bridgebio

hope through
rigorous science

Corporate presentation

January 2022

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BridgeBio Pharma: Hope through rigorous science

Our mission: To **discover**, **create**, **test** and **deliver** transformative medicines to treat patients who suffer from genetic diseases and cancers with clear genetic drivers

Context #1 | Still Day 1 for innovation within genetic medicine

MACROMOLECULES → **MOLECULAR SYSTEMS** → **CLINICAL DIAGNOSIS** → **NEW THERAPEUTIC MODALITIES**

DNA

- gnomAD
- ENCODE3

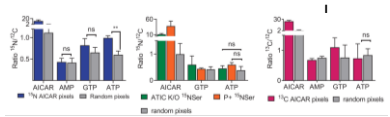
RNA

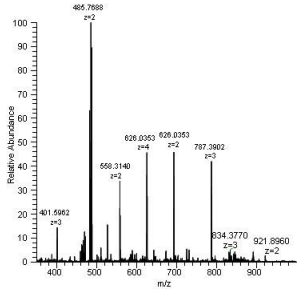
- GTEx
- Single cell sequencing advances

PROTEIN

- CryoEM
- DeepMind

- Mass spectrometry + metabolomics give us 1st snap of purine bio-synthesis





- Whole genome sequencing of rare disease patients in UK Biobank
- Expanded sequencing led to novel causal variants in 28 genetic disorders

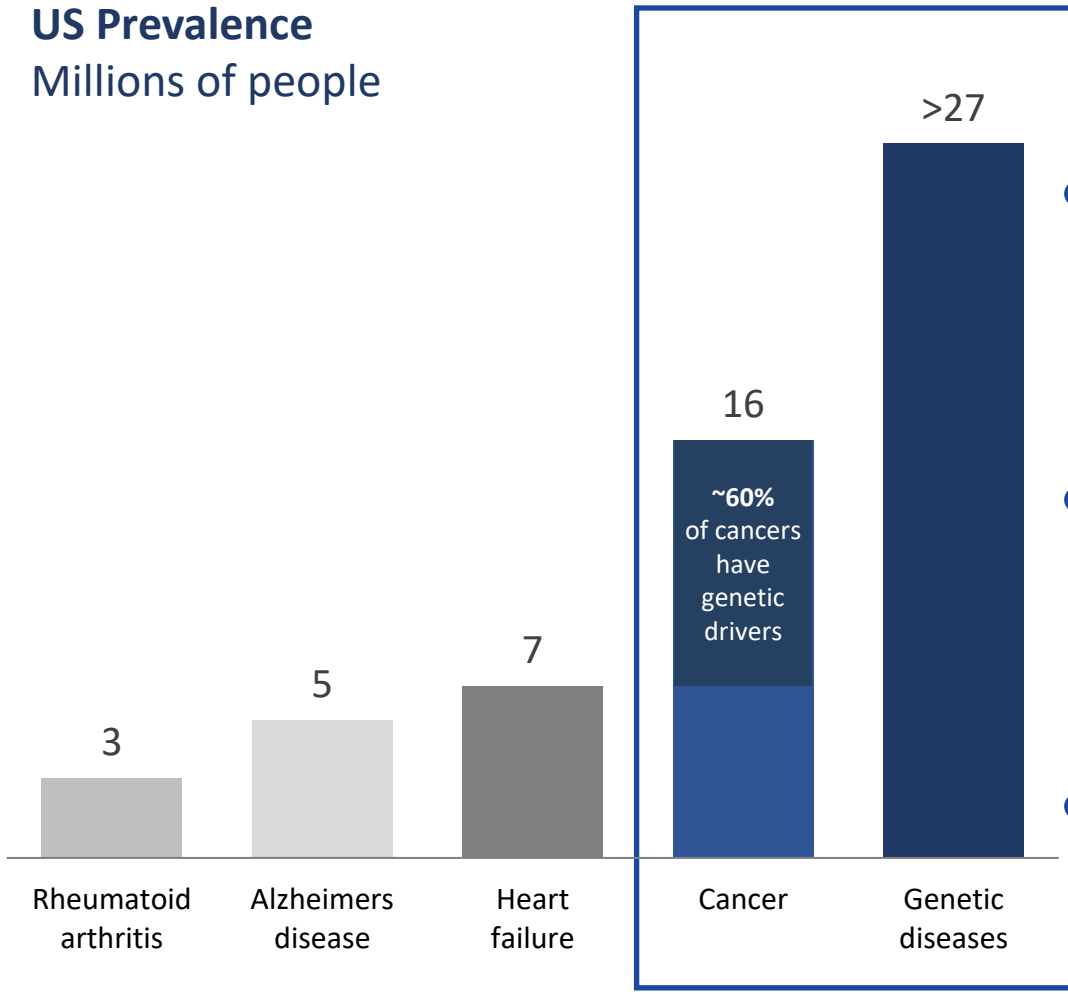
- Antisense oligonucleotides coming of age
- Gene therapy continues maturing

>25 FDA approvals for drugs targeting rare genetic diseases or genetically defined cancers in 2020 & 2021

Source: Evaluate

Context #2 | A vast opportunity to help patients…

US Prevalence
Millions of people



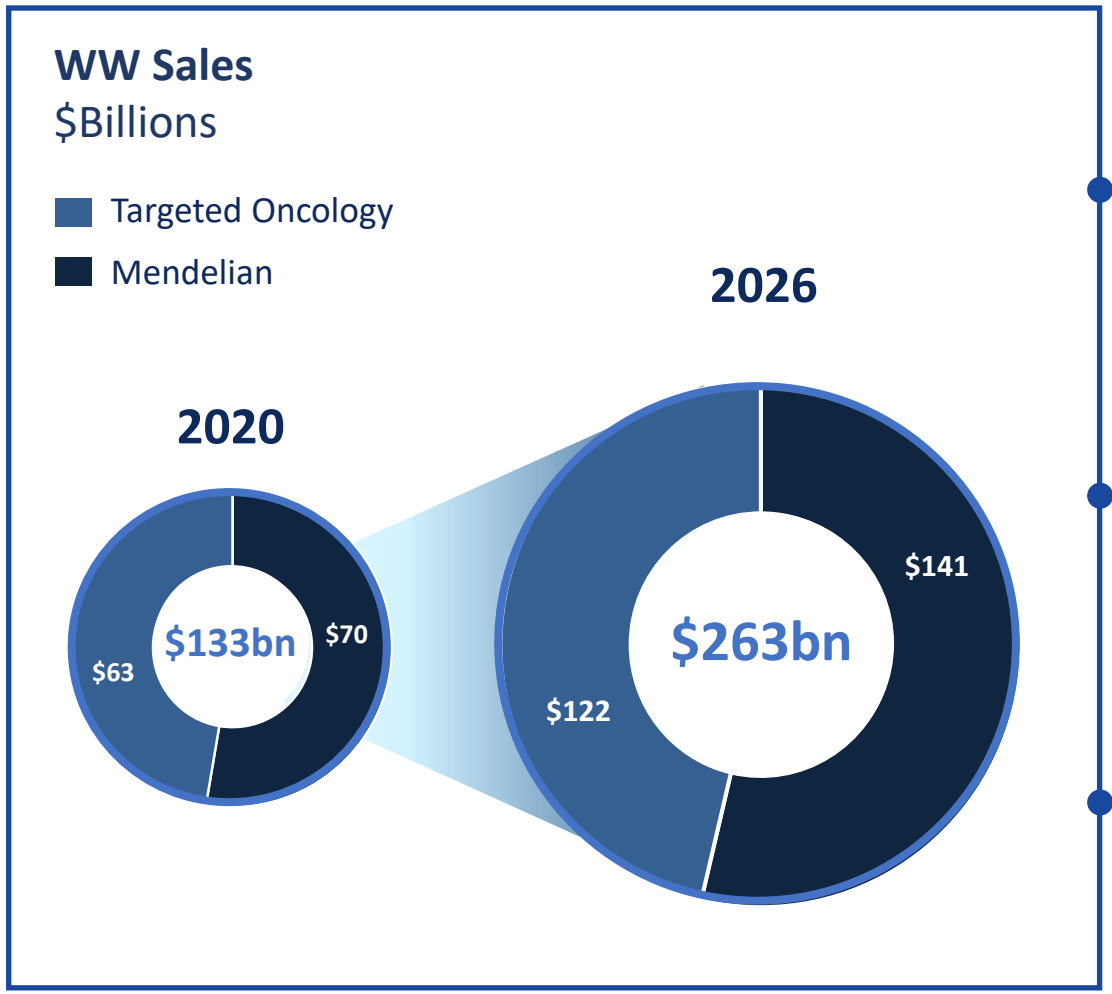
>27 million Americans are living with a genetic disease

50% of people affected are children

Only 5% of these diseases have an approved therapy option

Source: Global Genes, American Cancer Society, American Heart Association, Alzheimer's Association, Arthritis Foundation, Bailey *et al., Cell* 2018

Context #2 (cont'd) | …in several large and growing rare genetic disease markets



$263 billion Projected sales in 2026

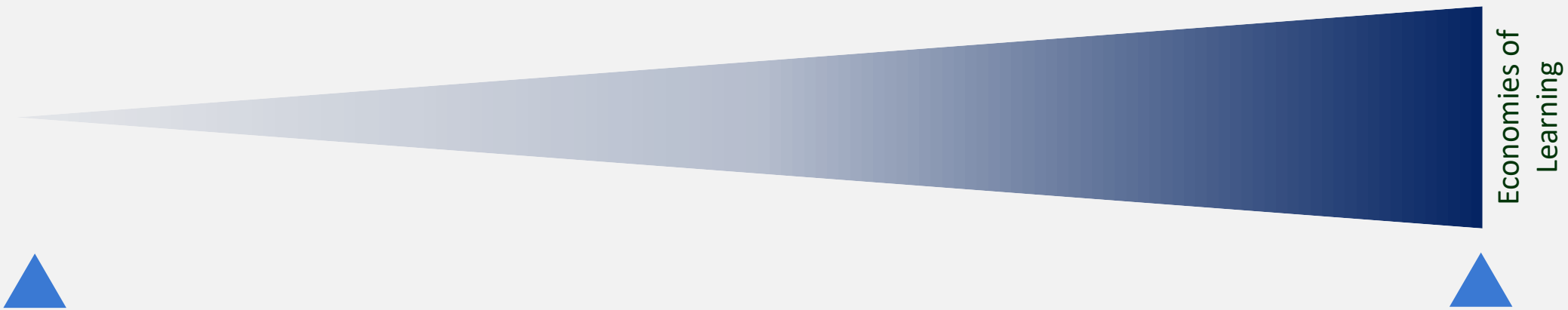
12% 2020 – 2026 CAGR

6x Size of projected rheumatoid arthritis, Alzheimer's, heart failure markets

Source: Evaluate Pharma. WW sales include US, EU and Japan. CAGR = Compound annual growth rate.

What does a sustainable genetic medicine innovation ecosystem look like? Criteria #1

Criteria #1: Need to solve for diseconomies of scale early, and economies of scale late

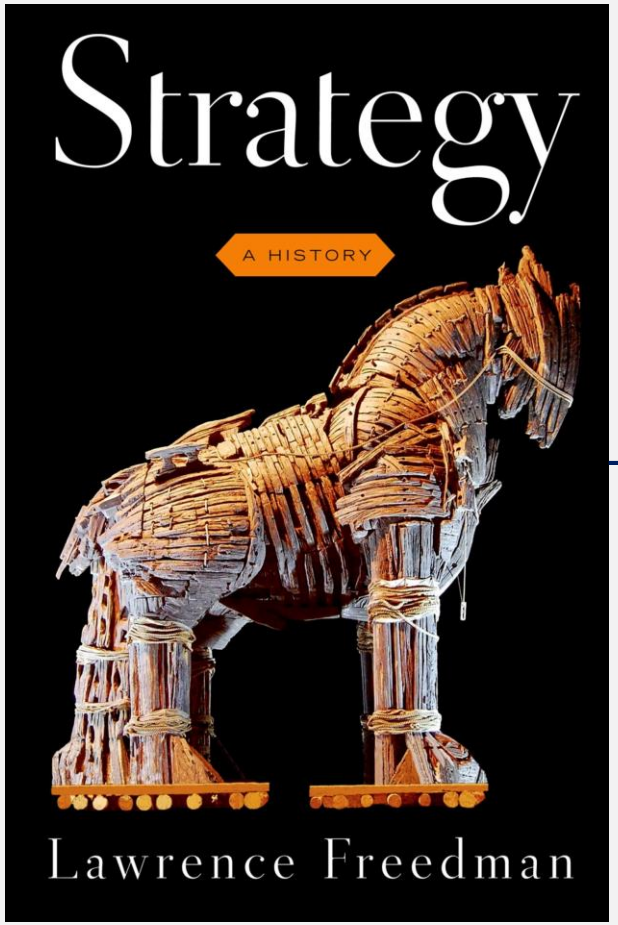


Decentralized R&D enables focus at the level of each asset driving value (Biotech)

Scale and economies of learning can drive value in a commercial organization (consolidation)

What does a sustainable genetic medicine innovation ecosystem look like? Criteria #2

Criteria #2: Each program needs to be NPV positive and supported by beautiful science



- Each program is NPV positive
  - **Realistic market size estimates**
    Only 2.3% of brands today >$2 Bn
  - **Capital efficient**
    IND cost < $15 Mn for small molecule
- Beautiful science
  - **High POTS programs**
    More like engineering, less biology
  - **Product market fit**
    Therapies which match patient need

Source: Evaluate Pharma

Reaffirming our core principles

- **Target well-described diseases at their source, and connect all the dots using science and clinical data**
- **Execute with experienced, product-focused R&D leadership**
- **Use central resources to keep things cheap and efficient per program**
- **Diversify risk**
- **Retain focus at the level of individual diseases and assets**

We believe BridgeBio is one of the most efficient and productive biotech companies in the genetic medicine space

In less than 7 years since inception, BridgeBio has delivered…

2 Nulibry (fosdenopterin) for injection; TRUSELTIQ (infigratinib) capsules
APPROVED PRODUCTS

30+
ACTIVE R&D PROGRAMS ACROSS 4 MODALITIES

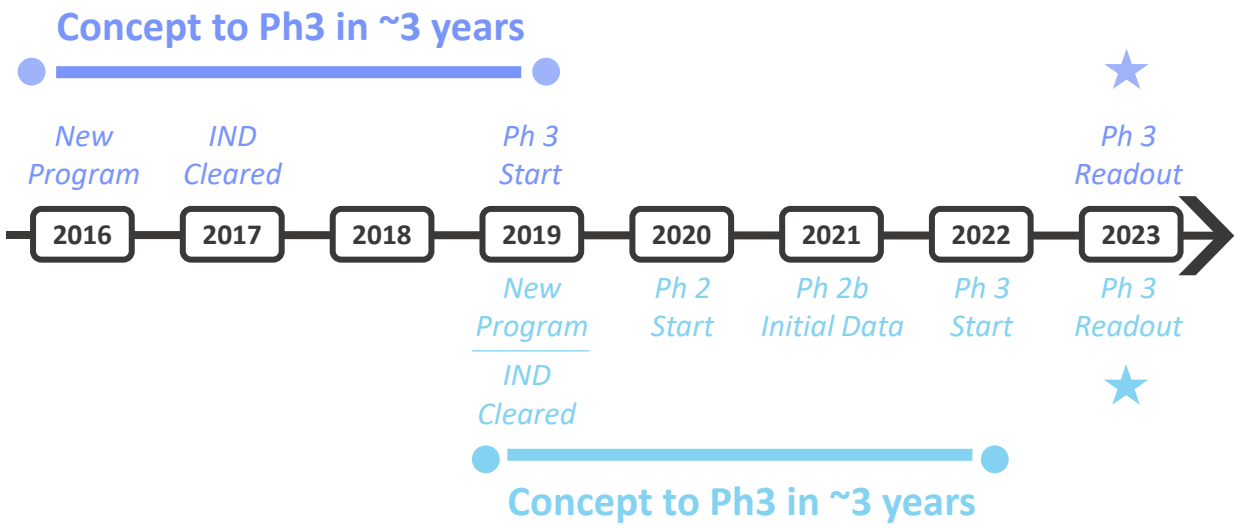
20+
ONGOING CLINICAL TRIALS ACROSS >450 SITES

540+
FULL-TIME EMPLOYEES

15
INDs (AVERAGE ~3 PER YEAR)

Select Programs:

ATTR



ADH1

…building the framework for efficient, repeatable results

Leadership team of world-renowned drug hunters

Scientific insight and judgment from industry leaders with a proven track record

Charles Homcy, MD
Founder and Chairman of Pharmaceuticals
MyoKardia GBT

Frank McCormick, PhD
Founder and Chairman of Oncology
ONYX PHARMACEUTICALS UCSF

Richard Scheller, PhD
Chairman of R&D
Genentech 23andMe

Len Post, PhD
Advisor
BIOMARIN LEAD THERAPEUTICS

Phil Reilly, MD, JD
Advisor
THIRD ROCK VENTURES bluebirdbio

Experienced team of R&D operators responsible for 100+ INDs and 20+ approved products

Mendelian / Cardio-renal

Uma Sinha, PhD
Chief Scientific Officer
GBT PORTOLA PHARMACEUTICALS

Robert Zamboni, PhD
Chemistry
MERCK FROSST

Jonathan Fox, MD, PhD
Chief Medical Officer, Eidos
MyoKardia AstraZeneca

Oncology

Eli Wallace, PhD
Chief Scientific Officer, Oncology
Peloton Therapeutics ARRAY BIOPHARMA

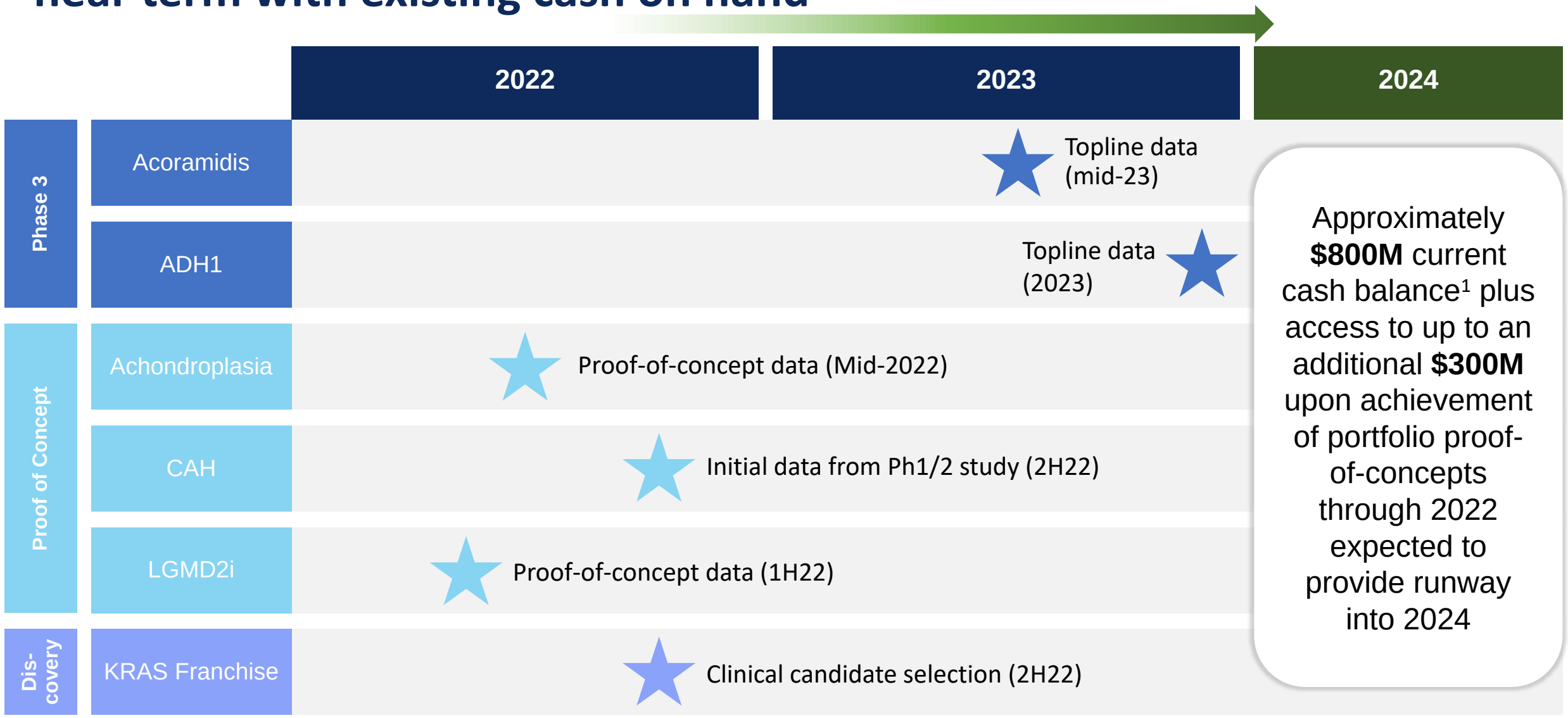
Pedro Beltran, PhD
SVP, Oncology
AMGEN UNITY BIOTECHNOLOGY

We have a diversified pipeline with a rich, uncorrelated catalyst map

4 commercial / late-stage drugs, 5 POCs and 5+ additional early-stage catalysts

Approved Products	Phase 3 Topline Data	Phase 2 Proof-of-Concept Readouts	Early-Stage Pipeline Catalysts
Nulibry™ (fosdenopterin) for injection	ATTR-CM Mid-2023	Achondroplasia Mid-2022	PKAN Phase 1 1H22
		LGMD2i 1H22	PH1 Phase 1 2022
TRUSELTIQ™ (infigratinib) capsules	ADH1 2023	RDEB 1H22	1 – 2 KRAS clinical candidates 2H22
		CAH 2H22	2 – 3 addt'l clinical candidates 2022
		Canavan 2H22	SHP2i combo data 2023

We believe BridgeBio is poised to deliver on multiple catalysts over the near term with existing cash on hand



Approximately **$800M** current cash balance[1] plus access to up to an additional **$300M** upon achievement of portfolio proof-of-concepts through 2022 expected to provide runway into 2024

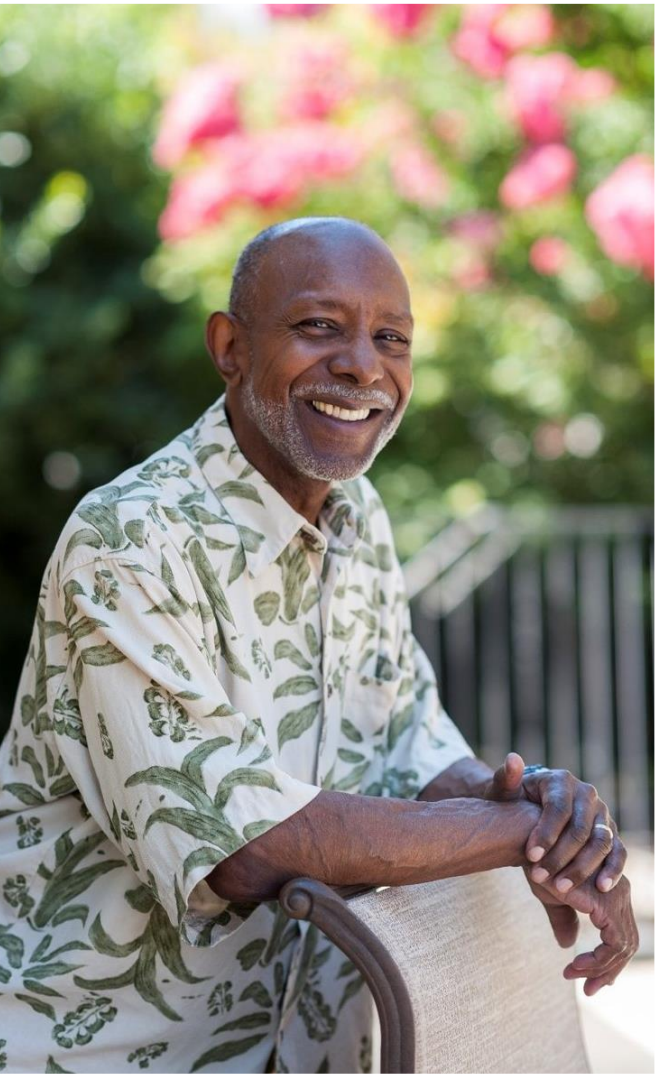
[1]Unaudited cash, cash equivalents and marketable securities

BridgeBio's pipeline, including potential best-in-class candidates

	Indication	Drug Mechanism	Pt. pop. (US+EU)	Partner
Mendelian	MoCD type A	NULIBRY™ (Synthetic cPMP, fosdenopterin)	100	MEDISON
	Achondroplasia	Low-dose FGFRi (infigratinib)	55k	
	LGMD2i	Glycosylation substrate (ribitol)	7k	
	RDEB	Recombinant COL7 (BBP-589)	3k	
	PKAN / organic acidemia	Pank activator (BBP-671)	7k	
	VM / LM	Topical PI3K inhibitor (BBP-681)	117k	
	Netherton	Topical KLK inhibitor (BBP-561)	11k	
	PTEN autism	PI3Kb inhibitor (BBP-472)	120k	
	8 undisclosed small molecule programs		>500k	
	4 undisclosed antisense oligonucleotide programs		>250k	
Precision Cardiorenal	ATTR amyloidosis	TTR stabilizer (acoramidis)	>400k	AstraZeneca
	ADH1	CaSR antagonist (encaleret)	12k[1]	
	PH1 / frequent stone formers	GO1 inhibitor (BBP-711)	5k / 1.5m	
	Undisclosed DCM small molecule program		>250k	
	Undisclosed DCM AAV gene therapy program			
Precision Oncology	FGFR2+ cholangiocarcinoma (2L)	TRUSELTIQ™ (FGFRi, infigratinib)	4k	
	FGFR2+ cholangiocarcinoma (1L)	FGFRi (infigratinib)		HELSINN
	FGFR3+ adjuvant urothelial	FGFRi (infigratinib)	21k	
	FGFR1-3+ tumor agnostic	FGFRi (infigratinib)	24k	
	FGFR1-3+ gastric cancer	FGFRi (infigratinib)	41k[2]	
	MAPK / RAS-driven cancer	SHP2i monotherapy (BBP-398)	>500k	
		SHP2i combo therapy (BBP-398)		Bristol Myers Squibb
	KRAS-driven cancer	KRAS G12C dual inhibitor	>500k	
		PI3Kα:RAS Breaker		
		KRAS G12Di		
	Solid tumors	GPX4i	>500k	HELSINN
Gene Therapy	CAH	AAV5 gene therapy (BBP-631)	>75k	
	Canavan	AAV9 gene therapy (BBP-812)	1k	
	TMC1 hearing loss	AAV gene therapy (BBP-815)	2k	
	Galactosemia	AAV gene therapy (BBP-818)	>7k	
	TSC1/2	AAV gene therapy	100k	
	Cystinuria	AAV gene therapy	30k	
	3 capsid discovery collaborations			

[1]US carriers
[2]China + Japan patient population

Acoramidis for transthyretin (TTR) amyloidosis (ATTR)



Len
Living with ATTR-CM

Prevalence

>400k

Worldwide

Pathophysiology

Systemic disease most commonly presenting as cardiomyopathy or peripheral neuropathy

Genetic Driver

Destabilized TTR leading to amyloid accumulation

Therapeutic Hypothesis

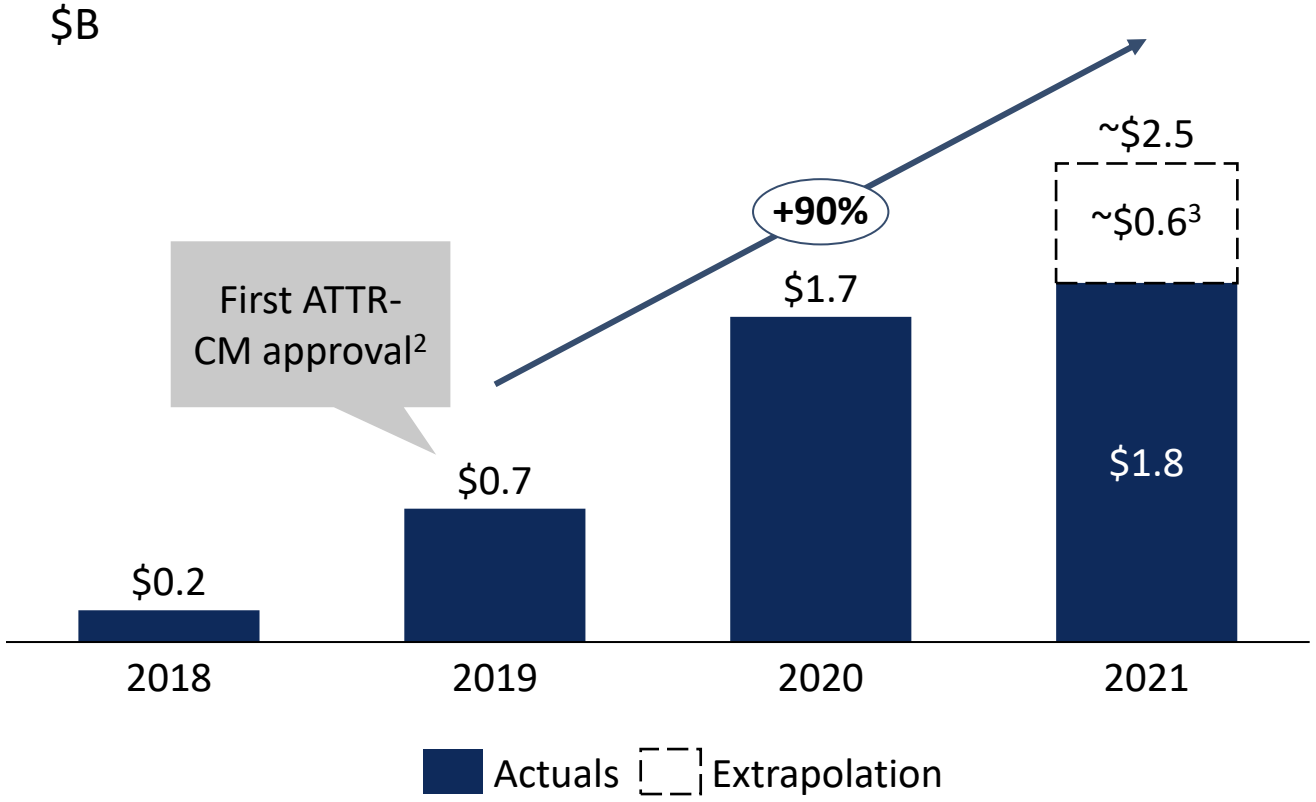
TTR stabilizer designed to mimic protective T119M mutation

Design Criteria for Optimal Therapy

- Near-complete stabilization of TTR
- Preservation of TTR tetramer
- Oral Dosing

Following first ATTR-CM approval in 2019, ATTR has become a $2B+ market with substantial remaining upside

Global annual ATTR market sales[1]



Significant ATTR market growth driven by:

- Increasing diagnosis in established geographies *(~30K ATTR-CM US patients currently diagnosed vs. <5k before first approval[4])*
- Launch and patient finding in new geographies

[1]ATTR market includes all approved drugs for ATTR-PN and ATTR-CM
[2]First ATTR-CM sales occurred in Q2 2019
[3]Assumes Q1 '21 – Q3 '21 growth annualized for Q4 '21
[4]Pfizer press release and transcript

Acoramidis was designed to treat ATTR at its source

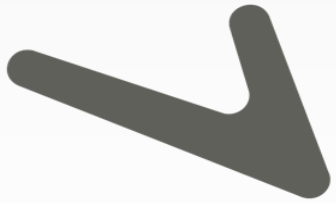
Disease mechanism

Native TTR circulates in blood as a tetramer

~130 known destabilizing mutations

Protective T119M mutation

Dissociation into monomers initiates pathogenesis



Monomers aggregate, causing disease

Therapeutic hypothesis

Acoramidis was designed to mimic protective T119M mutation by stabilizing TTR tetramers to slow or halt disease progression

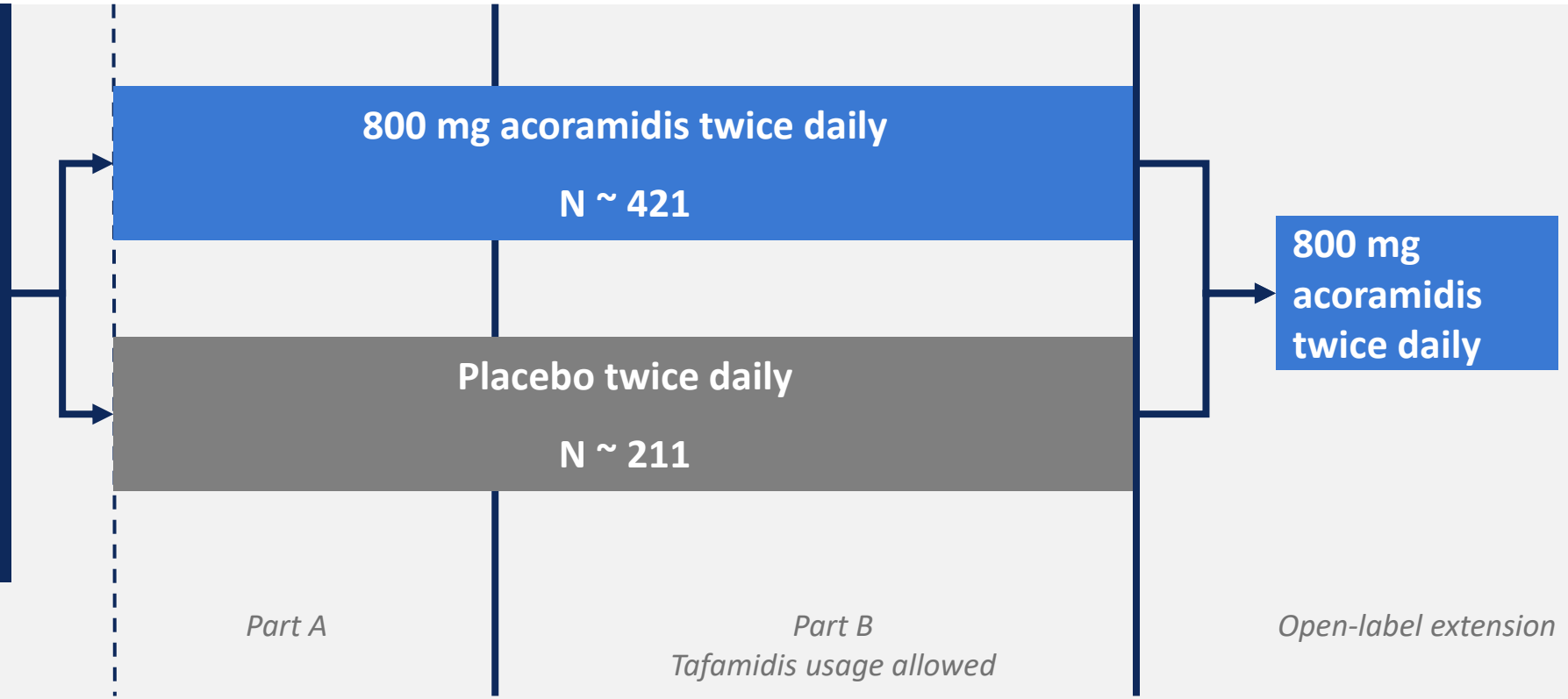
ATTRibute-CM still set to provide 30-month mortality and CV hospitalization data despite its 12-month 6MWD primary endpoint miss

12-month endpoints:
Primary: Change in 6MWD
Key secondary: Change in KCCQ

30-month endpoints:
Primary: Hierarchical composite[1]
Key secondary: Change in 6MWD, KCCQ

Key eligibility criteria

- Subjects with diagnosed ATTR-CM (WT or mutant)
- NYHA Class I-III
- ATTR-positive biopsy or ^{99m}Tc scan
- Light chain amyloidosis excluded if diagnosis by ^{99m}Tc



6MWD = Six-minute walk distance KCCQ = Kansas City Cardiomyopathy Questionnaire NYHA = New York Heart Association
^{99m}Tc = Technetium labeled pyrophosphate (PYP) or bisphosphonate (e.g., DPD) CV = cardiovascular-related
[1]Primary analysis will use the Finkelstein-Schoenfeld method

Summary of Part A results

Based on data available at Month 12, acoramidis demonstrated relative to placebo:

? No improvement in functional status as measured by 6MWD

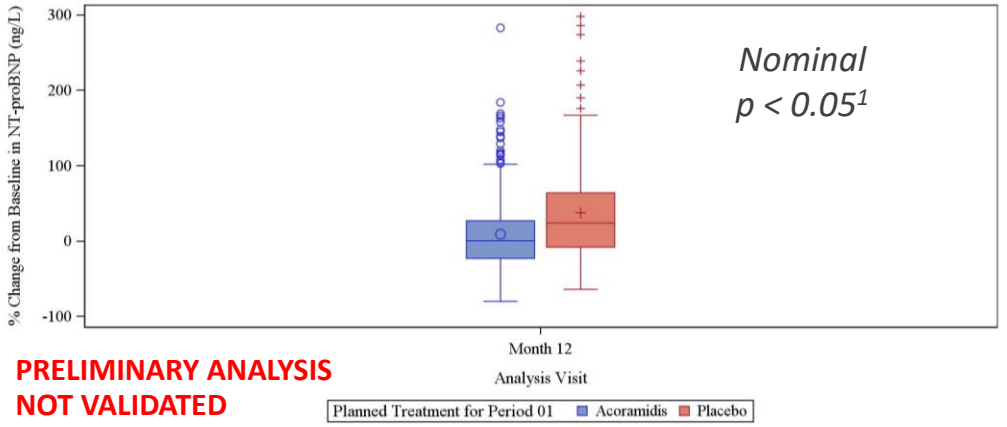
✓ Positive improvement in KCCQ-OS

✓ Positive reduction in NT-proBNP

✓ Positive improvement in serum TTR

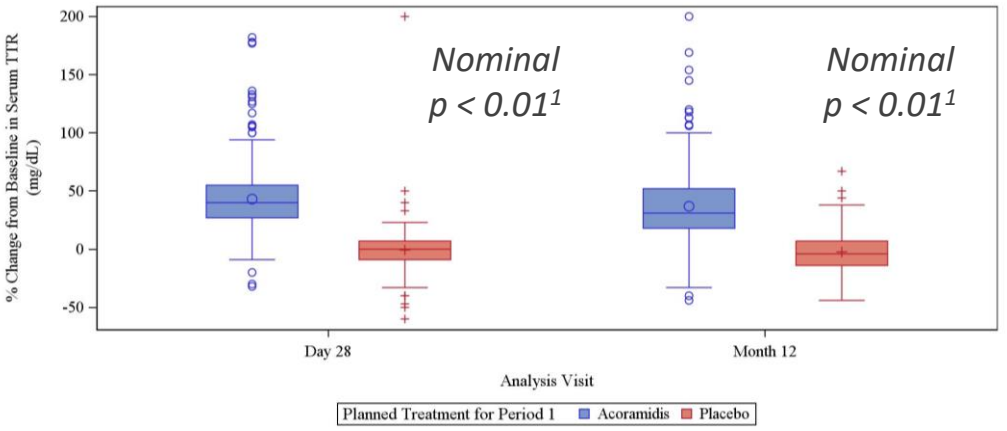
✓ No safety signals of clinical concern and lower rates of SAEs and AEs leading to death

Percent change from baseline in NT-proBNP at Month 12[2]



Note: to facilitate a focused review of the vast majority of the data, outliers greater than 300% change from baseline are not included in this plot.

Percent change from baseline in serum TTR by treatment and visit[2]



Note: to facilitate a focused review of the vast majority of the data, outliers greater than 200% change from baseline are not included in this plot.

[1]Inference analysis (p-value) based on absolute change from baseline between groups
[2] Modified intent-to-treat (mITT) population defined as all randomized subjects who have received at least one dose of IMP and have at least one post baseline efficacy evaluation. mITT population pre-specified to exclude subjects with baseline eGFR < 30 mL/min/1.73 m^2

Was this a spurious 6MWD result or are patients too healthy? – baseline characteristics and changes over time

Baseline Trait	ATTRibute-CM (mITT)[1]	ATTR-ACT[2]
Age		
Mean	77.0	74.3
Median	78.0	74.6
NYHA Class		
Class I	11.2%	8.4%
Class II	72.7%	59.6%
Class III	16.1%	32.0%
6MWT (m)		
Mean	360	352
NT-proBNP (ng/L)		
Median	2778	3062
KCCQ-OS		
Mean	71.4	66.7[3]
Serum TTR (mg/dL)		
Mean	23.2	21.5[4]
Genetic TTR status		
Variant	9.7%	24.0%
Wildtype	90.3%	76.0%
Geography		
US	19.3%	63.3%
Ex-US	80.7%	36.7%

NT-proBNP increase, KCCQ decline, and AE-driven death all point to decreases in health over time, unlike the 6MWD

[1]BridgeBio, data on file. [2]Maurer MS, et al. N Engl J Med. 2018;379(11):1007-16. [3]Tafamidis CDER NDA filing. [4]Approximated from Hanna M, et al. HSFA 2019.

Frequently asked questions

Question	Answer
Were there differences between your technetium-scanned patients and the biopsy confirmed?	No meaningful difference in baseline characteristics or rate of decline
Was the variability in 6MWD substantially different in ATTRibute-CM than previous ATTR-CM cohorts?	Standard deviation in baseline 6MWD (~100 m) and standard deviation in change-from-baseline at Month 12 (~60 m) were both similar to previous cohorts
Was the standard of care for ATTRibute-CM participants different than in previous ATTR-CM studies?	No ATTR-specific therapies were permitted during Part A of ATTRibute-CM. Use of heart rhythm control medications was restricted in accordance with best clinical practice
Do you anticipate substantial tafamidis usage or trial discontinuation in Part B of ATTRibute-CM?	A low single-digit percentage of participants in ATTRibute-CM have initiated tafamidis. The proportion of completed Month 12 visits in ATTRibute-CM was comparable to ATTR-ACT. We will continue to monitor these metrics during Part B

Next steps for ATTRibute-CM

- Work to ensure the ongoing fidelity of the trial to Part B endpoint, and seek to monitor critical event rates, adjusting duration if necessary (next month)
- Continue to evaluate hypotheses regarding unexpected 6MWD result

Low-dose FGFR inhibitor (infigratinib) for achondroplasia

Miguel
Living with achondroplasia

Prevalence

55k

US & EU

Pathophysiology

Up-regulation of STAT1 and MAPK in the growth plate cause cranial, spinal, and stature symptoms

Genetic Driver

Gain of function of FGFR3

Therapeutic Hypothesis

Low dose inhibition of FGFR3

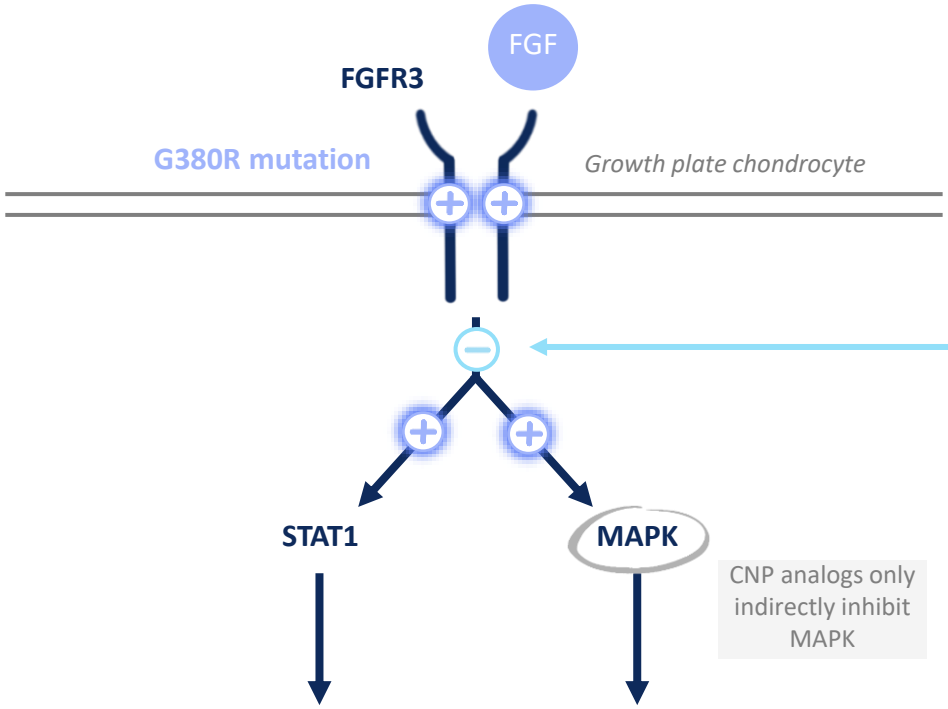
Key Differentiation

- Directly target FGFR3 to normalize both STAT1 and MAPK pathways
- Differentiated pre-clinical efficacy in mouse model
- Oral Dosing

Low-dose infigratinib is designed to treat achondroplasia directly at its genetic source

Disease Mechanism

- **ACH FGFR3** gain-of-function mutation causes 2-3x overactivation of the receptor



Symptoms

- Disproportionate short stature
- Narrowed foramen magnum
- Spinal stenosis

Therapeutic Hypothesis

Low-dose infigratinib has the potential to:

- Directly inhibit the causal gain-of-function mutation in FGFR3
- Normalize both the STAT1 and MAPK signaling pathways
- Reverse all key drivers of symptoms

Source: Ornitz DM et al., Developmental Dynamic 2017, Richette Joint Bone Spine 2007, Unger Curr Osteoporos Rep 2017, Hoover-Fong Am J Gen Med 2017

Improved all the key drivers of clinical symptomology in validated ACH mouse model

FGFR3 WT
No treatment

FGFR3$^{Y367C/+}$
No treatment

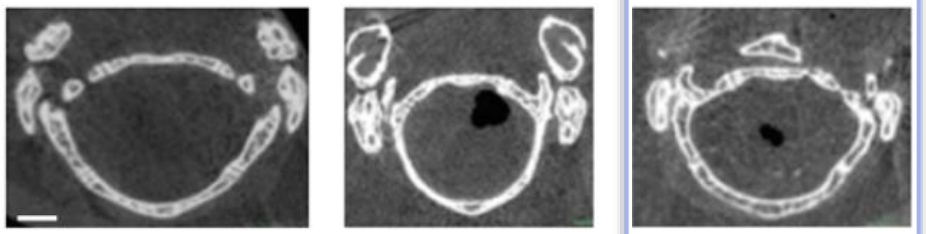
FGFR3$^{Y367C/+}$
Infigratinib tx

1 Cranial bone issues

17% increase in FM area

6% increase in AP skull length

May lead to **decrease in foramen magnum stenosis** and fewer surgeries

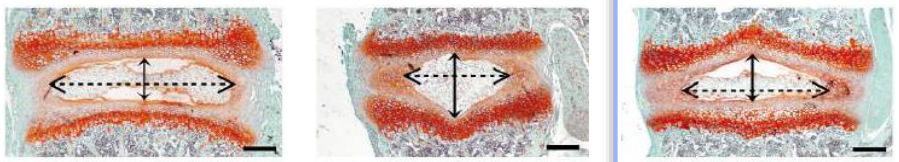


2 Disorders of the spine

12% increase in L4-L6 length

73% increase in disc width

May lead to **decrease** in **spinal stenosis**, possibly **reducing need for surgery**

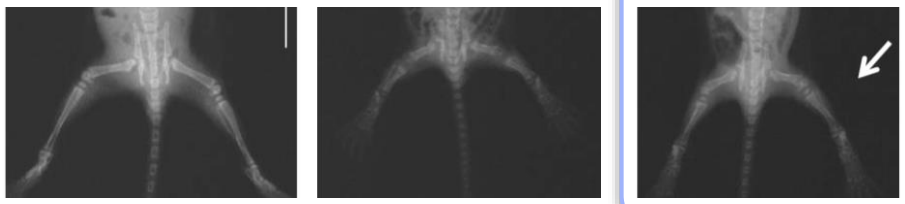


3 Disproportionate short stature

21% increase in femur length

33% increase in tibia length

May lead to **increased stature** and **proportionality**

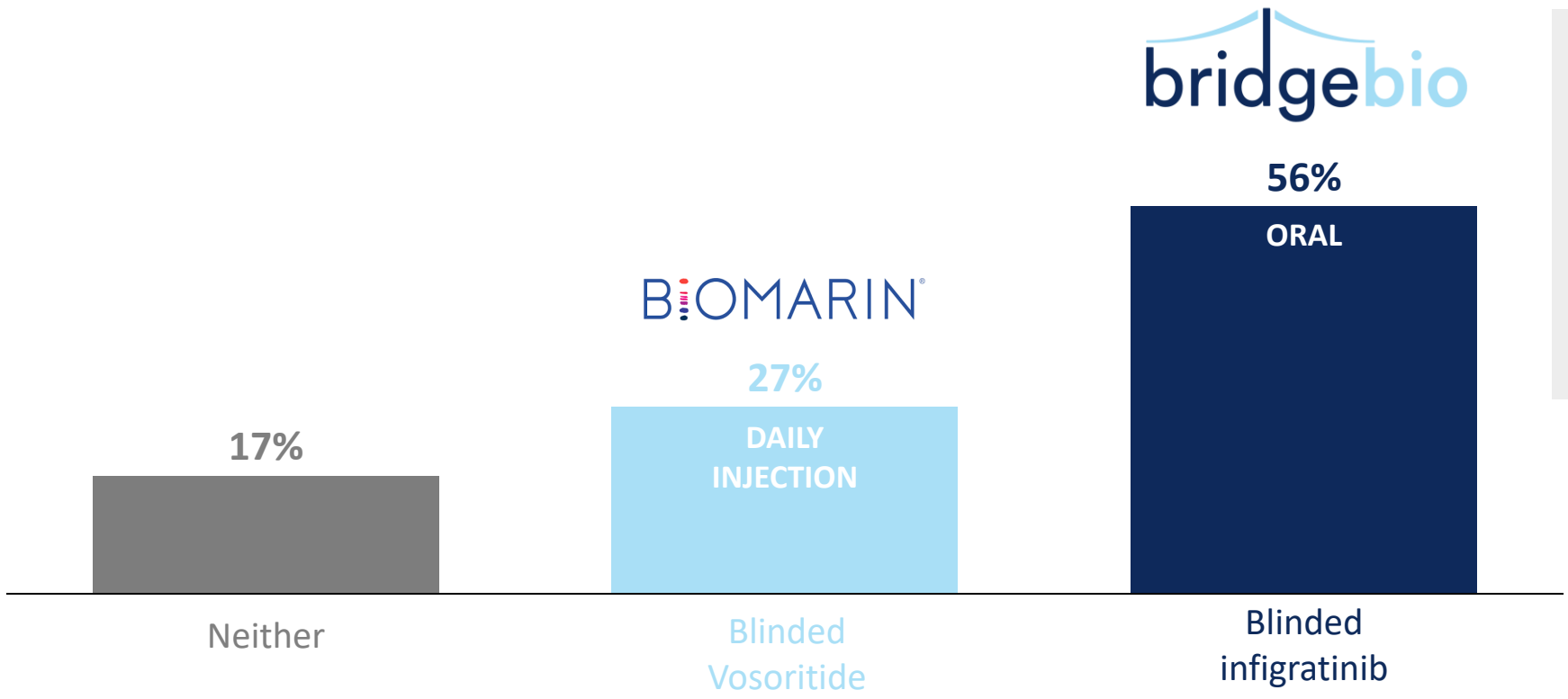


Source: Komla-Ebri et al., J Clin Inv 2016
Note: percent increase compared to vehicle treated FGFR3Y367C/+ mouse, infigratinib treatment with 2mg/kg subcutaneous dose

HCP survey suggests oral route of administration with efficacy equivalent to vosoritide takes majority market share

Vosoritide vs. low-dose infigratinib showing equivalent efficacy

% of children with achondroplasia who would receive each product[1]

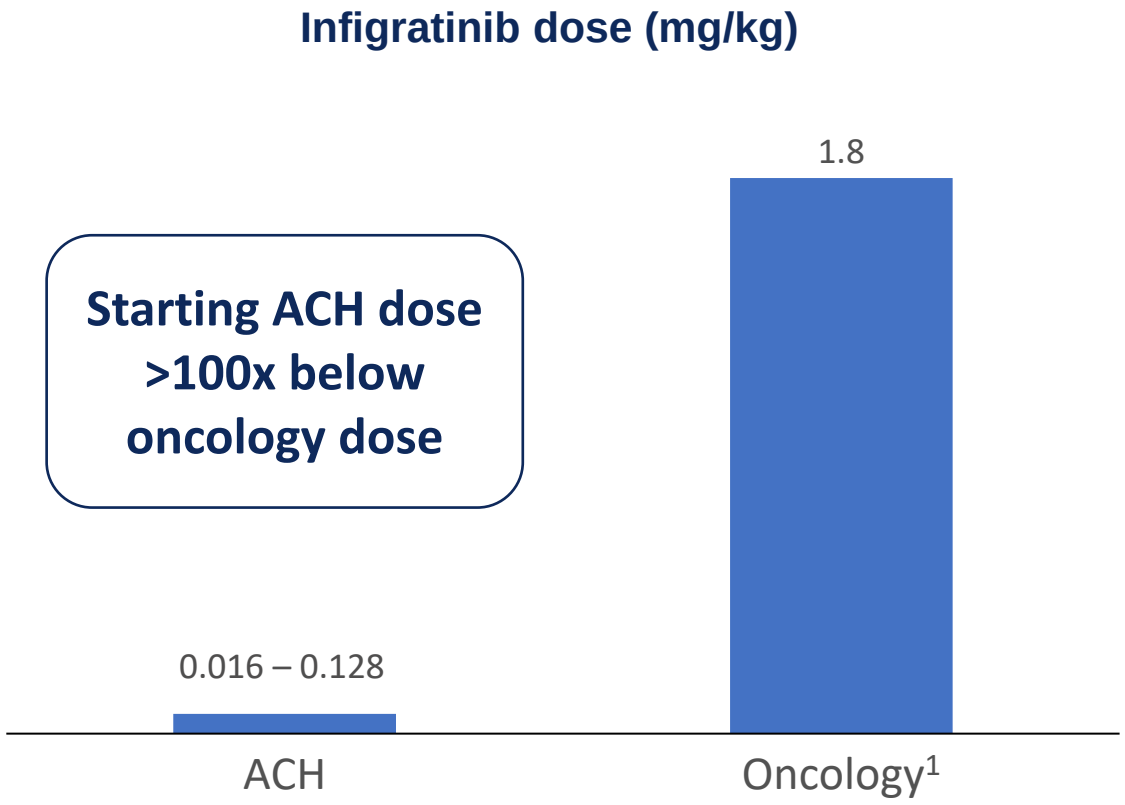


Clear share preference for an **oral solution** for achondroplasia vs. daily injection for children

Source: US market research testing blinded product profiles for vosoritide and infigratinib among HCPs who treat children with achondroplasia; responses weighted by specialty (31 endos, 23 geneticists).
1 Question text: Imagine that Product A [blinded vosoritide] has been on the market for some time and Product B [blinded infigratinib with equivalent efficacy] has just now been approved. Consider the children you manage with ACH not already receiving therapeutic treatment: what percentage of these children would receive each product?

Low dose infigratinib in Achondroplasia is safe and does not result in meaningful changes in phosphate

Achondroplasia dose much lower than in oncology where hyperphos has been observed

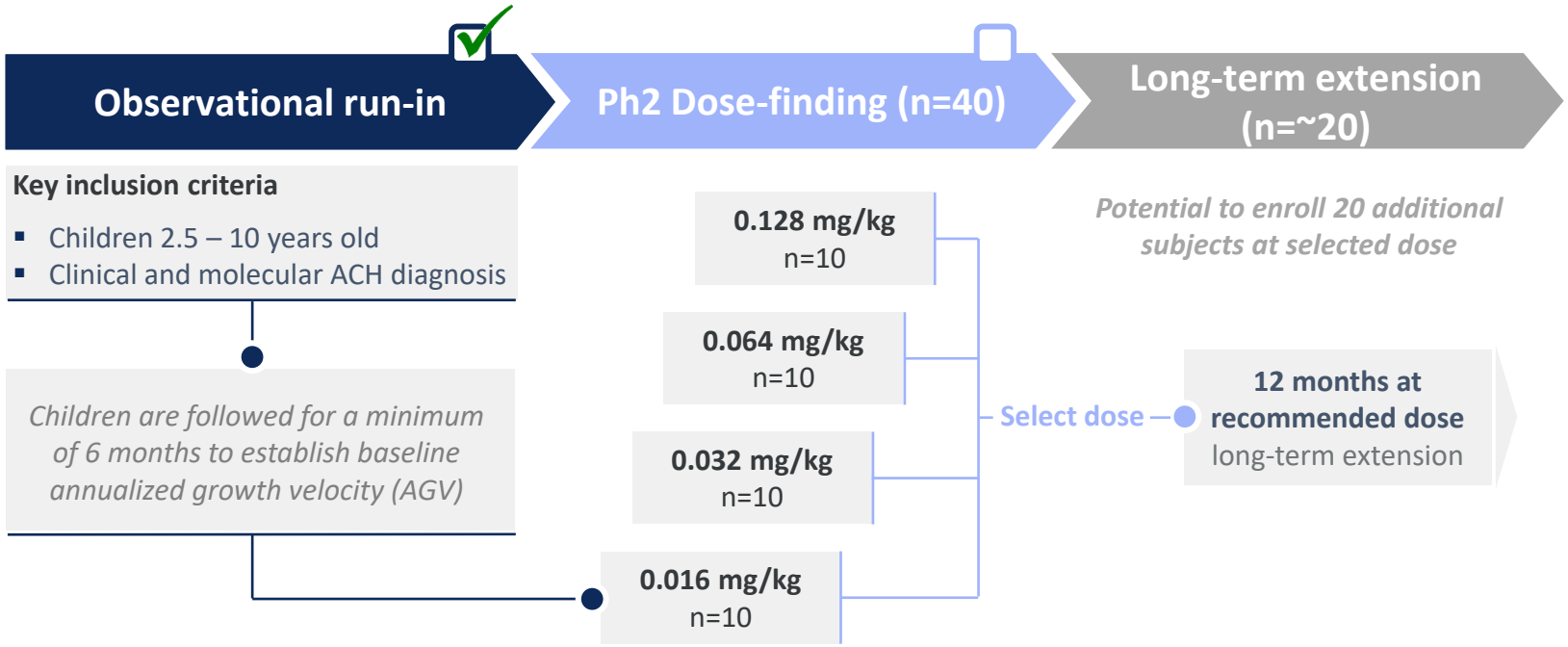


All 4 dose cohorts in our study have been cleared for safety by the DRC

Cohort	Dose (mg/kg)	Enrolled	Safety cleared by Data Review Committee
1	0.016	8 children	✓
2	0.032	13 children	✓
3	0.064	12 children	✓
4	0.128	12 children	Cohort open now

Source: Demuynck B et al. ENDO 2020, Data on file. [1]Approximate based on 70kg adult

The PROPEL clinical program is enrolling with data expected in Mid-2022



Next Steps

Clinical proof-of-concept readout

Mid-2022

Following POC, Phase 3 trial start

2023

Primary objectives

- Collect baseline annualized growth velocity (AGV)

- Identify safe therapeutic dose for expansion / pivotal study
- Safety and tolerability
- Change from baseline in AGV

- Long-term safety and efficacy

Future indications

- Infigratinib has potential applications beyond Achondroplasia
- Exploring additional FGFR-driven skeletal dysplasias including hypochondroplasia
- Pre-clinical data in non-achon indication expected in 2022

Encaleret for autosomal dominant hypocalcemia type 1 (ADH1)

Alexis and Jackson
Living with ADH1

Prevalence

12k

US

Pathophysiology

Decreased blood calcium, elevated urine calcium, and lowered parathyroid hormone secretion

Genetic Driver

Hyperactivation of calcium-sensing receptor (CaSR)

Therapeutic Hypothesis

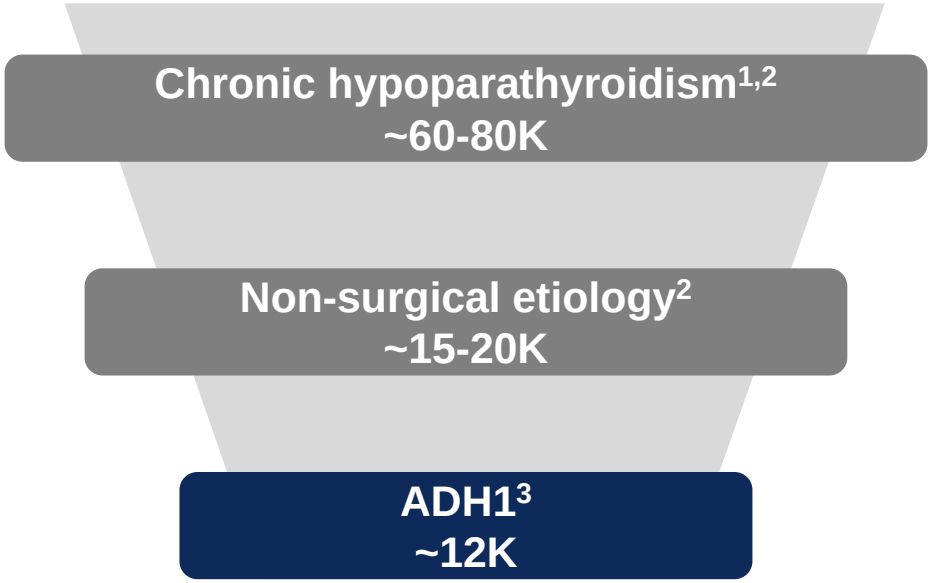
Selectively antagonize CaSR to normalize downstream effects

Design Criteria for Optimal Therapy

- Directly target CaSR to potentially resolve key symptoms
- Phase 2 data suggests potential to normalize blood Ca and urine Ca
- Oral Dosing

ADH1 is a genetic cause of hypoparathyroidism resulting from gain-of-function variants in the CaSR which disrupt calcium homeostasis

US ADH1 Addressable Market



ADH1 Clinical Manifestation

Presenting symptoms

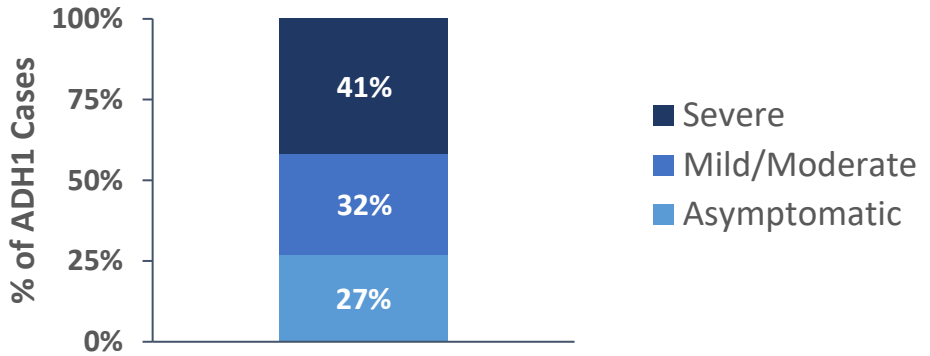
- Hypocalcemic seizures
- Paresthesia
- Tetany
- Muscle cramps

Long-term complications

- Nephrocalcinosis
- Nephrolithiasis
- Chronic kidney disease

Median age of ADH1 dx[4]: 25 (0-77) years

Symptom presentation[4]

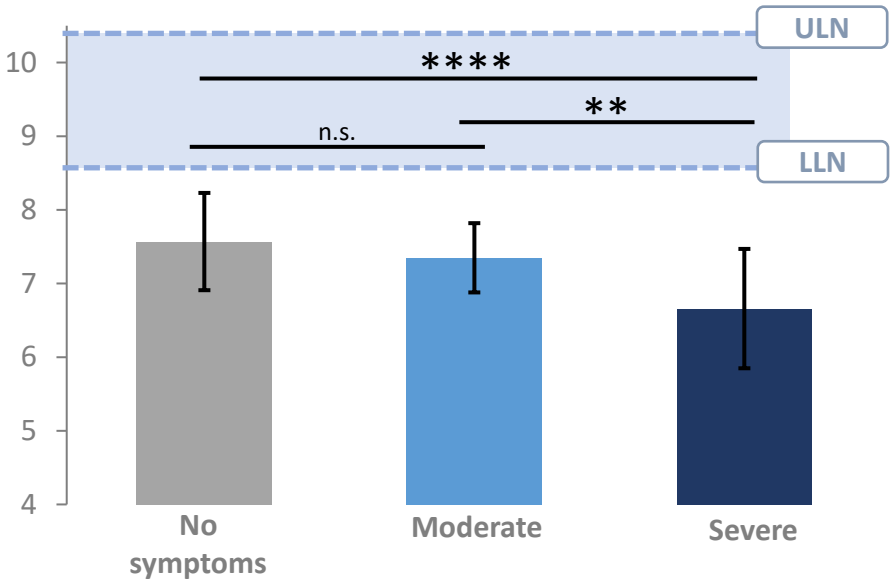


[1]Powers, et al. J Bone Miner Res. 2013. [2]Mannstadt, et al. Nat Rev Dis Primers. 2017. [3]Dershem, et al. Amer Jour of Hum Genetics 2020. [4]Roszko, et al., ASBMR Annual Meeting, 2021. Abbreviations: dx = diagnosis. Age of dx presented as median (range)

ADH1 symptom severity is associated with blood calcium levels and current treatment inadequately addresses symptom burden

Blood calcium at clinical presentation

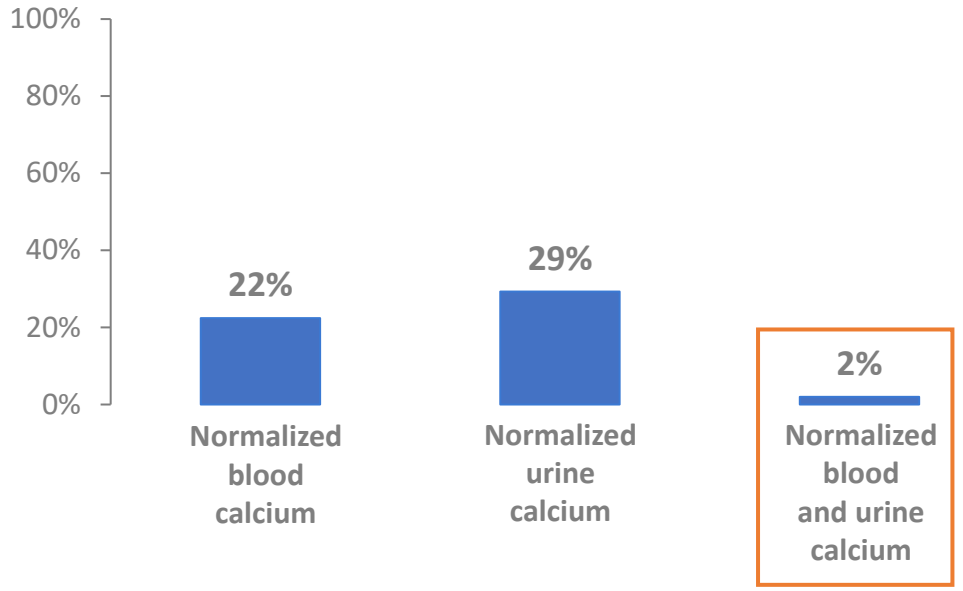
Blood corrected calcium
mg/dL, mean



Severely symptomatic individuals exhibited significantly lower blood calcium compared to asymptomatic and moderately symptomatic[1]

ADH1 medical intervention

Individuals on calcium and/or active vitamin D
%

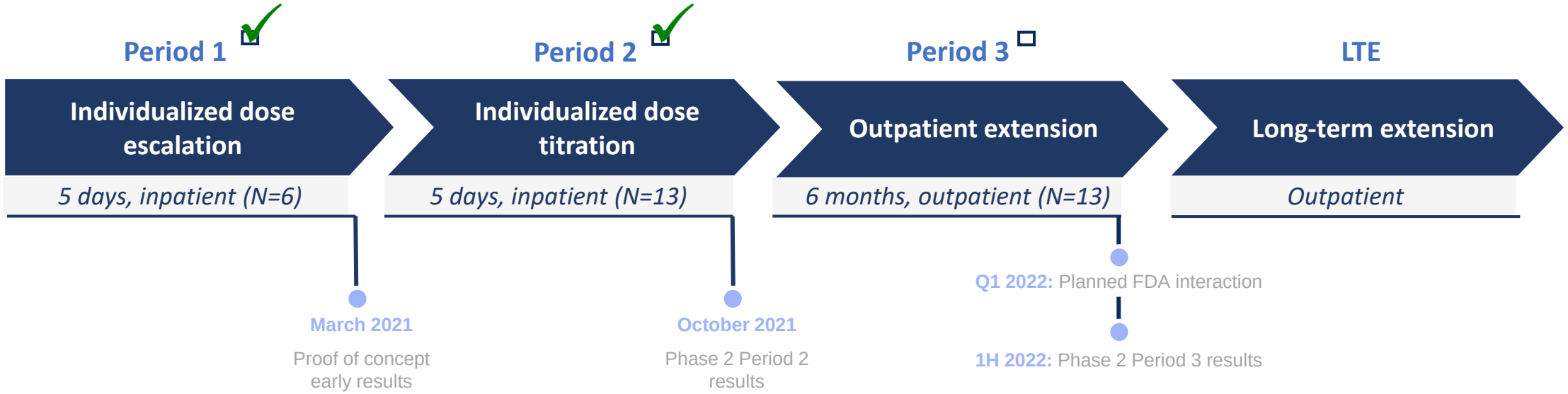


Only 2% of individuals normalized both blood and urine calcium[1]

ULN = upper limit of normal, LLN = lower limit of normal. ** p-value <0.01. **** p-value < 0.0001. n.s. = not statistically significant.

Source: 1. Roszko, et al., ASBMR Annual Meeting, 2021.

Encaleret Phase 2 study design



Key study objectives:

- Safety and tolerability
- Blood calcium concentration
- Urine calcium concentration
- Intact parathyroid hormone concentration

Additional measures:

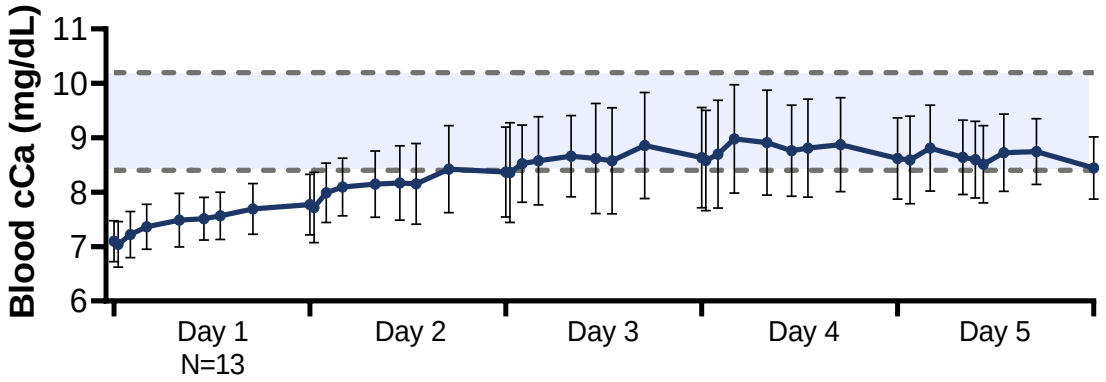
- Blood 1,25-$(OH)_2$ Vitamin D, magnesium, and phosphate
- Urine creatinine, cAMP, citrate, phosphate, sodium, magnesium
- Bone turnover markers (serum collagen C-telopeptide, serum procollagen Type 1 N-propeptide)

Encaleret normalized mean blood and urine calcium and increased mean PTH during Period 2

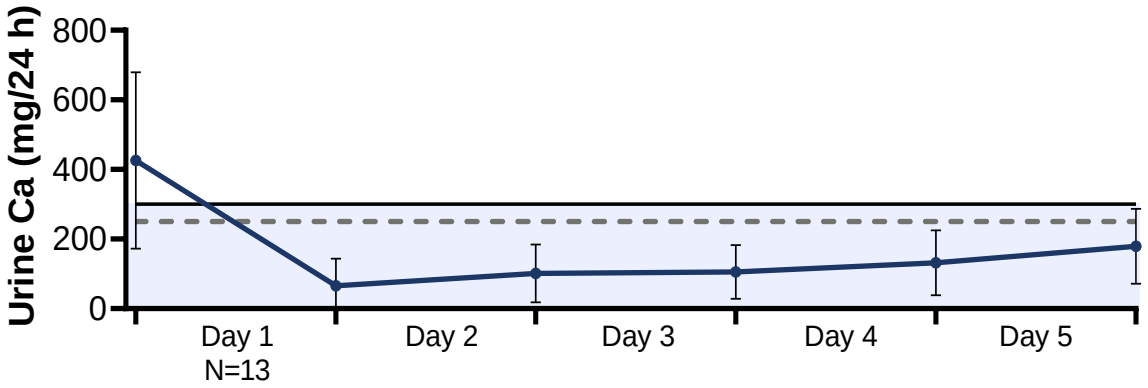
Mean responses on Day 1 through Day 5 in Period 2 (N=13)

Normal Range

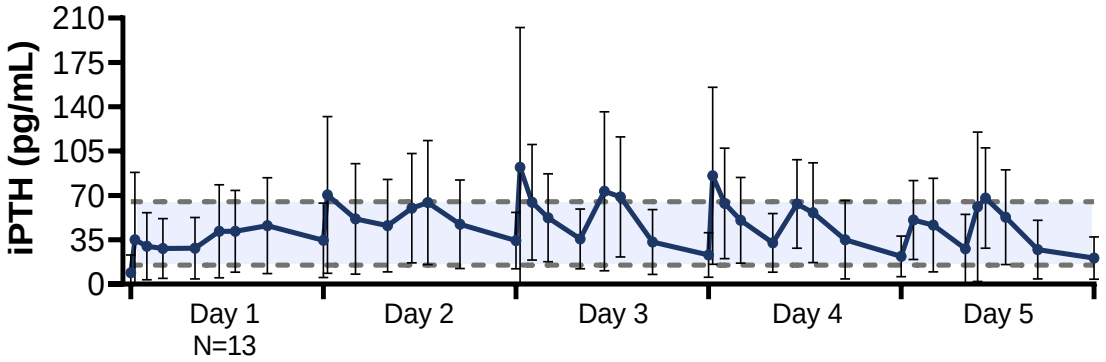
Blood Calcium



Urine Calcium



PTH



- Encaleret was generally well-tolerated when administered once or twice daily over 5 days, with no serious adverse events reported
- Consistent improvements in mineral homeostasis suggest encaleret may become an effective treatment for ADH1

Data reported as mean±SD. Values below limit of assay quantitation recorded as "0". Shading reflects normal range. Solid line for urine calcium reflects the upper limit for men and dashed line reflects upper limit for women

Encaleret continues to be generally well-tolerated with no serious adverse events reported[1]

	Period 1 N = 6	Period 2 N=13
Number of subjects experiencing any Serious Adverse Event	**0 (0%)**	**0 (0%)**
Number of subjects experiencing any Adverse Event	**6 (100%)**	**10 (77%)**
Mild	6 (100%)	10 (77%)
Moderate	1 (17%)	0 (0%)
Severe	0 (0%)	0 (0%)
Number of Adverse Events Reported	**19**	**12**
Mild	18 (95%)	12 (100%)
Moderate	1 (5%)	0 (0%)
Severe	0 (0%)	0 (0%)
Treatment-related Adverse Events[2]	**3 (16%)**	**8 (67%)**
Hypocalcemia	1 (33%)	0 (0%)
Hypophosphatemia	2 (67%)	7 (88%)
Hypercalcemia	0 (0%)	1 (12%)

[1]Data as of September 3, 2021. [2]Treatment-related adverse events were transient and resolved with dose-adjustment. Treatment-related AEs were counted as the number of events per period and are presented as a percentage of the total number of AEs. The most common AEs (≥ 2 subjects) were hypophosphatemia, hypocalcemia, and headache

Summary reported Phase 2 data and next steps

Summary of Encaleret Development Program

- In 13 participants, encaleret normalized mean blood calcium and 24-hour urine calcium excretion, increased PTH, and decreased phosphate into the normal range during both Periods 1 and 2
- Individualized BID dosing in Period 2 resulted in a decrease in the mean Day 5 encaleret dose as compared to Period 1
- Encaleret was generally well-tolerated when administered once or twice daily over 5 days, with no serious adverse events reported
- Consistent improvements in mineral homeostasis suggest encaleret may become an effective treatment for ADH1
- Granted Fast Track Designation by FDA and Orphan Drug Designation by the FDA and EMA

Next Steps

- **Q1 2022**: Interact with regulatory authorities
- **1H 2022**: Present complete Phase 2 data
- **2022**: Initiate Phase 3 registrational study
- **2023**: Top line Phase 3 data

BBP-631: AAV5 gene therapy for congenital adrenal hyperplasia (CAH)

Maddie
Living with CAH

Prevalence

>75k

US & EU

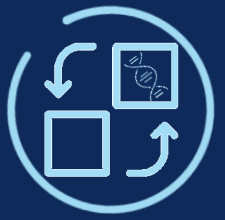
Pathophysiology

Inability to produce cortisol causes need for supraphysiologic doses of synthetic steroids, ~5x increase in mortality risk, hirsutism, Cushingoid symptoms

Genetic Driver

Loss of function of 21-hydroxylase (21-OH)

Therapeutic Hypothesis



AAV5 gene therapy to provide 21-OH

Design Criteria for Optimal Therapy

- Only known approach designed to induce endogenous cortisol and mineralocorticoid production
- Durable transgene delivery to the adrenal gland of NHPs
- Low threshold to correct phenotype

Research and manufacturing capabilities

Facility | 20,000 sq ft lab space in Raleigh, NC

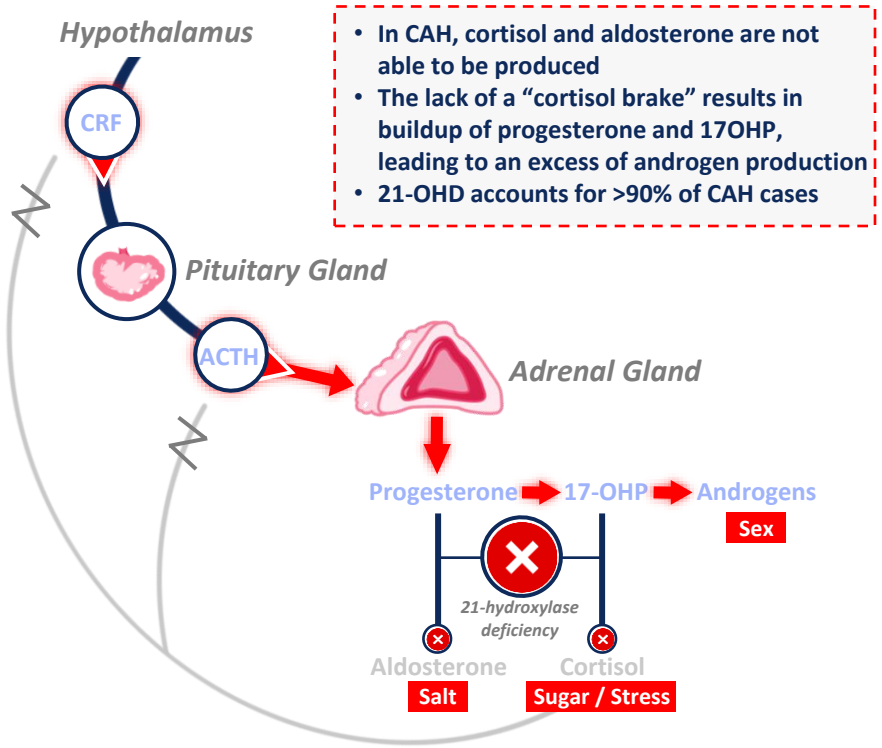
People | 60+ gene therapy employees (>50% in research or CMC)

Capabilities | Vector development, optimization, analytical development, and production (200L)

External Manufacturing | Dedicated GMP manufacturing suite at Catalent

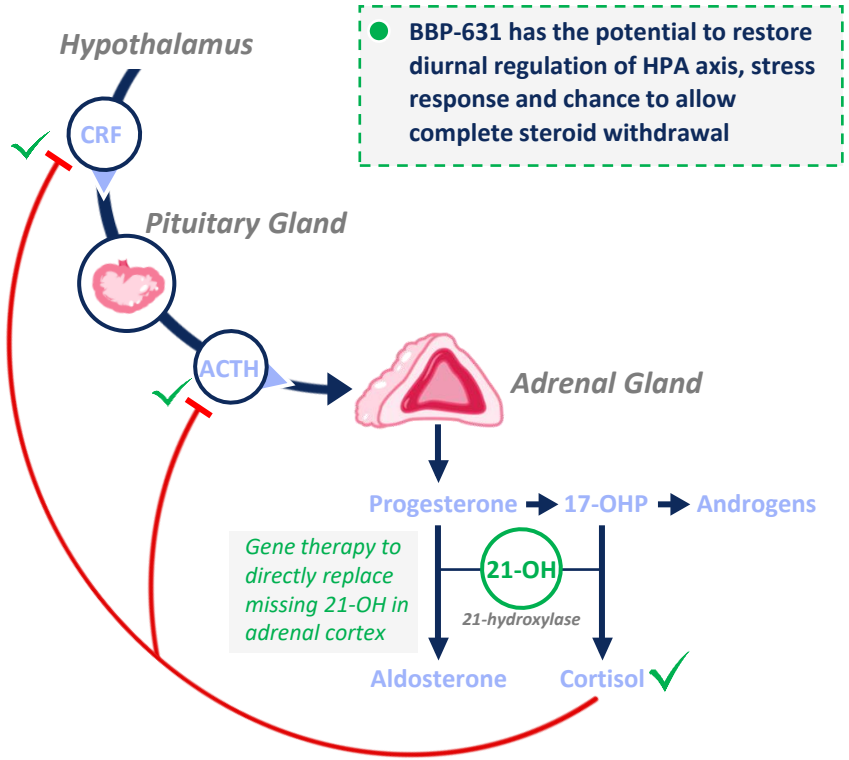
Gene therapy is the only known modality designed to treat CAH at its source and allow for production of endogenous cortisol

Hormonal dysregulation in HPA Axis due to 21-Hydroxylase Deficiency (21-OHD)



- In CAH, cortisol and aldosterone are not able to be produced
- The lack of a "cortisol brake" results in buildup of progesterone and 17OHP, leading to an excess of androgen production
- 21-OHD accounts for >90% of CAH cases

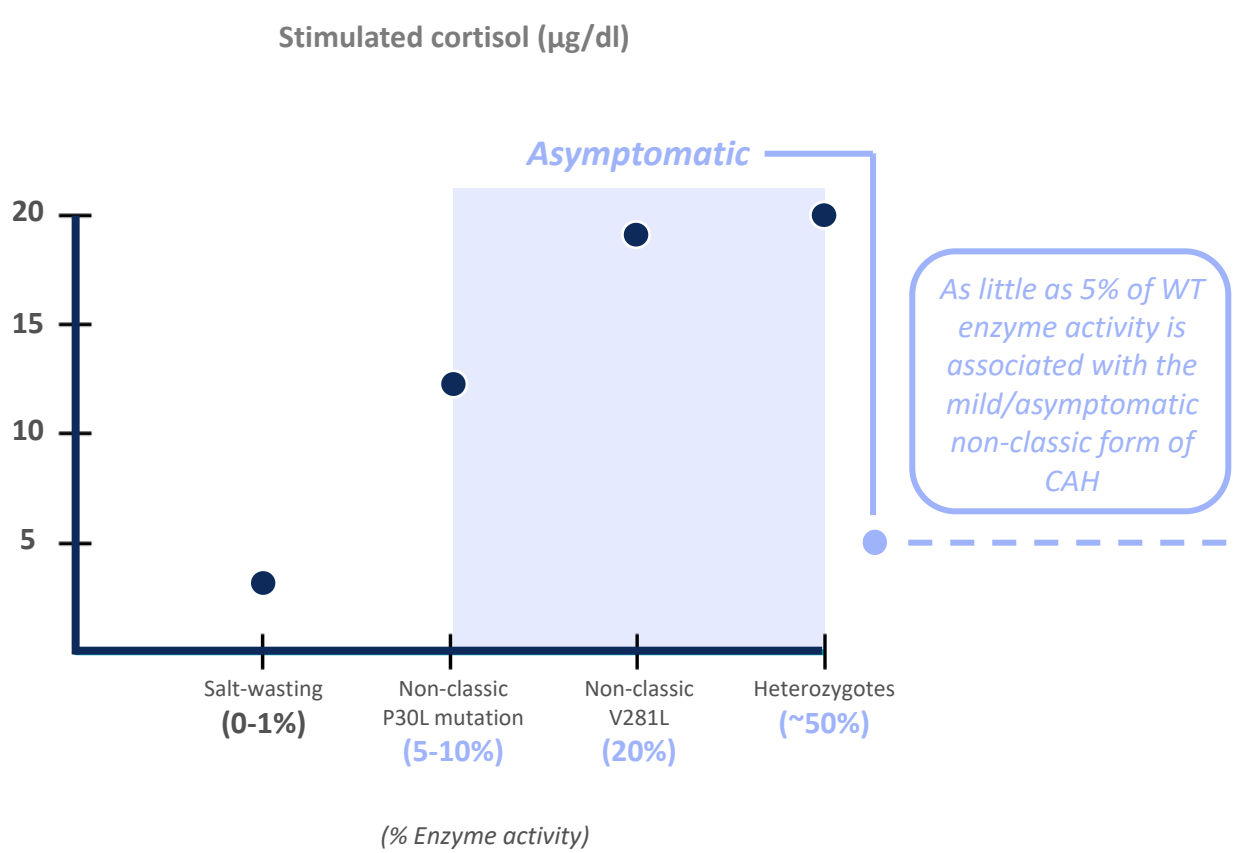
BBP-631 is designed to restore endogenous cortisol production



- BBP-631 has the potential to restore diurnal regulation of HPA axis, stress response and chance to allow complete steroid withdrawal

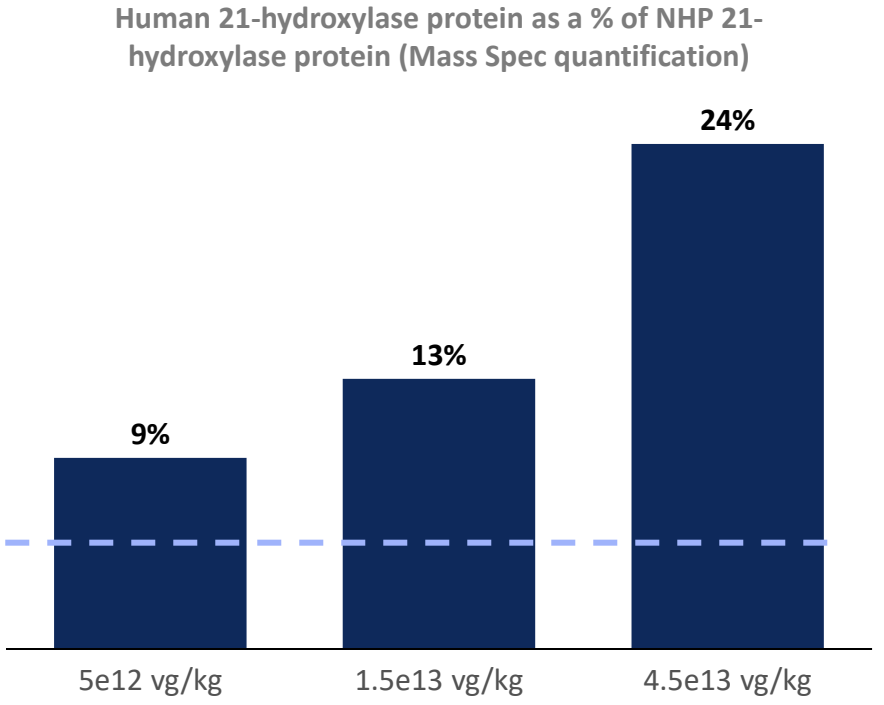
5-10% of WT enzyme may be sufficient for clinical impact

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



As little as 5% of WT enzyme activity is associated with the mild/asymptomatic non-classic form of CAH

NHP protein data suggests potentially therapeutic levels of 21-hydroxylase enzyme



- Mass-spec methods to quantify protein expression by identifying differential peptides between human and NHP 21-OH
- Data suggest dose-dependent enzyme expression in the adrenal cortex from 9%-24% of WT levels

Source: Perdomini, Gene Therapy 2017; ESGCT 2019; data on file

Phase 1/2 first-in-human trial design

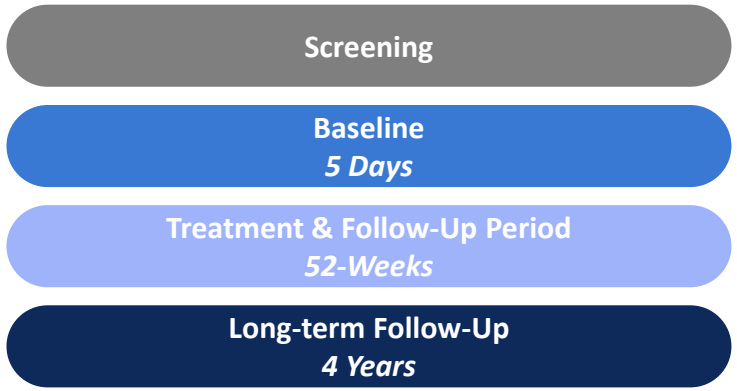
Status

- Trial enrollment underway

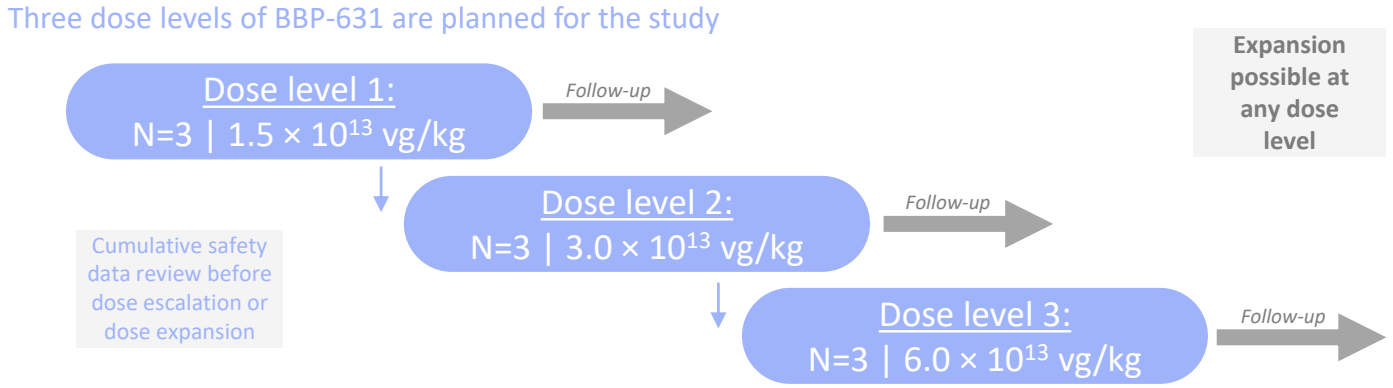
Eligibility

- Age >18 years with classic CAH (simple virilizing or salt-wasting) due to 21-Hydroxylase Deficiency (21-OHD)
- Screening/baseline 17-OHP levels > 5-10 × ULN

FIH Trial Design



Dose Escalation Design



Primary Objectives

- Evaluate safety
- Levels of endogenous cortisol (pre- and post-ACTH stimulation)
- Quality-of-life assessment

Limb-Girdle Muscular Dystrophy Type 2i (LGMD2i)

Seamus
Living with LGMD2i

Prevalence[1]

7k

US & EU

Pathophysiology

Progressive muscle weakness resulting in the loss of ability to perform routine daily functions

Genetic Driver

Loss of function of FKRP gene

Therapeutic Hypothesis

Add glycosylation substrate to drive residual enzyme activity

Design Criteria for Optimal Therapy

- Naturally occurring compound with strong safety profile
- First potential disease targeting therapy
- Oral dosing

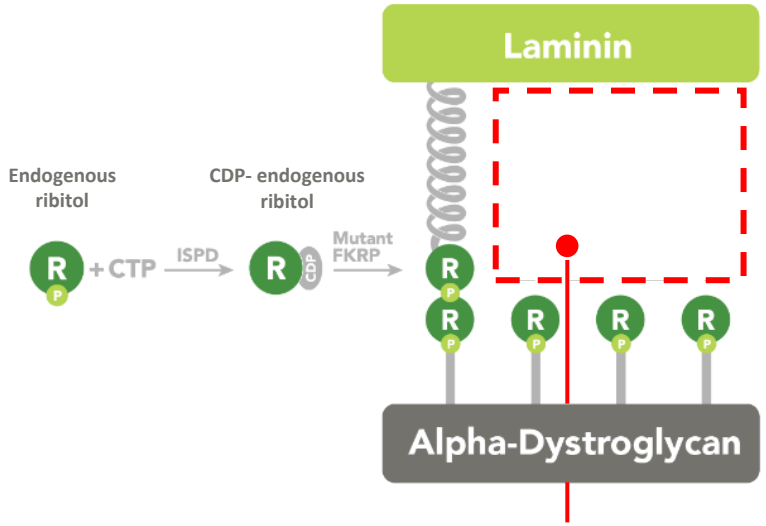
[1]Includes all patients with potentially treatable mutations

Ribitol (BBP-418) is being investigated as an upstream substrate to drive residual activity of the mutant FKRP enzyme

Disease Mechanism

Functional FKRP fully glycosylates alpha-dystroglycan (α-DG) which stabilizes cells by binding extracellular ligands

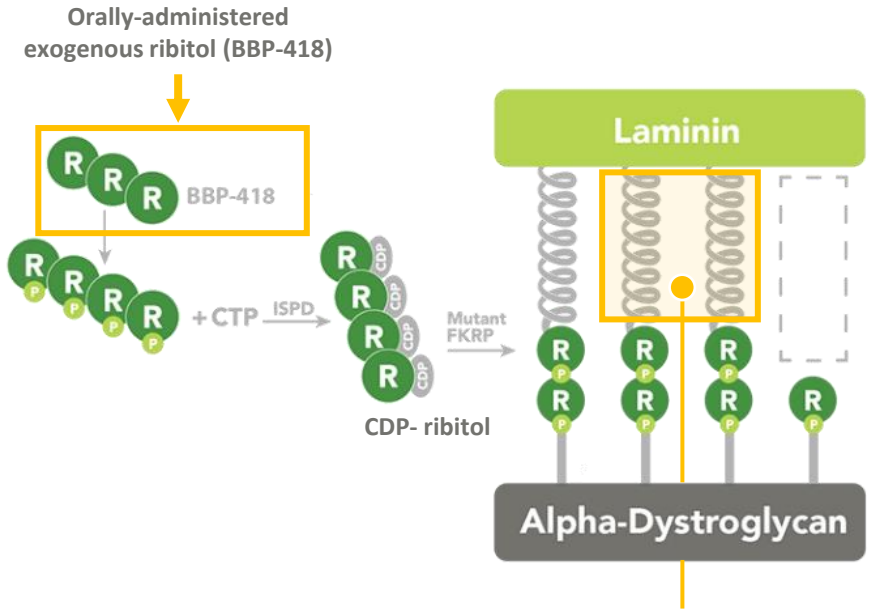
Partial loss of function mutation in FKRP result in dysfunctional, hypo-glycosylated α-DG in muscle cells which increases cell susceptibility to damage



Mutations in FKRP prevent addition of CDP-ribitol to alpha-dystroglycan (hypo-glycosylated α-DG) limiting α-DG's ability to function as a "shock absorber" for muscle fibers

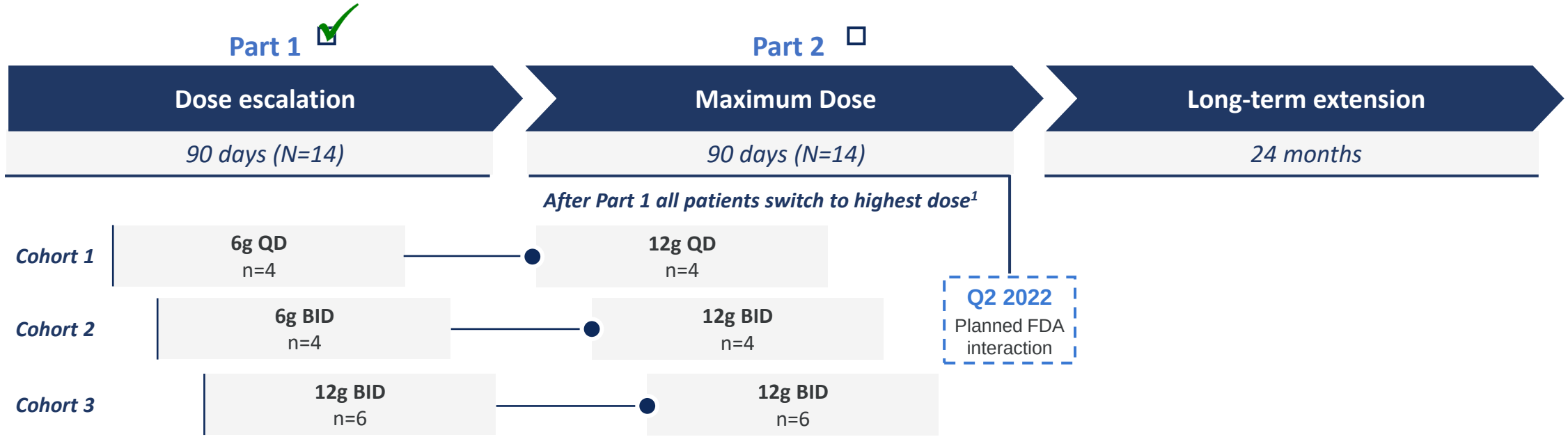
Therapeutic Approach

Supply supraphysiological levels of ribitol upstream to drive residual activity of mutant FKRP enzyme and increase α-DG glycosylation levels



Potential partial restoration of α-DG glycosylation

Ribitol (BBP-418) Phase 2 study design



Key study objectives:

- Safety and tolerability
- Dose selection for ph3
- Key biomarker parameters

Key endpoints:

- Creatine Kinase
- Ratio of glycosylated aDG to total aDG
- NSAD
- PUL2.0
- 10MWT
- FVC

Note: Doses were adjusted for weight using the following schema: 0-50 kg 6g BID, >50-70kg 9g BID, >70kg 12g BID. [1]Cohort 3 continues same dose

KRAS mutant-driven cancers

Basia

Living with pancreatic cancer (>90% KRAS-driven)

Prevalence

>500k

US & EU

Pathophysiology

RAS is the most frequently mutated oncogene, leading to abnormal cell proliferation and survival

Program Highlights

G12C dual inhibitor

MOA: first to directly bind and inhibit both GTP (active) and GDP (inactive) states of $KRAS^{G12C}$

PI3Kα:RAS Breaker

MOA: first to block RAS-driven PI3Kα activation with the potential to avoid adverse effects on glucose metabolism

G12D inhibitor

MOA: directly bind and inhibit $KRAS^{G12D}$ - the single most prevalent KRAS mutant

MOA = mechanism of action

KRAS mutations are implicated in 30% of all cancers, and we have multiple approaches against the target

Program	Mechanism of Action	Stage
$KRAS^{G12C}$ *First-In-Class*	▪ Inhibits both $KRAS^{G12C}$ GTP (active) and GDP (inactive) states; directly binds KRAS ▪ Differentiates from $KRAS^{G12C}$ GDP (inactive)-only inhibitors	Development Candidate 2022
PI3Kα Breaker *First-In-Class*	▪ Blocks specific interaction between RAS and PI3Ka ▪ RAS driver agnostic ▪ Blocks PI3K / AKT effector signaling	Development Candidate 2022
$KRAS^{G12D}$ *Best-In-Class*	▪ Potent and selective $KRAS^{G12D}$ inhibitor ▪ Directly binds KRAS	Lead Optimization
Pan-KRAS *First-In-Class*	▪ Potent pan-KRAS inhibitor ▪ Directly binds KRAS	Lead Optimization
$KRAS^{G12R}$ *First-In-Class*	▪ Potent and selective $KRAS^{G12R}$ inhibitor ▪ Directly binds KRAS	Lead Generation

All our programs are structure-based design approaches driven by protein:inhibitor co-crystal structures

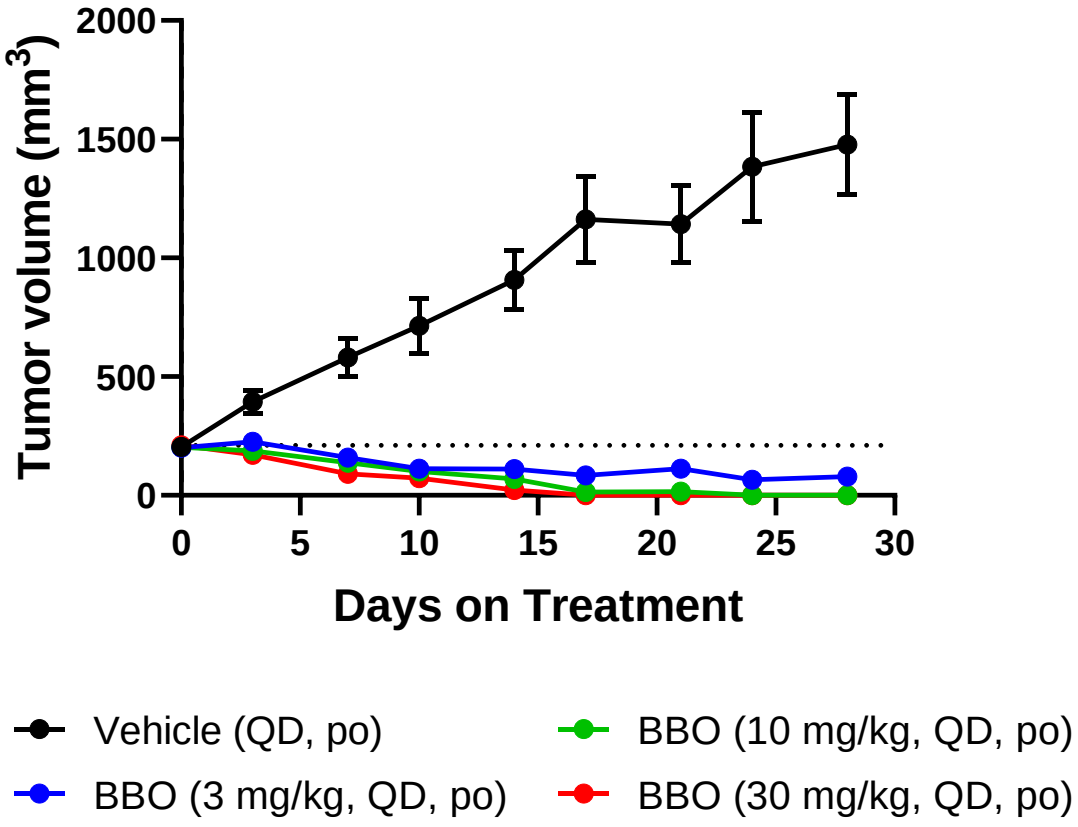
BridgeBio G12C inhibitors modify both GTP (active) and GDP (inactive) forms of $KRAS^{G12C}$

			BBP	AMG510	MRTX849
% modified	$KRAS^{G12C}$ GTP (active)	15’	100	0	0
		120’	100	0	0
	$KRAS^{G12C}$ GDP (inactive)	15’	100	80	73
		120’	100	83	80
$KRAS^{G12C}$: RAF1 Effector Binding IC_{50} (nM)			35	>100,000	20,000
H358 pERK IC_{50} @ 30’ (nM)			8	50	310

	GTP (active) / GDP (inactive) dual inhibitor e.g. BBP compounds	GDP (inactive) inhibitors e.g. AMG510, MRTX849
1 Blocks oncogenic signaling from $KRAS^{G12C}$ GTP (active)	✓	
2 Prevents $KRAS^{G12C}$ GDP (inactive) from cycling to $KRAS^{G12C}$ GTP (active)	✓	✓
3 Prevents resistance from residual $KRAS^{G12C}$ GTP (active) signaling	✓	

Note: Conclusions based on preclinical models

BBO KRAS^{G12C} inhibitor demonstrates potent efficacy in MIA PaCa-2 xenograft model

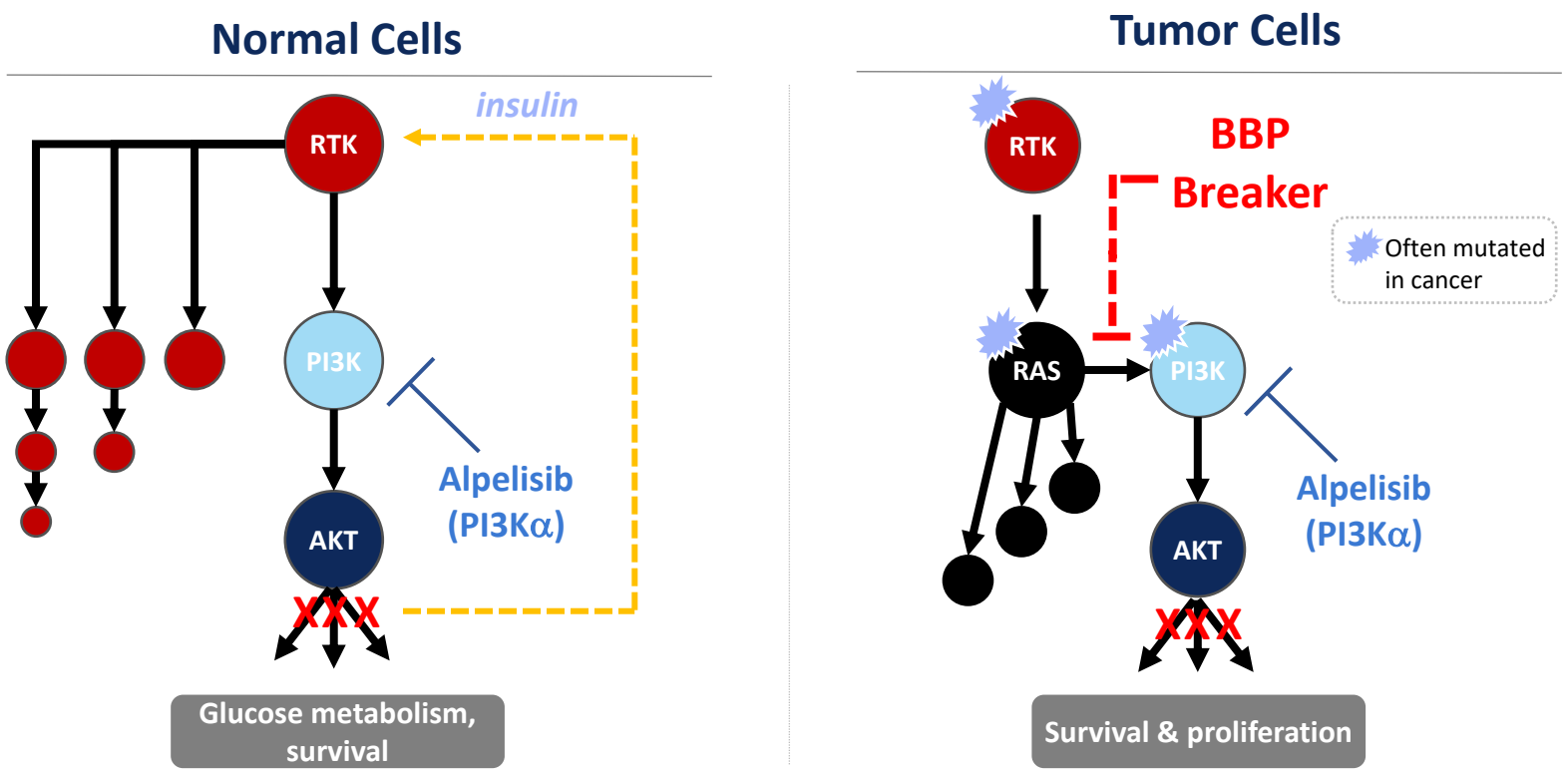


Group (n=10)	Day 28			
	Mean tumor regression	Complete regressions	P value vs vehicle	Body weight change
Vehicle	-	1/10	-	+10.4%
BBO (3 mg/kg)	60%	1/10	<0.0001	+7.1%
BBO (10 mg/kg)	100%	9/10	<0.0001	+4.7%
BBO (30 mg/kg)	100%	10/10	<0.0001	+5.6%

Two-way repeated measures ANOVA performed with Dunnett's multiple comparison test for statistical analyses (day 3 to 28)

Novel approach to target PI3Kα is tumor cell specific and differentiates from kinase inhibitors

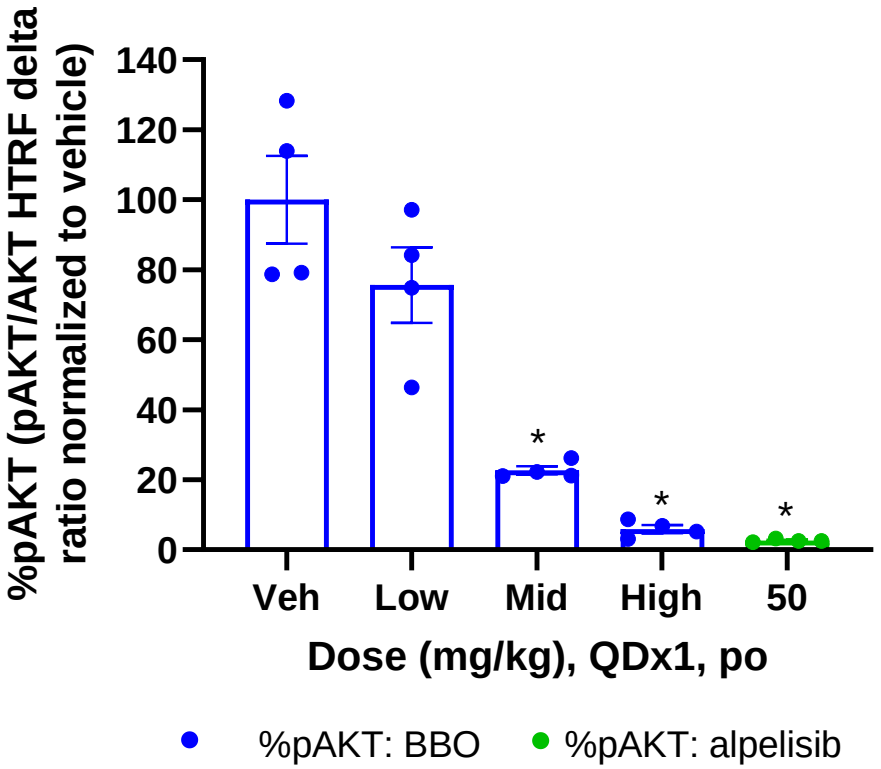
- PI3Kα kinase inhibitors ***block normal cell signaling*** as well as RAS-driven PI3Kα pathway activation in tumor cells, resulting in ***dose-limiting hyperglycemia and insulin-driven resistance***
- Our novel approach of inhibiting PI3Kα:RAS PPI with a ***"PI3Kα Breaker"*** should avoid hyperglycemia and insulin-driven resistance by specifically targeting tumor cells and may provide multiple therapeutic opportunities:
  - ***Tumors with RAS or PI3Kα helical mutations and RTK mutant/amplified drivers***
  - ***Potential combination with ERK pathway inhibition (BRAFi, MEKi, ERKi, $KRAS^{G12C}$i)***



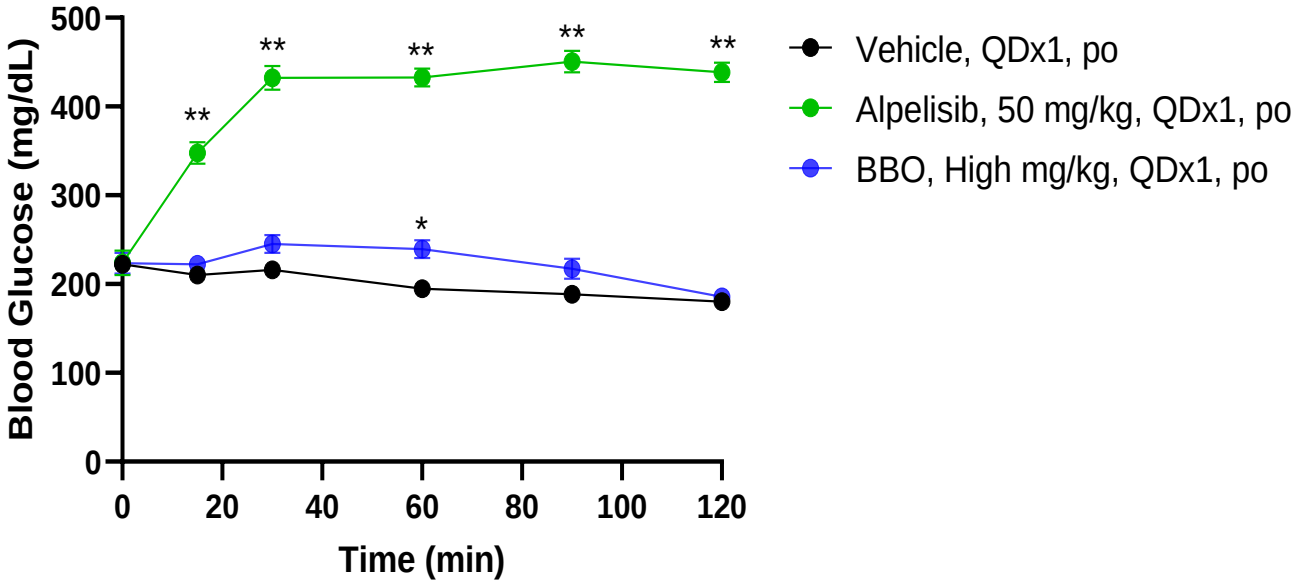
- Structural insights provide a novel approach to develop PI3Kα:RAS breakers
- PI3Kα:RAS breakers selectively bind to PI3Kα
  - PI3Kα amino acid sequence in the region of the binding pocket is unique amongst all the isoforms
  - No binding affinity to KRAS
- PI3Kα:RAS breakers do not affect kinase activity of PI3Kα

BBO induces strong pAkt inhibition in tumor xenograft model but does not induce hyperglycemia in non-tumor-bearing mice

Dose response



Blood glucose levels



Dose response: One-way ANOVA with Tukey's test vs vehicle *p<0.0001. Blood glucose levels: One-way ANOVA with Dunnett's multiple comparisons test vs vehicle: *p<0.01, **p<0.0001

BridgeBio is well capitalized with ~$800M in hand and access to up to ~$1.1B in capital to fund the portfolio through key readouts

- ✓ **Encaleret (CaSRi) for ADH1:** Ph2 proof-of-concept data
- ☐ **COL7 replacement for RDEB:** Data from Ph2 study (1H22)
- ☐ **Ribitol for LGMD2i:** Ph2 proof-of-concept data (1H22)
- ☐ **Low-dose infigratinib (FGFRi) for achondroplasia:** Ph2 proof-of-concept data (Mid-22)
- ☐ **AAV5 gene therapy for CAH:** Initial data from Ph1/2 study (2H22)
- ☐ **Acoramidis (ATTR stabilizer) for ATTR-CM:** Ph3 topline data (Mid-23)
- ☐ **Encaleret (CaSRi) for ADH1:** Ph3 topline data (2023)

BBIO is eligible to draw, at its option through YE 2022, $100M upon each of these POCs (up to a total of $300M) per the November 2021 loan agreement

Our current cash balance[1] plus access to up to an additional $300M upon achievement of portfolio proof-of-concepts through YE 2022 expected to provide runway into 2024

[1]Unaudited cash, cash equivalents and marketable securities