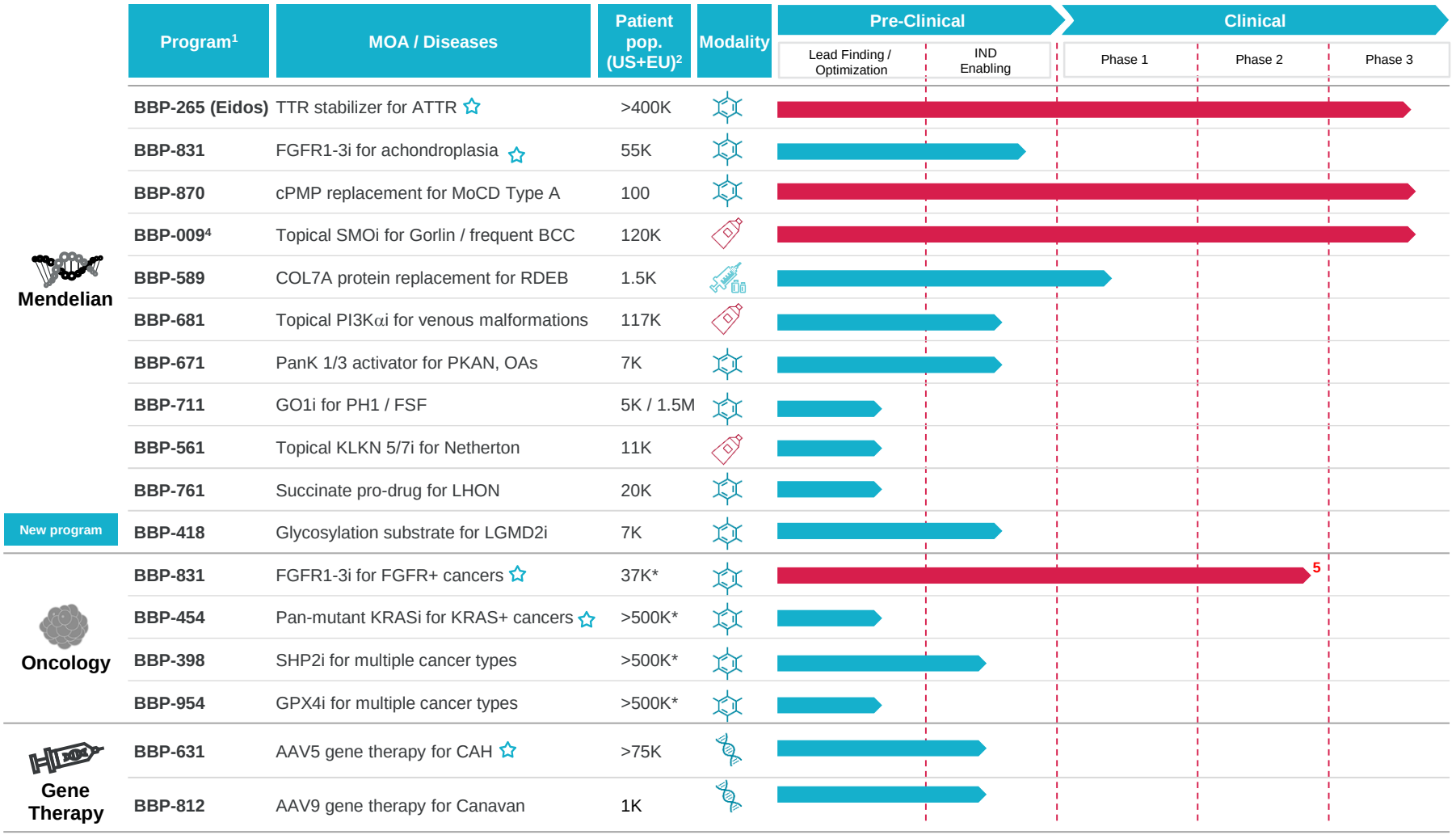
NOVEMBER 2019

**Forward-Looking Statements**

Statements in this Presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, expected manufacturing capabilities, strategy, regulatory matters, market size and opportunity, future financial position, future revenue, projected costs, prospects, plans, objectives of management, and the Company's ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "potential" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing therapeutic products, future results from the Company's ongoing and planned preclinical studies and clinical trials, the Company's ability to obtain adequate financing to fund its preclinical studies and planned clinical trials and other expenses, trends in the industry, the legal and regulatory framework for the industry and future expenditures. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in the Presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this Presentation is given. This Presentation discusses product candidates that are under preclinical study or clinical trial and which have not yet been approved for marketing by the U.S. Food and Drug Administration (the "FDA"). No representation is made as to the safety or effectiveness of these product candidates for the therapeutic use for which such product candidates are being studied.

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes 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 the Company believes its own internal research is reliable, such research has not been verified by any independent source.

# We have built a sizeable pipeline over the past four years




[1] Each of our programs is housed in a separate subsidiary; [2] Patient population: Prevalence except for asterisked figures which represent incidence; [3]A clinical trial we believe could support filing an application for marketing authorization, although the FDA and other regulatory authorities have not indicated their agreement or that additional trials will not be required; [4] We are party to an option agreement pursuant to which LEO Pharma A/S has been granted an exclusive, irrevocable option to acquire PellePharm, including the BBP-009 program. If the option is exercised by LEO Pharma A/S, we will no longer have rights to develop and commercialize BBP-009. See "Business — Our Material Agreements—BBP-009 (Patidegib): Option Agreement with LEO Pharma A/S." [5]Planned New Drug Application (NDA) submission for the treatment of cholangiocarcinoma (CCA) as a second-line or later therapy (2L)

# Where we are headed: Profile by year-end 2021

**“Shots on goal”**

Based on our projected 2019-2021 catalyst map

**Pipeline Advancement** + **Add New Programs**

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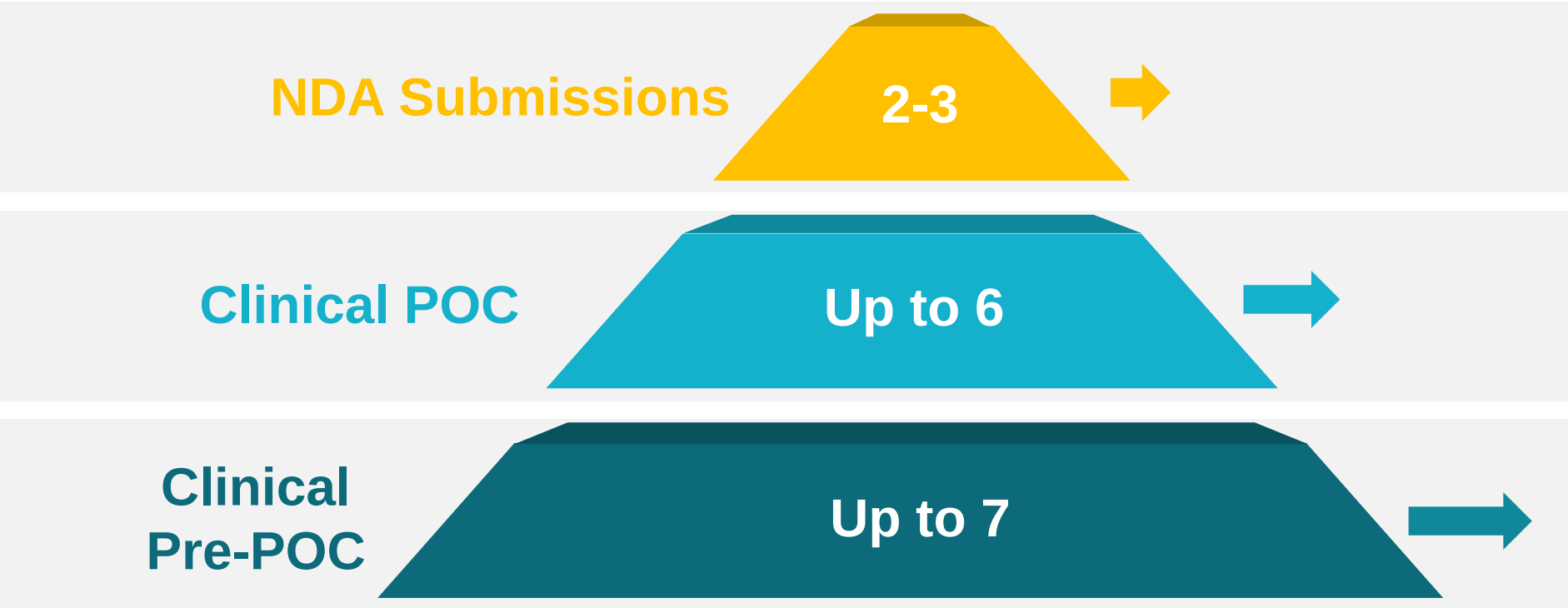
2-3 new programs/year




*NDAs:* BBP-831 (2L CCA), BBP-870, BBP-265
*Clinical Proof-of-Concept (POC):* BBP-831 (achon), BBP-631, BBP-009, BBP-681, BBP-589, 0-1 additional
*Clinical:* BBP-812, BBP-398, BBP-711, BBP-561, BBP-671, 1-2 additional
*Note:* The above represents potential non-risk adjusted outcomes



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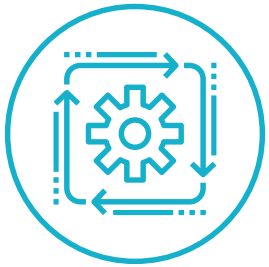
# BridgeBio: A product platform and current pipeline



## Product Platform

Systematic disease mapping

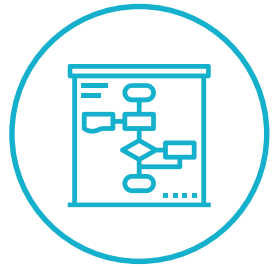
World-class R&D minds and capabilities

Partnered with leading institutions

Focus on capital efficiency

Best owner mentality

**Continued growth and terminal value**



## Current Pipeline

15 programs targeting diseases at their source

Four Phase 2 or Phase 3 clinical programs

Focus on Mendelian diseases and targeted oncology

Small molecules, biologics, gene therapies

5+ therapeutic areas

**Present value and near-term catalysts**



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# BridgeBio is led by an experienced team

**Neil Kumar, PhD — Co-Founder and CEO**
- Principal at Third Rock Ventures
- Founding management team at MyoKardia
- Associate principal at McKinsey
- PhD MIT; BS / MS Stanford University

**Frank McCormick, PhD, FRS — Chairman of Oncology**
- Director of the UCSF Cancer Center and former Associate Dean of the UCSF School of Medicine
- Former AACR President
- Co-founder & first CSO of Onyx Pharma ($9B+)
- PhD Cambridge; BS University of Birmingham

**Uma Sinha, PhD — Chief Scientific Officer**
- CSO for Global Blood Therapeutics
- Senior leader in Portola, Millennium, and COR Therapeutics
- PhD Georgia; BS Presidency College

**Phil Reilly, MD, JD**
- Management Committee member
- Highly respected clinical geneticist
- Co-founder and former interim CMO of Voyager Therapeutics
- SAB member and former interim CMO of bluebird bio
- Co-founder and board member of Edimer, Lotus
- MD Yale; JD Columbia; BA Cornell

**Andrew Lo, PhD**
- Investment Committee member
- Pioneering researcher in economics and financial engineering at MIT
- Founder and CSO of multi-billion dollar hedge fund

**Charles Homcy, MD — Chairman of Pharmaceuticals**
- World renowned expert in drug discovery
- Developed >10 marketed drugs
- Founder, CEO, director of multiple $500M+ biotechnology companies
- MD Johns Hopkins; BA Johns Hopkins

**Richard Scheller, PhD — Chairman of R&D**
- Former CSO and EVP of Research and Early Development at Genentech
- CSO of 23andMe
- Lasker Award winner for pioneering CNS research
- Stanford and HHMI Faculty
- PhD Caltech; BS Univ of Wisconsin

**Brian Stephenson, PhD — Chief Financial Officer**
- Partner at Capital IP
- Director / VP at Leerink
- Manager at McKinsey
- PhD / MS MIT; BS Brigham Young

**Hoyoung Huh, MD, PhD**
- Investment Committee member
- Leader of multiple $100M+ biotech companies including Epizyme, Geron, BiPar, Nektar
- Partner, McKinsey & Co.
- MD / PhD Cornell; BS Dartmouth

**Robert Zamboni, PhD**
- Medical Chemist for BridgeBio and portfolio companies
- ACS Heroes of Chemistry Award for discovery of Singulair® (montelukast sodium)
- Author of over 80 papers, holder of over 20 patents
- PhD McGill; BS Yale

## Companies

Genentech · Takeda MILLENNIUM · ONYX PHARMACEUTICALS · PORTOLA PHARMACEUTICALS · MyoKardia · MERCK FROSST · 23andMe · globalblood THERAPEUTICS · Epizyme · EXELIXIS pharmaceuticals, inc.

## Drugs

TECENTRIQ atezolizumab · OCREVUS ocrelizumab · VELCADE (bortezomib) · Kyprolis (carfilzomib) · Enbrel etanercept · VENCLEXTA venetoclax tablets · Kadcyla trastuzumab emtansine · Entyvio vedolizumab · Nexavar (sorafenib) tablets · Andexxa · PERJETA pertuzumab · INTEGRILIN (eptifibatide) · SINGULAIR (montelukast, MSD) · VIOXX (rofecoxib, MSD) · ARCOXIA (etoricoxib)



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# Industry-leading R&D experts who have led 100+ INDs and the approval of 20+ marketed drugs

**Robert Zamboni, PhD**

- ACS Heroes of Chemistry Award for discovery of Singulair
- Developed Vioxx and Arcoxia (marketed in Europe)
- Holds over 20 patents
- Involved in DP antagonist and Catk inhibitor
- Several dozen development programs
- Retired from Merck in 2005 as VP of Medicinal Chemistry

**Anjali Pandey, PhD**

- 11 INDs and 1 NDA filed
- SVP of Medicinal Chemistry and Chemical Development at Portola
- Director of Chemistry at COR and Millennium
- 25+ years experience in industry

**Hector Rodriguez, PhD**

- 7 INDs filed for first in class agents in oncology, CV and inflammation
- Senior Director and founding member of biochemistry groups at Myokardia, Calithera, and Arresto
- Founder and SAB member of Edgewise Therapeutics

**Athiwat Hutchaleelaha, PhD**

- 2 marketed drugs including Bevyxxa and Andexxa from preclinical discovery through commercialization
- 20+ years in large and small molecule development at Global Blood Therapeutics, Portola, Millennium and COR

**Andreas Betz, PhD**

- Preclinical development of small molecule protease and kinase inhibitors
- Lead enzymologist in discovery and development of Bevyxxa
- 20+ years experience in industry at COR, Pharmacia-Pfizer, Chiron and Global Blood Therapeutics

**Uma Sinha, PhD**

- CSO of Global Blood Therapeutics, VP, Head of Biology and VP, Translational Biology at Portola
- 21 INDs and 4 marketed drugs, co-inventor of Andexxa
- 30+ years in biotech industry
- Discovery and preclinical development of small molecules in hematology, CV and inflammatory diseases.

**James Kanter**

- 25+ INDs filed at companies including Millennium, Exelixis, Pharmacofore, Gilead and Ardelyx
- 5 NDAs including Velcade, Sovaldi, Vemlidy and Vitekta
- Managed 4 drug substance commercial products
- 12+ drug substance, 3 drug product validations in NA, Europe and Asia

**Jesper Jernelius, PhD**

- 11+ INDs filed with Roche, Gilead and Medivation
- 3 NDAs for marketed drugs with Gilead (Sovaldi), Amgen (Kyprolis), and Medivation (Talazoparib)

**Satish Rao, PhD**

- 8 INDs filed at Endocyte, ARYx, and Scios
- 20+ years experience in DMPK and bioanalytical in industry, CROs, and academia

**Ben Collman**

- 11+ INDs and 3 NDAs filed at Pfizer, Abbott/AbbVie, Gilead and Ardelyx
- Worked on 8 marketed drugs including Lyrica, Steglatro, Xeljanz, Daurismo, Vizimpro, Technivie, Biktarvy, and Ibsrela
- 18+ years experience in CMC



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# BridgeBio: A new model for the genetic disease space

*Our model*

**Fit-for-purpose program building**
Minimum viable program startup with extreme willingness to fail.

**Aligned agendas**
Incentives at the level of each program for program management teams and scientists.

**Play-calling on the field**
Decentralized decision-making left to the most appropriate decision makers.


*The genetic disease space*

**Deep understanding of a privileged target space**
Comprehensive mapping of the Mendelian disease space allows us to identify high value opportunities and novel approaches.

**Unencumbered target selection**
New opportunities not limited by potential peak-year sales or existing infrastructure.

**Capabilities to enter the "chasm of death"**
Unparalleled team of experienced translational scientists and company builders that enables us to pursue ultra-early-stage academic assets.

**We believe performing more "reps" with the BridgeBio approach will create "flywheel momentum"**

**Mastery of executional efficiency**
The right MVC 'minimum viable corporation' structure, amount of capital, and talent phenotypes

**Reputation**
Recognition from academics and top-tier talent that we are an ideal partner

# We advanced our first two programs from academia to Ph 3 trials in three years

## Academic origins

## World-class biotech R&D

## Advancement to pivotal trials, value inflection

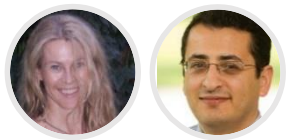
### BBP-265
TTR stabilizer for ATTR (Eidos)

PNAS

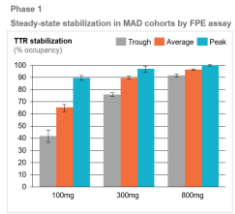
AG10 inhibits amyloidogenesis and cellular toxicity of the familial amyloid cardiomyopathy-associated V122I transthyretin

Sravan C. Penchala[a,1], Stephen Connelly[b,c,1], Yu Wang[a,1], Miki S. Park[a], Lei Zhao[a], Aleksandra Baranczak[c], Irit Rappley[c], Hannes Vogel[d], Michaela Liedtke[e], Ronald M. Witteles[e], Evan T. Powers[c], Natàlia Reixach[b], William K. Chan[a], Ian A. Wilson[b], Jeffery W. Kelly[c], Isabella A. Graef[a,2], and Mamoun M. Alhamadsheh[a,2]

[a]Department of Pharmaceutics and Medicinal Chemistry, University of the Pacific, Stockton, CA 95211; Departments of [b]Integrative Structural and Computational Biology and [c]Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, CA 92037; and [d]Department of Pathology and [e]Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA 94305



SPARK AT STANFORD




IPOS

Eidos, Avrobio shoot for $201M as biotech IPOs continue to roll forward on Nasdaq

by JOHN CARROLL — on May 29, 2018 07:13 AM EDT

MarketWatch

Eidos Therapeutics stock soars in debut

By Emily Bary

Published: June 20, 2018 10:52 a.m. ET

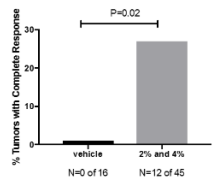
### BBP-009
Topical SMOi for Gorlin / BCC (PellePharm)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhibiting the Hedgehog Pathway in Patients with the Basal-Cell Nevus Syndrome

Jean Y. Tang, M.D., Ph.D., Julian M. Mackay-Wiggan, M.D., Michelle Aszterbaum, M.D., Robert L. Yauch, Ph.D., Josslyn Lindgren, M.S., Kris Chang, B.A., Carol Coppola, R.N., Anita M. Chanana, B.A., Jackleen Marji, M.D., Ph.D., David R. Bickers, M.D., and Ervin H. Epstein, Jr., M.D.

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BIOTECH RESEARCH CRO MEDTECH

Biotech

LEO Pharma inks $760M rare skin disease R&D deal with PellePharm

by Conor Hale | Nov 20, 2018 6:00am



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# Track record of capitally efficient value creation

**BBP-265**
TTR stabilizer
for ATTR (Eidos)

Cost: $25M

Time: 2 years

**IPO at $625M post**
**(6/19/2018)**

**BBP-009**
Topical SMOi for
Gorlin / BCC
(PellePharm)

Cost: $26M

Time: 3.5 years

**Up to $760M* for late-stage funding, option to acquire and milestones**

*Note: Total deal value of $760M; BridgeBio owns 43.3% of PellePharm (as of 12/31/2018)

# Key portfolio value drivers

| Program / MOA | Disease | Patient population, '000s (US+EU) | Description |
|---|---|---|---|
| **BBP-265 / TTR stabilizer** | Transthyretin Amyloidosis | 400 | • Potentially most potent TTR stabilizer designed for the treatment of ATTR<br>• One of the largest Mendelian diseases |
| **BBP-831 / FGFR1-3i** | Achondroplasia | 55 | • Only known oral FGFR1-3i in clinical development for achondroplasia*<br>• No approved standard of care in the US or EU<br>• Strong pre-clinical data and only oral product in development<br>• Also being pursued for a variety of FGFR-driven cancers |
| **BBP-454 / Pan-mutant KRASi** | KRAS+ Cancers | 500 | • Pan-mutant KRAS inhibitor program for KRAS-driven cancers<br>• ~30% of all cancers are driven by KRAS mutations, including large proportions of lung, colorectal and pancreatic tumors |
| **BBP-631 / AAV5 21-OH gene replacement** | Congenital Adrenal Hyperplasia | 75 | • Gene therapy product candidate for CAH<br>• Likely one of the largest gene therapy markets, with prevalence >75,000 in the US and EU<br>• High unmet need, with poor treatment options and lifelong risk of potentially fatal adrenal crisis |
| **Total patient population for key portfolio value drivers** | | 1,030 | **These four assets alone could provide novel treatment options for over 1M people in the US and EU** |

*Based on clinicaltrials.gov search



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# Our cash balance provides runway through key value inflections across the portfolio

ESTIMATED

| 2019 | | 2020 | 2021 |
|---|---|---|---|
| **1H** | **2H** | **FY** | **FY** |
| ✓ Initiate BBP-265 (AG10) Ph3 in ATTR-CM | ✓ Initiate achondroplasia observational run-in study (infigratinib) | ❑ Topline Ph1/2 data from BBP-589 in RDEB | ❑ Topline AG10 Ph3 data in ATTR-CM (12m 6MWD) |
| ✓ Initiate BBP-009 Ph3 in Gorlin | ✓ Announce new program (BBP-418 for LGMD2i) | ❑ Updated infigratinb Ph2 CCA data | ❑ Topline BBP-009 Ph3 data in Gorlin |
| ✓ Initiate infigratinib Ph3 in 1L CCA | ✓ CAH gene therapy (BBP-631) NHP data at ESGCT | ❑ Initiate infigratinib adjuvant urothelial carcinoma Ph3 study | ❑ Infigratinib Ph2 PoC data in achondroplasia |
| ✓ Initiate BBP-589 Ph1/2 in RDEB | ❑ AG10 Ph2 ATTR-CM OLE data at AHA (November 16) | ❑ Initiate dosing in infigratinib Ph2 in achondroplasia | ❑ CAH gene therapy (BBP-631) clinical PoC data |
| | ❑ Initiate BBP-870 rolling NDA in MoCD Type A | ❑ Submit infigratinib NDA for 2L CCA | ❑ Infigratinib approval and launch in 2L CCA |
| | | | ❑ BBP-870 approval and launch in MoCD Type A |

We are also on track to file multiple INDs in 2020, which will set the stage for the next wave of clinical catalysts



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# AG10 (BBP-265): Potentially most potent transthyretin stabilizer for the treatment of transthyretin amyloidosis

## Mechanism of Disease

Native transthyretin circulates in blood as a tetramer

Dissociation into toxic monomers initiates pathogenesis

Monomers aggregate and deposit as amyloid, causing disease
**ATTR-CM, ATTR-PN**

**Impact on patients:**

- Progressive, fatal cardiomyopathy (median life expectancy 3-5 yrs) and polyneuropathy
- Both manifestations includes significant disability
- We believe the diagnosed population of ATTR-CM is growing rapidly due to awareness and accurate, non-invasive, diagnostic methods

## Mechanism of Drug

AG10 stabilizes TTR tetramer, potentially preventing disease

Dissociation into toxic monomers initiates pathogenesis

Monomers aggregate and deposit as amyloid, causing disease
ATTR-CM, ATTR-PN


AG10 is designed to bind TTR in a way that mimics a naturally-occurring protective mutation

## Program Highlights

**400k+**
ATTR-CM patients worldwide

**10k+**
ATTR-PN patients worldwide

### Clinical status:

| Pre-IND | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|

**ATTR-CM Ph3 study ongoing** (FPI 1Q19)

**ATTR-PN Ph3 study expected 2H19**

### Catalysts:

- Ph2 ATTR-CM OLE data in 2H19
- Ph3 ATTR-CM 12-month data in 2021
- Potential ATTR-CM NDA submission in 2021

### Key data:

- Ph2 ATTR-CM data presented in 2H18
  - Normalized serum TTR in all actively treated patients at d28
  - TTR stabilization of ≥90% in all actively treated pts at d28
- Ph3 ATTRibute study initiated in 1Q19
  - Potential registration on 12m 6MWD endpoint, followed by 30m CV outcome/hospitalization endpoint



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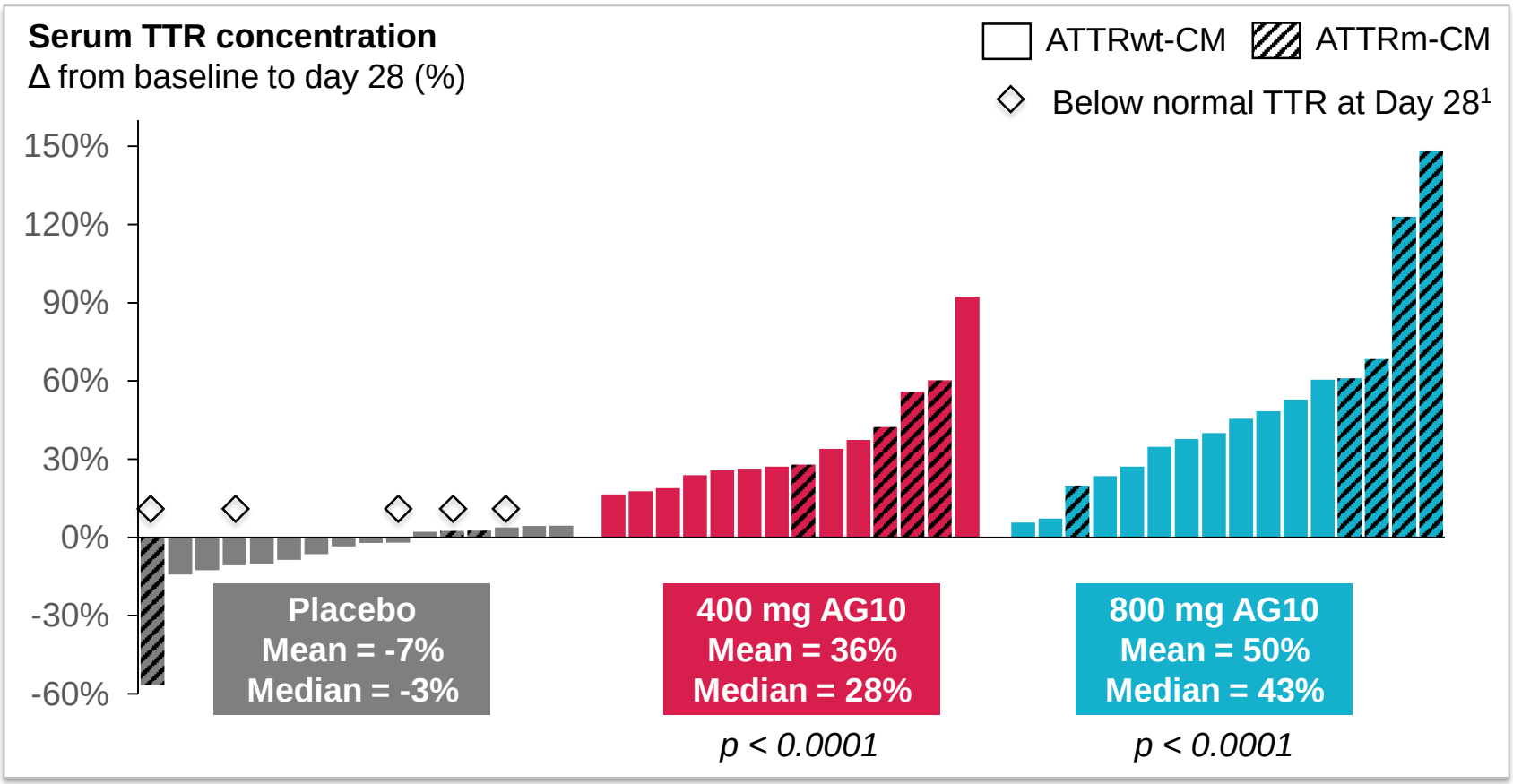
# Treatment with AG10 restored serum TTR concentrations to normal range in all subjects




- **Dose-dependent increase in serum TTR concentrations in AG10-treated subjects**
- **Greater treatment effect observed in ATTRm subjects – final TTR concentrations normalized to comparable levels as treated ATTRwt subjects**

1 Normal reference range for serum TTR 20-40 mg/dL (3.6-7.3 µM)

Source: AG10 data on file



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# AG10 Ph2 open label extension will provide long-term safety and efficacy data

## Overview of AG10 Phase 2 OLE data

### Study design

47 ATTR-CM patients (NYHA Class II and III) continued onto Phase 2 OLE. Data cut as of 8/31/2019:

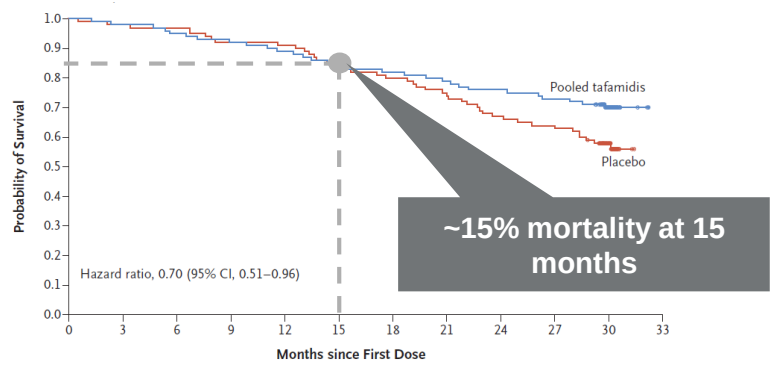
- Median 65 weeks from Phase 2 initiation
- Median 51 weeks from OLE initiation

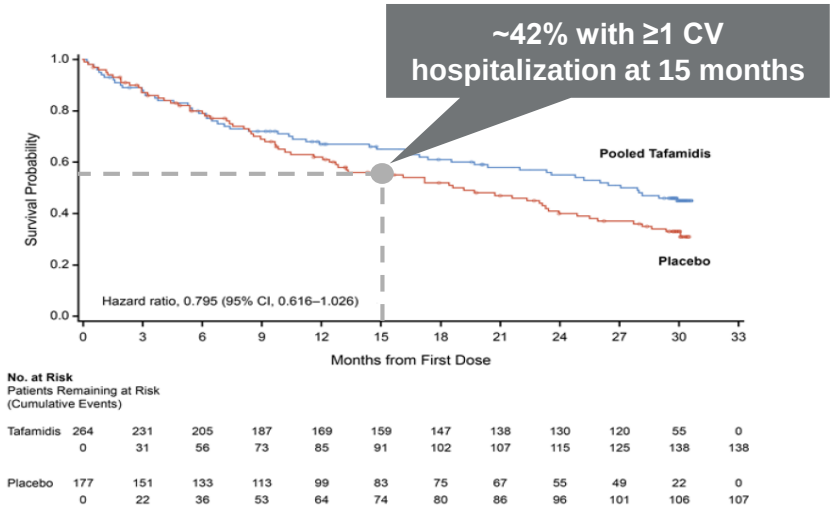
### Outcomes

Safety and tolerability

- Adverse events
- Clinical events and vital signs (e.g., death, cardiovascular hospitalization)
- Clinical laboratory parameters (including NT-proBNP and TnI)
- Pharmacokinetics and Pharmacodynamics
- Serum TTR levels, TTR stabilization

## Benchmark natural history



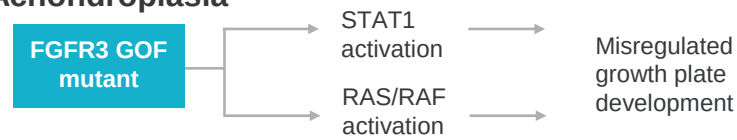




Adapted from Maurer, M.S. et al. N Engl J Med. 2018;379:1007–16.

# Infigratinib (BBP-831): Oral FGFR1-3 inhibitor to treat achondroplasia and FGFR-driven cancers

## Mechanism of Disease

### Achondroplasia

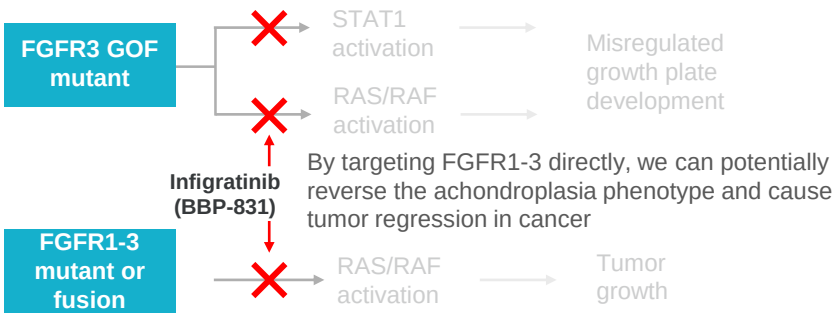



**Impact on patients:**
- Short stature, spinal compression, narrow foramen magnum
- Increased risk of infant death, sleep apnea, infections
- No currently approved therapies in the US or EU

### Oncology


**Impact on patients:**
- Poor survival, multiple comorbidities that impact QoL

## Mechanism of Drug




## Program Highlights

**55k**

Achondroplasia pts in US+EU

**37k**

Annual new FGFR1-3+ oncology diagnoses in US+EU

### Clinical status:

Pre-IND | Phase 1 | Phase 2 | Phase 3

**ACH Ph1/2 planned for 2020**

**Oncology Ph3 enrolling (1L CCA)**

### Catalysts:

- Achondroplasia IND acceptance and FPI 2020 (expected)
- Achondroplasia clinical data 2021
- Potential oncology NDA in 2020 (2nd line cholangiocarcinoma, CCA)

### Key data:

- Achondroplasia:
  - Strong preclinical data with effects on stature, foramen magnum and lumbar disc width in mouse model
  - Only known oral therapy in development
  - Anticipate active dose significantly lower than oncology
- Meaningful clinical data in oncology indications CCA and UC (26.9% and 25.4% ORR respectively)



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# Infigratinib showed significant improvements in key disease features in the achondroplasia mouse model

## Preclinical data from infigratinib

**Ph1/2 clinical study to initiate by 2020 for infigratinib, the only oral asset in development**

Percent increase compared to non-treated mouse

| Asset | Company | Status | Mouse model | Tibia length | Femur length | Foramen magnum area | L4-L6 height |
|---|---|---|---|---|---|---|---|
| Infigratinib | bridgebio | Pre-Ph1/2 | FGFR3$^{Y367C/+}$ | 33% | 21% | 16% | 12% |

Source: Komla-Ebri et al. J Clin Inv 2016
Note: Infigratinib dose of 2mg/kg

## Preclinical data from other investigational achondroplasia therapies

Percent increase compared to non-treated mouse

| Asset | Company | Status | Mouse model | Tibia length | Femur length | Foramen magnum area | L4-L6 height |
|---|---|---|---|---|---|---|---|
| Vosoritide (BMN111) | BIOMARIN | Pivotal | FGFR3$^{Y367C/+}$ | 7% | 5% | No known publically available data | 3% |
| TransCon CNP[1] | ascendis pharma | Ph1/2 | FGFR3$^{Y367C/+}$ | 12%* | | | |
| TA-46 | Therachon achieving potential | Ph1/2 | FGFR3$^{ach/+}$ | 9%* | 7%* | | |

Source: Lorget et al. Am J Hum Genet 2012, Garcia et al. Science Trans Med 2013, Breinholt ENDO 2017
Note: subcutaneous doses, percent increase compared to vehicle treated FGFR3Y367C/+, FGFR3ACH/+ mouse unless otherwise noted
1 Based on vosoritide continuous infusion; *Value estimated using DigitizeIt



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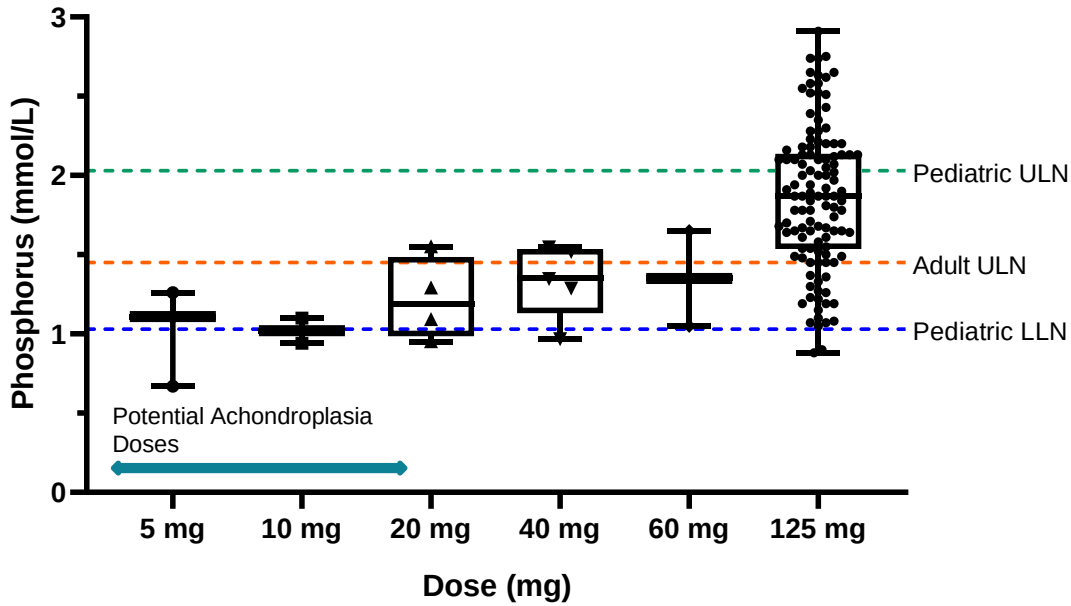
# Human clinical data suggests potential activity in achondroplasia below the threshold for on-target adverse events

We expect our active achondroplasia dose could be >50x lower than our oncology dose, well below known toxicity thresholds in humans




5 mg, n=3
10 mg, n=2
20 mg, n=4
40 mg, n=5
60 mg, n=2
125 mg, n= 114

**Pediatric**
ULN = 2.03 mmol/L
LLN = 1.03 mmol/L
**Adult**
ULN =1.45 mmol/L
LLN = 0.8 mmol/L

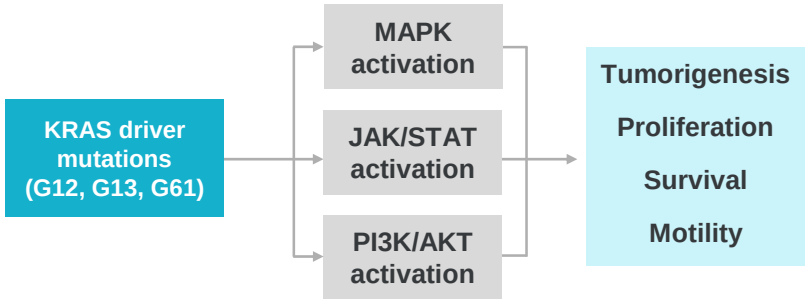
| | | | | | | |
|---|---|---|---|---|---|---|
| Human mg | 5 | 10 | 20 | 40 | 60 | 125 |
| Human mg/kg | 0.083 | 0.167 | 0.333 | 0.667 | 1.000 | 2.083 |
| Mouse sq mg/kg | 0.257 | 0.514 | 1.029 | 2.058 | 3.086 | 6.430 |

**Pediatric normal ranges: source** https://www.healthcare.uiowa.edu/path_handbook/appendix/heme/pediatric_normals.html
Age range 1 – 15 years of age

Source: ASHG 2019

# BBP-454: Pan-mutant KRAS inhibitor to treat lung, colon, and pancreatic cancer

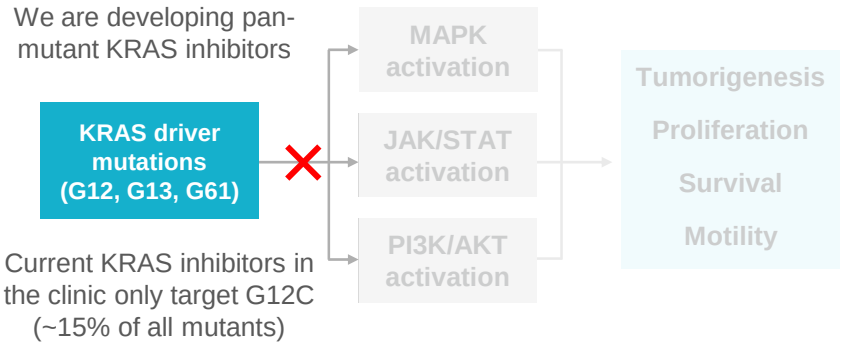
## Mechanism of Disease




**Impact on patients:**

- KRAS is one of the well-known monogenic drivers of cancer
- ~30% of all cancers carry KRAS mutations (high proportions of lung, colorectal, pancreatic)

## Mechanism of Drug




## Program Highlights

**500k+**

Patients/year in US+EU are diagnosed with KRAS+ cancer

| Tumor type | KRAS+ frequency |
|---|---|
| NSCLC | 30% |
| Colorectal cancer | 45% |
| Pancreatic cancer | 98% |

### Development status:

| Pre-IND | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|

**BBP-454**

### Catalysts:

- Development candidate selection and IND filing

### Key info:

- Platform-like approach to KRAS inhibition driven by a world class research coalition:
  - Led by globally recognized RAS expert Frank McCormick
  - Discovery partnerships with NCI RAS initiative and Lawrence Livermore National Labs
- Two pan-mutant approaches being optimized
  - C185 binders block membrane tethering and activation
  - H95 binders trigger KRAS degradation
- Multiple novel pockets discovered through computational chemistry
- Co-crystal structure solved for H95 compound series



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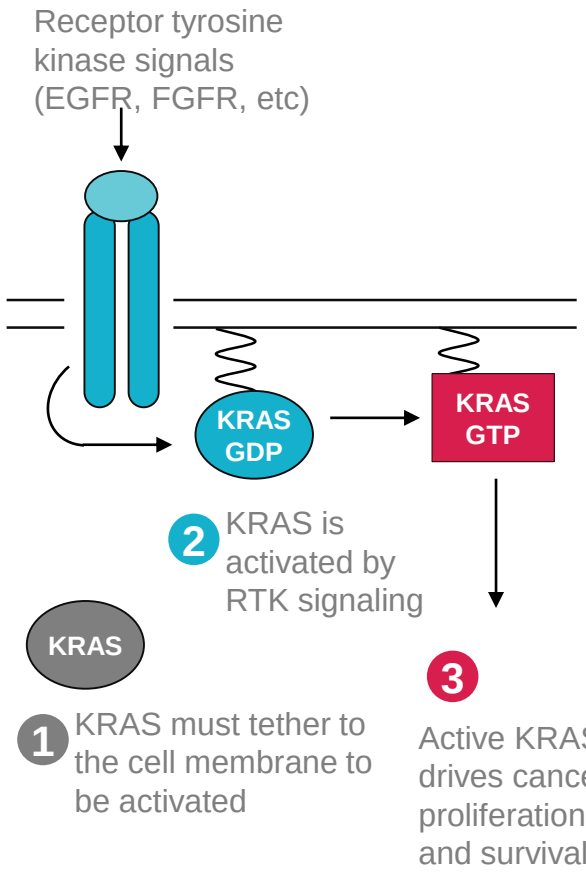
# We have two shots on goal with our pan-mutant KRAS inhibitor programs – each with a unique and novel MOA

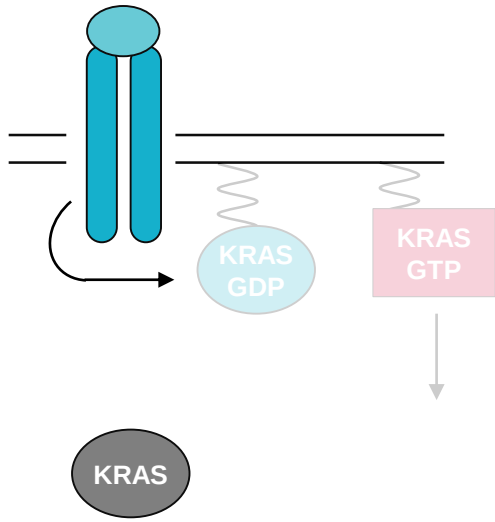
## KRAS activation in cancer is a multi-step process




## Our two programs target different steps of the KRAS activation process

### 1st approach: C185 targeting

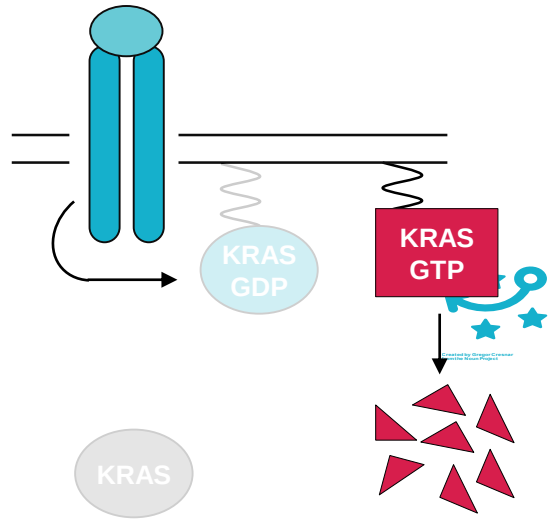
- Blocks KRAS from tethering
- Blocks activated KRAS GTP from signaling




**KRAS tethering is blocked – cancer growth is inhibited**

### 2nd approach: H95 targeting

- Directly binds activated KRAS
- Triggers KRAS degradation, blocking the signal




**Activated KRAS is degraded – cancer growth is inhibited**



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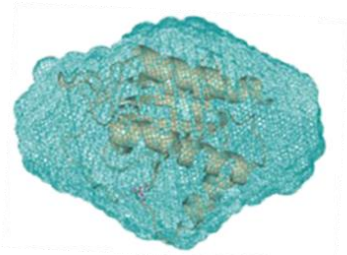
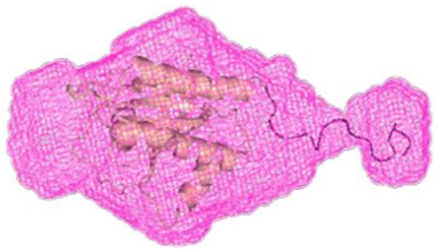
# We've built out our C185 screening cascade with additional biophysical and cellular assays, enabling major advances

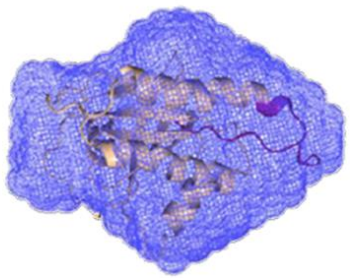
## Small angle X-ray scattering supports our hypothesis



KRAS without HVR



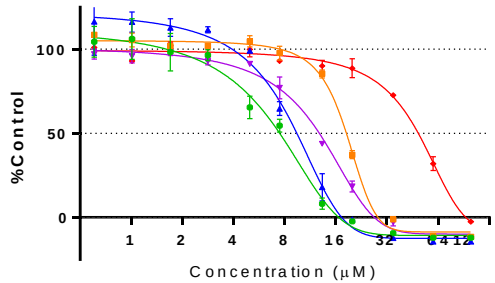
Full KRAS



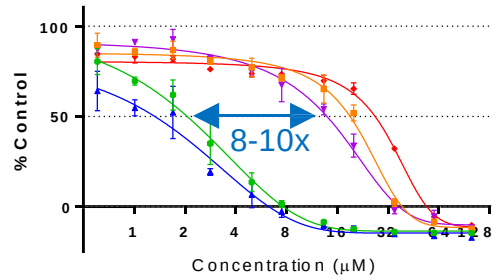
Full KRAS + our compound

## RASless MEFs are our first pass selectivity screen

*2017*

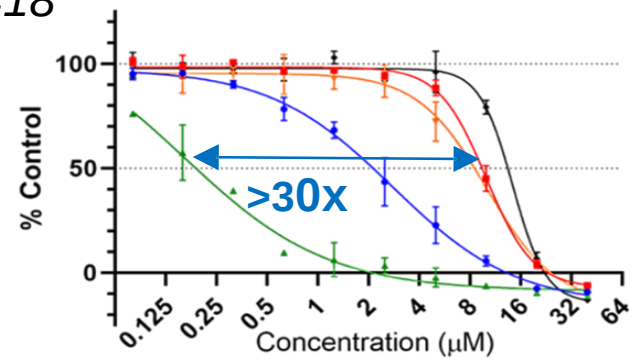



*Q218*




| | |
|---|---|
| **IC50** | 1.5uM |
| **Selectivity** | 8-10x |

*Q418*




| | |
|---|---|
| **IC50** | 250nM |
| **Selectivity** | >30x |



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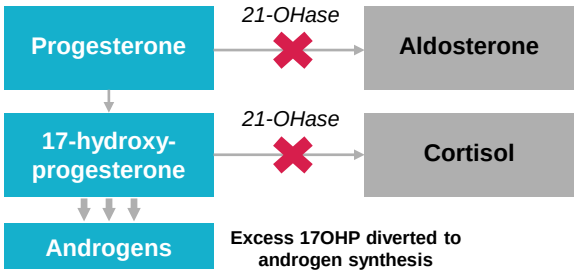
# BBP-631: Gene therapy for CAH caused by 21OH deficiency

## Mechanism of Disease

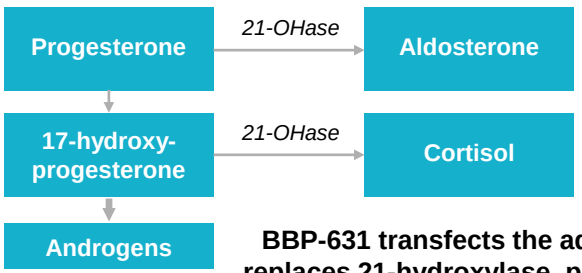
**Steroid synthesis pathway**




**Impact on patients:**

- Adrenal crises (can be fatal)
- Lifelong treatment with supraphysiologic steroid, which can cause significant morbidity (CV disease, obesity, bone disease)
- Abnormal sexual development, infertility

## Mechanism of Drug




**BBP-631 transfects the adrenal glands and replaces 21-hydroxylase, potentially restoring production of aldosterone and cortisol and reducing excess synthesis of androgens**

## Program Highlights

**75K+**

Patients with CAH in US+EU

**1 / 11,000**

Newborns born with CAH

**Development status:**

| Pre-IND | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|

**BBP-631**

**Catalysts:**

- IND filing in 2020
- Anticipated clinical proof-of-concept data in 2021

**Key info:**

- Durability of expression shown in NHP studies; sustained vector copy number and RNA expression out to at least 6 months
- Clinical GMP manufacturing underway at Paragon; in-house process development and analytical capabilities being developed
- Vector construct designed by Dr. Guangping Gao, a world leader in AAV design
- Genotype-phenotype studies show that 5-10% of enzyme activity may be sufficient for clinical impact



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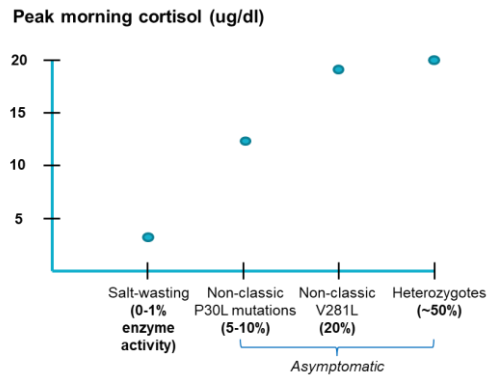
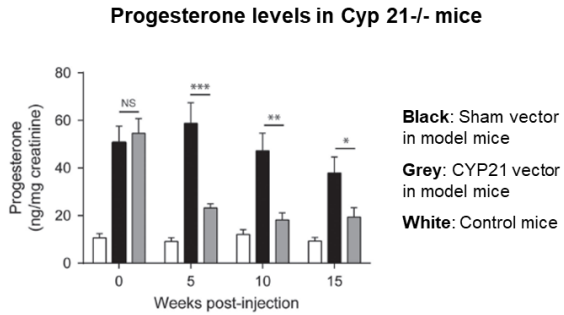
# BBP-631 NHP experiments show durable transgene expression; 5-10% of WT enzyme may be sufficient for clinical impact

## Genotype-phenotype studies show that >5-10% of enzyme activity results in nonclassical CAH




- Due to the high enzymatic efficiency/selectivity of 21-OHase, **only a small amount of enzyme is required to rescue the phenotype**

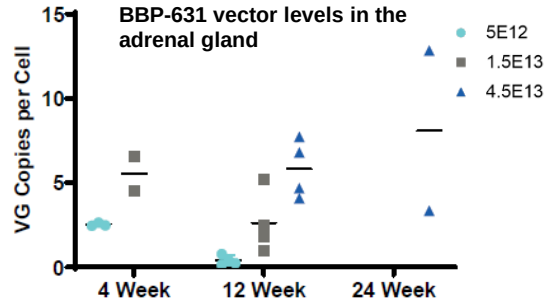
## Mouse studies show a VGC of only 0.13 at 18 wks was sufficient for phenotypic reversal



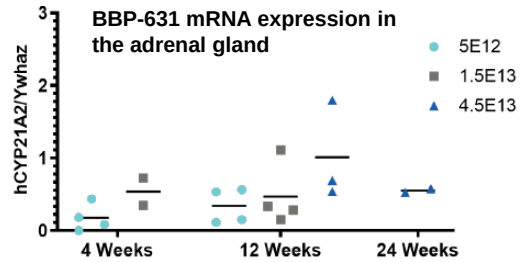

VGC from the whole adrenal gland was 0.13 at wk 18

- At 15 weeks in treated mice, **progesterone** (the key substrate of 21OHase in mice) was **significantly reduced vs untreated mice**

## Ongoing NHP studies show sustained VGC and RNA out to at least 6 months




- Mean vector genome copies per cell appear stable at 24 wks



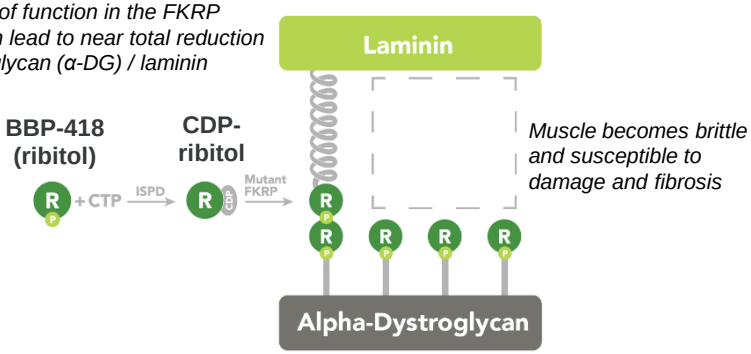

- Transgene expression is dose-dependent and stable out at 24 wks

Source: ESGCT 2019

# ML Bio Solutions overview: BBP-418 (ribitol) for Limb-girdle muscular dystrophy type 2i (LGMD2i)

## Mechanism of Disease

*Partial loss of function in the FKRP enzyme can lead to near total reduction in α-dystroglycan (α-DG) / laminin binding*



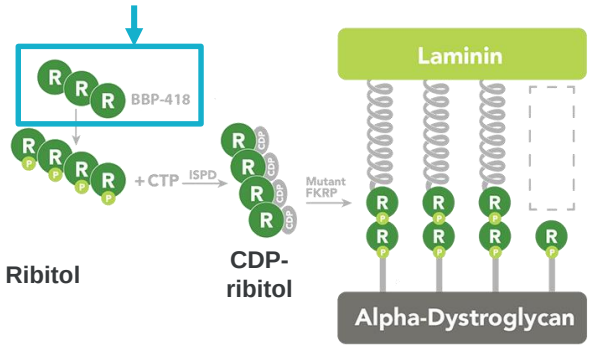

*Muscle becomes brittle and susceptible to damage and fibrosis*

**Impact on patients:**

- Progressive muscle weakness, leading to loss of ambulation, respiratory function, and cardiac function
- Increased mortality in even the mildest forms of the disease
- No currently approved therapies

## Mechanism of Drug

**Exogenous BBP-418 (ribitol) partially restores glycosylation**




## Program Highlights

**7000+**

LGMD2i pts in US+EU

### Development status:

| Pre-IND | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|

BBP-418

### Catalysts:

- Natural history study start 2H19
- IND filing in 2020

### Key info:

- In preclinical tolerability studies of BBP-418 in LGMD2i mice, a ~20x window between minimum effective dose and maximum tolerated dose was observed.
- Preclinical studies of BBP-418 in the mouse model of severe LGMD2i (P448L) showed:
  - **Clear BBP-418 uptake in target tissues and efficient conversion into FKRP substrate:** 4x increases in '418 levels in heart and in leg tissue with similar increases in ribitol-5P and CDP-ribitol
  - **Restored *α-DG* glycosylation in skeletal, cardiac, and diaphragm muscle**
  - **Improved disease pathology and function:** Increase in running time and distance, increase in muscle, decrease in fibrosis, and increase in respiratory function
- **FDA Orphan Drug Designation** for the treatment of LGMD2i



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# Mechanism of disease and therapeutic rationale

## We have a clear quantitative understanding of LGMD2i pathophysiology…

| | |
|---|---|
| **FKRP mutants result in partial loss of enzyme** | • ~70% or more of enzyme function can be lost<br>• May result in complete loss of α-DG glycosylation |
| **Up to 100% loss of α-DG glycosylation** | • Results in dissociation of muscle fibers from the extracellular matrix<br>• Muscles become “brittle” |
| **Patients with mutation have 4-12% muscle mass** | • 30-40% is average for an adult without FKRP mutations |
| **Reduction in strength by 33-100%** | • Based on strength testing across flexors/extensors in human subjects |
| **45%+ lose ambulation, 30%+ cardiomyopathy Increased mortality** | • For the mildest form<br>• Severe forms impact respiratory & brain function |

## …and a therapeutic rationale based on quantitative understanding of our product candidate, BBP-418

| | |
|---|---|
| **Dose of 2g daily dissolved in water** | • Based on the human equivalent dose from animal studies in the severe form of LGMD2i |
| **Leads to >6x CDP-ribitol in target tissues** | • Based on animal PK studies and ~70-90% BBP-418 to FKRP substrate conversion rate in human muscle |
| **Leading to a 2x or greater increase in catalytic rate of mutant FKRP** | • Based on our estimates from preclinical studies in the severe LGMD2i mouse model |
| **50%+ magnitude of benefit on symptoms** | • Given significant functional benefits observed in the treated severe LGMD2i mouse model |



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# Detailed corporate milestone calendar

| | 2019 | 2020 | 2021 |
|---|---|---|---|
| ★ BBP-265 / TTR stabilizer | Ph 3 CM Initiation✓<br>Ph 3 PN Initiation<br>Ph 2 OLE Data | | Ph 3 CM Data |
| ★ BBP-831 / FGFR 1-3 inhibitor | 1L CCA FPI | Achondroplasia Ph 1/2 FPI<br>2L+ CCA NDA<br>Adjuvant UC Phase 3 FPI | Achondroplasia PoC Data<br>2L+ CCA Approval |
| ★ BBP-631 / CAH gene therapy | | IND | POC Data |
| ★ BBP-454 / Pan-mutant KRASi | H95 Crystal Structure✓ | | |
| BBP-870 / cPMP replacement | Rolling NDA | | Approval + PRV |
| BBP-009 / Topical SMO inhibitor | Gorlin Ph 3 1st Pt Dosed✓<br>HF-BCC Ph 2b Initiation | | Gorlin Ph 3 Data |
| BBP-681 / Topical PI3Ka inhibitor | | IND | |
| BBP-589 / COL7 protein replacement | Ph 1/2 1st Pt Dosed✓ | Ph 1/2 PoC Data | |
| BBP-812 / Canavan gene therapy | | IND | |
| BBP-398 / SHP2 inhibitor | | IND | |
| BBP-711 / GO1 inhibitor | | IND | |
| BBP-561 / KLKN5/7 inhibitor | | | IND |
| BBP-671 / PanK1/3 activator | | | IND |
| BBP-954 / GPX4 inhibitor | | | IND |
| BBP-671 / Succinate prodrug | | | IND |

★ Key value driver ✓ Achieved



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