bridgebio

hope through
rigorous science

Corporate presentation

November 2020

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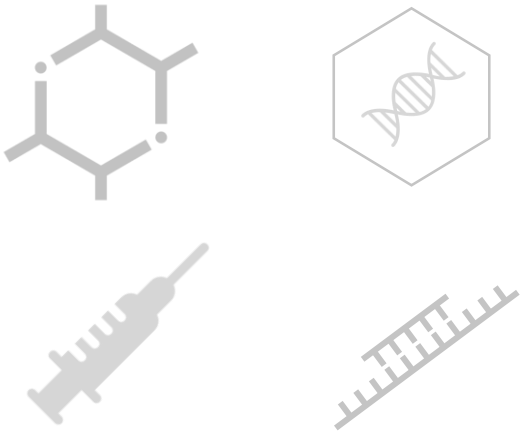
BridgeBio Pharma: Hope through rigorous science

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

BridgeBio corporate overview

Strategy

Platform

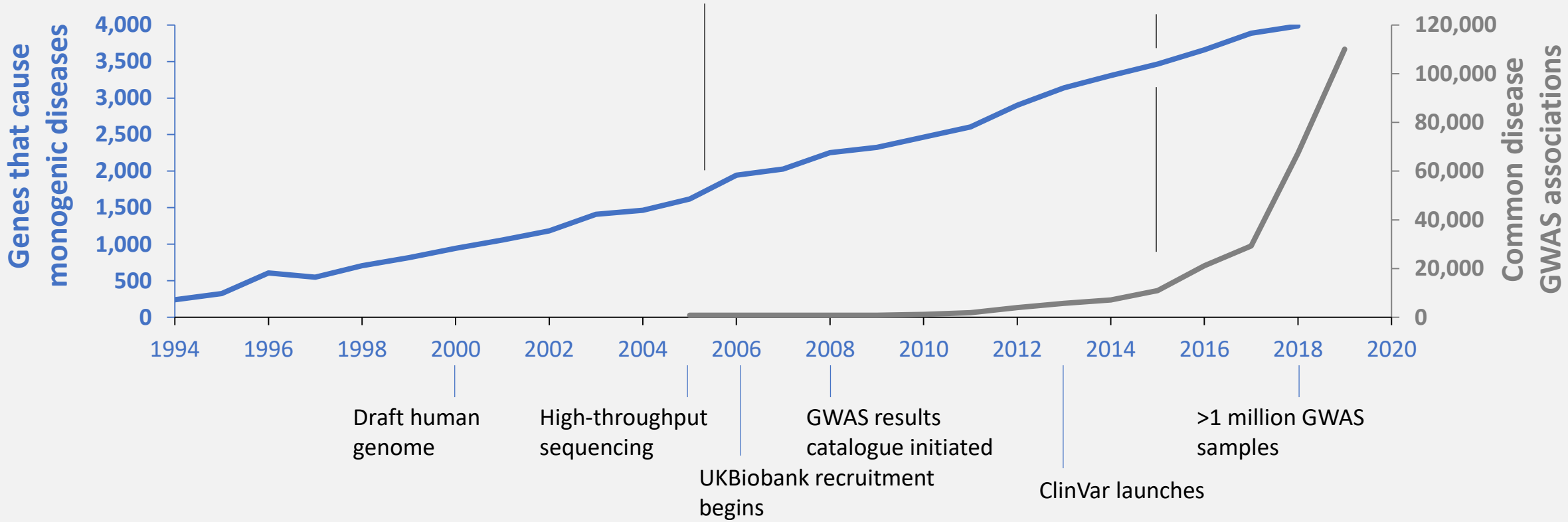


Products

We are at Day 1 in the era of genetic medicine

Hundreds of monogenic disease-causing variants are discovered every year…

…and common disease associations are increasing exponentially



Source: Claussnitzer *et al., Nature* 2020

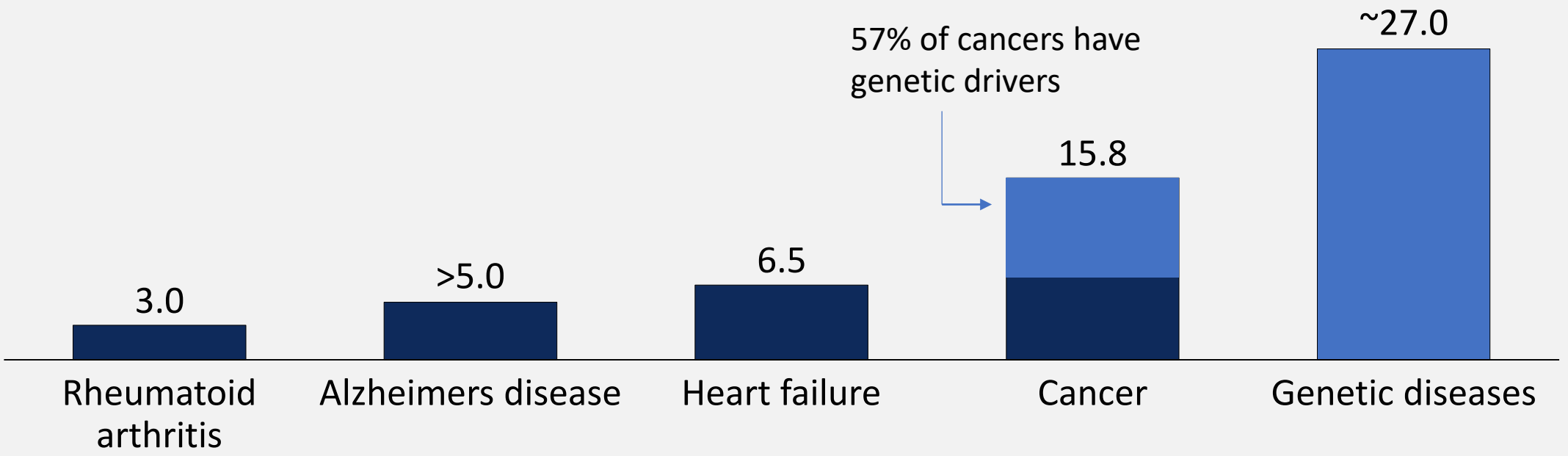
A vast opportunity to help patients

~27 million Americans are living with a genetic diseases

50% Of people affected are children

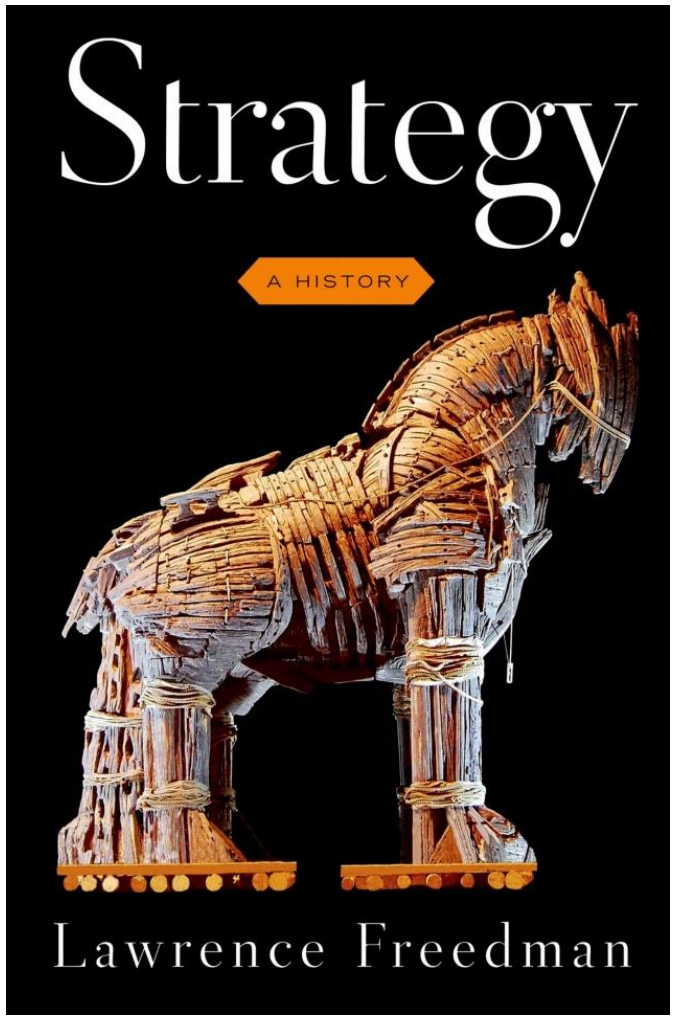
Only 5% Of these diseases have an approved therapy

US prevalence, mn



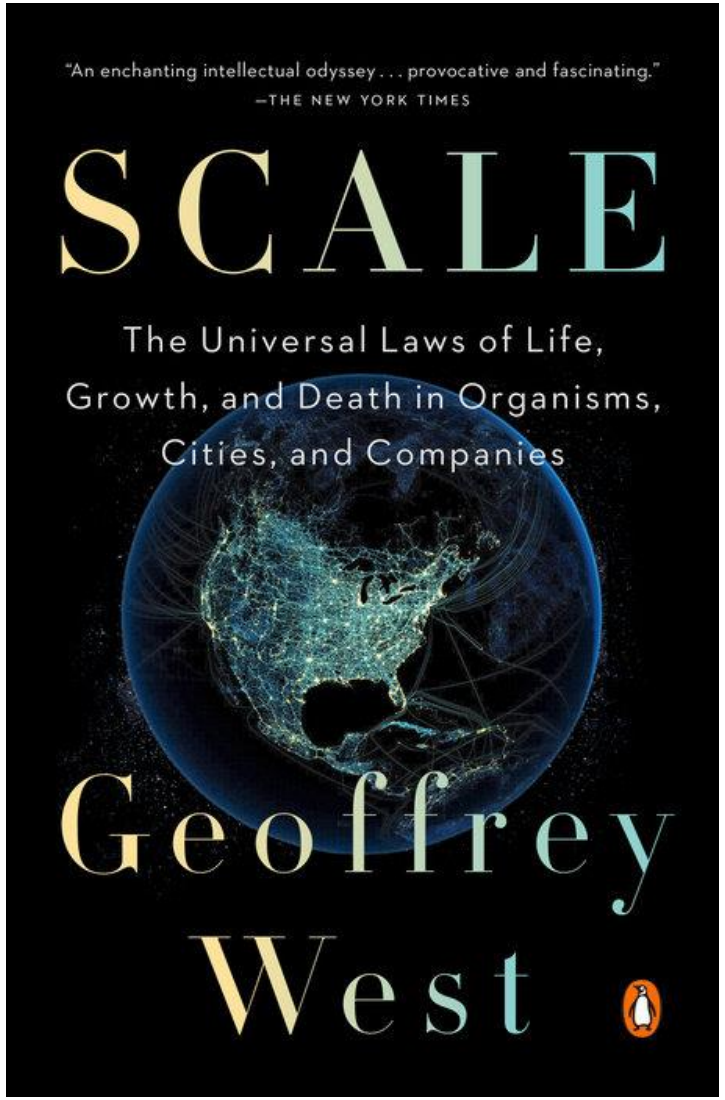
Source: Global Genes, American Cancer Society, American Heart Association, Alzheimer's Association, Arthritis Foundation, Bailey *et al., Cell* 2018

Our strategy is simple



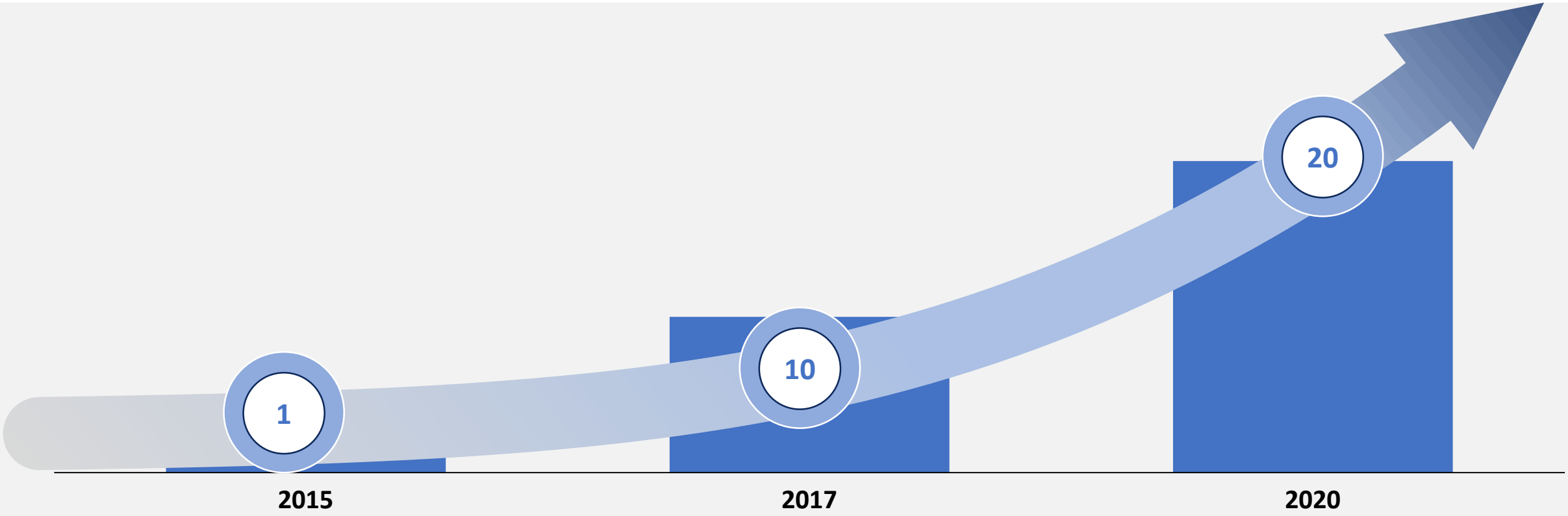
History teaches us about strategy:		BBIO applications:
1. Right playing field	→	1. Genetic disease
2. Right tenets	→	2. Beautiful science, NPV positive
3. Stay adaptive	→	3. No initial focus on TA, disease, or modality. Repeated application

Our organizational principles enable scale



History teaches us about growth:		BBIO applications:
1. Simple rules repeated at many levels	→	1. Simple rules – put patients first, think independently and let science speak, be efficient
2. De-centralized cities grow with *returns to scale*, centralized companies slow with economies of scale	→	2. De-centralized approach – small teams that focus and are incented at the level of each asset, scale that allows for rapid failure, learning

Result: Pipeline momentum



- BridgeBio founded
- 1 pipeline program

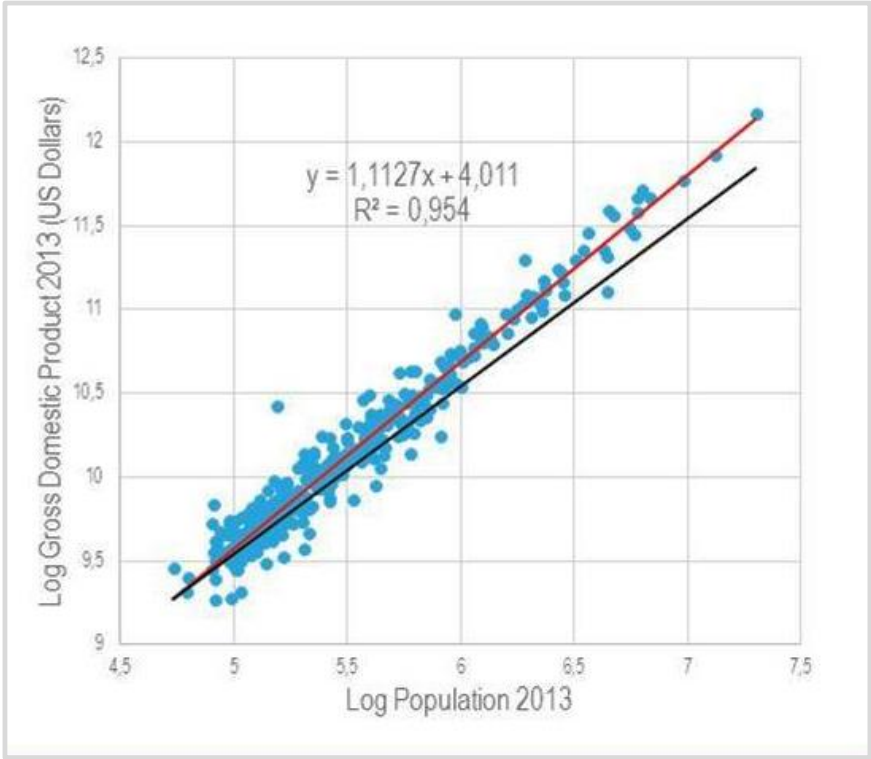
- 10 pipeline programs
- 3 clinical compounds

- 20+ programs
- Multiple $1B+ opportunities in Ph3
- Two NDA submissions
- >10 INDs in 5 years

Increasing returns to scale – BridgeBio since IPO

Achievement:

- NDA for MoCD Type A accepted, ODD & Fast Track received for 2L CCA program
- 7 INDs filed
- Twelve new clinical trials initiated (18 total), >400 trial sites across 26 countries
- 8 new programs, including LGMD2i and ADH1, both in the clinic
- TTR clinical data, DEB clinical data, CAH and Canavan pre-clinical data, achon pre-clinical data, TIO data



BridgeBio corporate overview

Strategy

Platform

Products

BridgeBio drug engineering basics: our platform

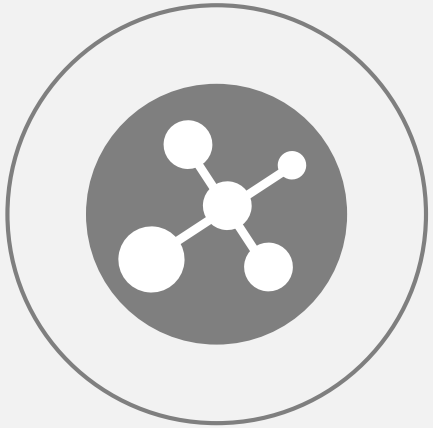
Discover

Novel genetic disease targets

Well described diseases than can be targeted at their source

Create

Medicines with industry-leading research capabilities



Tailored therapeutic technologies to create first or best-in-class medicines

Test

Our drugs through global development footprint

Broad clinical development capabilities across therapeutic areas and geographies

Deliver

Our products to patients through commercial infrastructure

Building the capabilities to deliver genetic medicines to patients globally

Discover

Capabilities to identify new genetic disease targets at scale

Our target identification engine is driven by three core areas of strength:

Computational genomics / statistical genetics

- Mining of large genotype-phenotype databases
- *De novo* target discovery
- Target validation
- Indication expansion

Systematic disease mapping

- Manual annotation and prioritization of the 7K known genetic diseases

Partnering with top academic researchers

- >15 current partnerships

Johns Hopkins University

The University of Texas MD Anderson Cancer Center
Making Cancer History®

Boston Children's Hospital
Until every child is well™

Cincinnati Children's™

Stanford University

Discover

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

Create

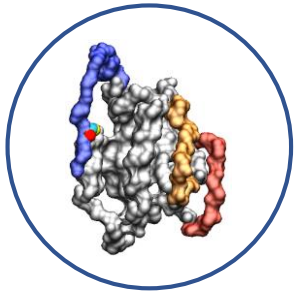
We select the optimal therapeutic modality to target each disease at its source

Industry-leading capabilities across 4 modalities:

Medicinal chemistry

- Molecular dynamics
- Reversible and irreversible chemistry
- Topical formulations

Optimal use: Inhibition of GOF or allosteric activation of LOF mutations



Gene therapy

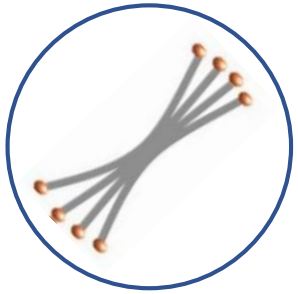
- Vector optimization
- Novel capsid engineering
- Analytical assay development

Optimal use: Replacement of intracellular protein in LOF diseases

Therapeutic proteins

- Large protein manufacturing
- Formulation expertise
- Comparability assay development

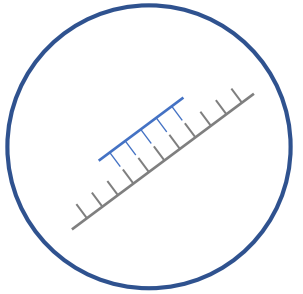
Optimal use: Replacement of extracellular protein in LOF diseases



Antisense oligonucleotides

- Target mapping with functional genomics
- Activity screening assay development
- Novel backbone and base chemistry

Optimal use: Inhibition of GOF or activation of WT allele in LOF diseases



GOF = gain-of-function, LOF = loss-of-function, WT = wild type

Create

Research leaders with a productive history developing novel therapeutics

Mendelian	Oncology	Gene therapy

Uma Sinha, PhD
Chief Scientific Officer

GBT
PORTOLA PHARMACEUTICALS

Robert Zamboni, PhD
Chemistry

MERCK FROSST

Eli Wallace, PhD
Chief Scientific Officer, Oncology

Peloton Therapeutics
ARRAY BIOPHARMA

Pedro Beltran, PhD
SVP, Oncology

AMGEN
UNITY BIOTECHNOLOGY

Clayton Beard, PhD
SVP, Research and Development

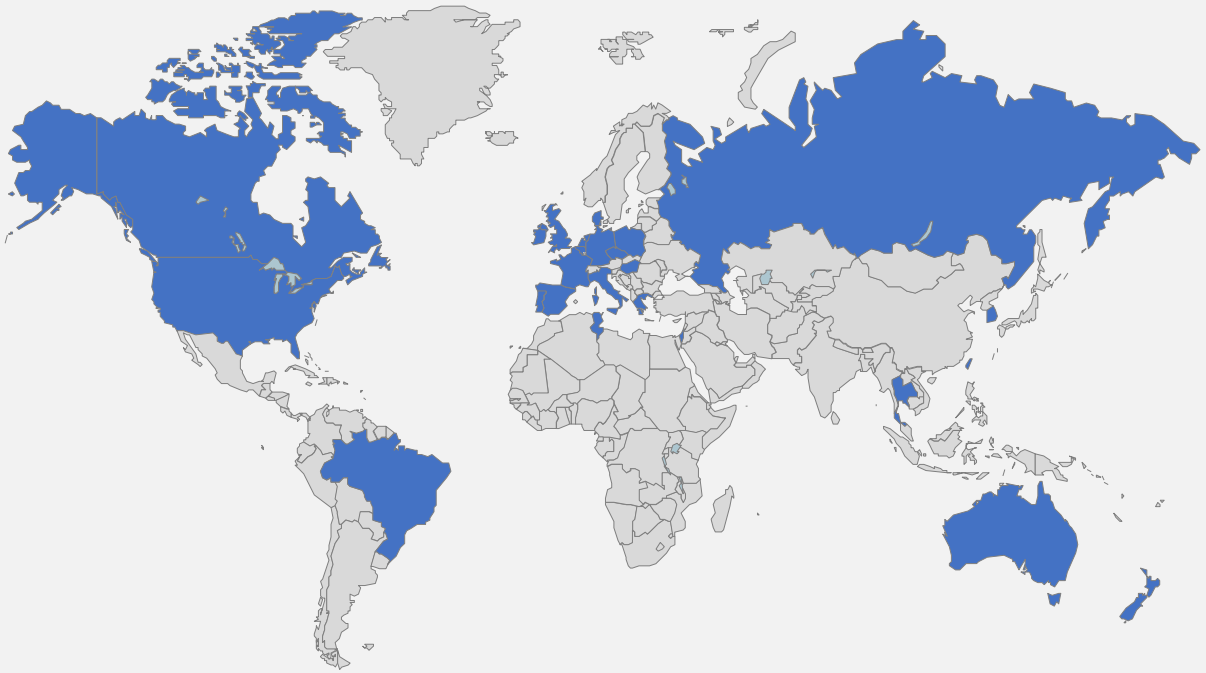
PRECISION BIOSCIENCES
NOVARTIS

Our global clinical development footprint

Test

- **18 ongoing trials** across 5 different therapeutic areas, >400 trial sites, and 26 countries
- **Creative clinical and regulatory strategy,** e.g., unique, nested Phase 3 trial design for acoramadis in ATTR
- **Central operations toolkit** for enrollment, protocol quality, site activation, CRO quality, regional performance
- **Expert, dedicated R&D teams** in each therapeutic area
  - **Cardio/renal:** Jonathan Fox, MD, PhD
  - **Oncology:** Susan Moran, MD
  - **Gene Therapy:** Adam Shaywitz, MD, PhD

Countries with BridgeBio trial sites



Deliver

Building capabilities to deliver our products to patients across the globe

- **Global commercial infrastructure** to leverage our drug and disease expertise
- **Diagnostic partnerships** to identify patients in need of our medicines
- **Disease awareness strategies** including close partnerships with patient advocacy groups
- **Country-specific Early Access Programs** (EAP) and patient assistance programs
- **Commercial partners in strategic geographies:**

FGFRi and SHP2i in China: LianBio

TTR in Japan: Alexion

MoCD type A in Israel: Medison Delivering Innovative Healthcare

Key people: Matt Outten (CCO), Jennifer Cook (BOD), Brent Saunders (BOD)

The platform is delivering

Discover
Novel genetic disease targets

20+
Disclosed programs in the pipeline

Create
Medicines with industry-leading research capabilities

>10
INDs since 2015

Test
Our drugs through global development footprint

18
Clinical trials across the globe

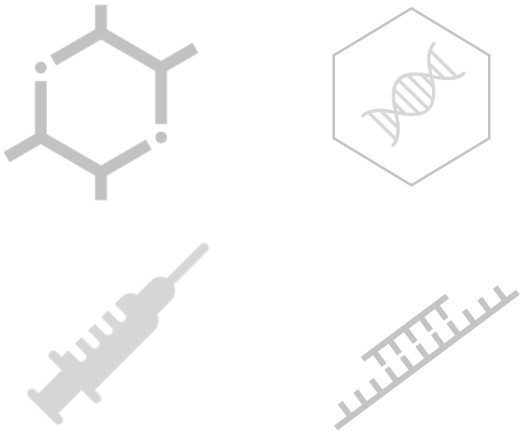
Deliver
Our products to patients through commercial infrastructure

2
Product launches expected in 2021

BridgeBio corporate overview

Strategy

Platform



Products

Our pipeline of 20+ development programs spans multiple therapeutic areas and drug modalities

Small molecule | Topical small molecule | Biologics | Gene therapy

Portfolio segment	Program	Drug mechanism	Diseases	Patient pop. (US+EU)	Modality	Preclinical: Discovery	Preclinical: IND-enabling	Clinical: Phase1	Clinical: Phase 2	Clinical: Phase 3
Mendelian	**Acoramidis**	TTR stabilizer	ATTR-CM	>400K	Small molecule					NDA filed
	Fosdenopterin	cPMP replacement	MoCD type A	100	Small molecule					NDA filed
	Infigratinib	Low-dose FGFR1-3i	Achondroplasia	55K	Small molecule					
	Encaleret	CaSR antagonist	ADH1 / HP	12K[1] / 200K	Small molecule					
	Zuretinol	Synthetic retinoid	IRD (RPE65 or LRAT)	3K	Small molecule					
	BBP-418	Glycosylation substrate	LGMD2i	7K	Small molecule					
	BBP-711	GO1 inhibitor	PH1 / FSF	5K / 1.5M	Small molecule					
	BBP-671	PanK activator	PKAN / OA	7K	Small molecule					
	BBP-761	Succinate prodrug	LHON	20K	Small molecule					
	BBP-472	PI3Kβi	PTEN autism	120K	Small molecule					
Genetic Dermatology	**Patidegib[2]**	Topical SMOi	Gorlin / BCC	120K	Topical small molecule					
	BBP-589	Recombinant COL7	RDEB	1.5K	Biologics					
	BBP-681	Topical PI3Kai	VM / LM	117K	Topical small molecule					
	BBP-561	Topical KLK 5/7i	Netherton	11K	Topical small molecule					
Targeted Oncology	**Infigratinib**	FGFR1-3i	FGFR+ tumors	37K	Small molecule					
	BBP-398	SHP2i	Multiple tumors	>500K	Small molecule					
	BBP-454	Pan-mutant KRASi	KRAS+ tumors	>500K	Small molecule					
	BBP-954	GPX4i	Multiple tumors	>500K	Small molecule					
Gene Therapy	**BBP-631**	21-OH gene therapy	CAH	>75K	Gene therapy					
	BBP-812	ASPA gene therapy	Canavan	1K	Gene therapy					
	BBP-815	TMC1 gene therapy	Genetic hearing loss	10K	Gene therapy					

1 US carriers; 2 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.

Four core value drivers over the next 12-18 months

Program	Patient population	Status	Upcoming event(s)
Acoramidis: TTR stabilizer for ATTR	>400K	ATTR-CM Ph3 ongoing	❑ Topline Ph3 part A data late-2021 / early-2022 ❑ Topline Ph3 part B data 2023
Low-dose infigratinib (FGFRi) for achondroplasia	55K	Enrolling Ph2 study	✓ Dose first child ❑ Phase 2 data 2021
Gene therapy for congenital adrenal hyperplasia (BBP-631)	>75K	GLP tox ongoing	❑ File IND ❑ Phase 1/2 data 2021
Encaleret: CaSR inhibitor for autosomal dominant hypocalcemia type 1 (ADH1)	12K	Ph2 ongoing	✓ FPI in Ph2 study ❑ Phase 2 data 2021

$711mn in cash and equivalents as of September 2020 expected to provide runway into 2022

A pipeline with multi-blockbuster potential

$1B+
opportunities
in the pipeline

1) **Acoramidis** for ATTR CM and PN
2) **Low-dose infigratinib** for achondroplasia
3) **AAV5 gene therapy** for congenital adrenal hyperplasia
4) **High-dose infigratinib** for adjuvant urothelial carcinoma
5) **Pan-mutant KRAS inhibitor** for KRAS+ cancer
6) **SHP2 inhibitor** for RAS and kinase mutant cancer
7) **GPX4 inhibitor** for multiple tumor types
8) **GO1 inhibitor** for frequent kidney stone formers

Acoramidis (AG10) for transthyretin (TTR) amyloidosis (ATTR)

Art
ATTR-CM patient

Seeking to address large and growing need in ATTR, a progressive and fatal disease affecting >400K patients

Designed to target the disease at its source by stabilizing TTR, a genetically and clinically validated mechanism

Advancing acoramidis, a potential best-in-class drug that mimics naturally occurring rescue mutation

Acoramidis has been **well-tolerated and demonstrated near-complete TTR stabilization** in Phase 1 and Phase 2 studies

Executing Phase 3 study with top-line data expected in late-2021 / early-2022

Acoramidis was designed to treat ATTR at its source

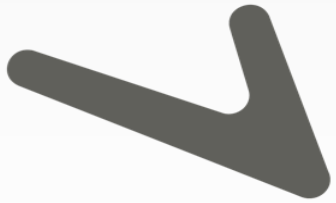
Disease mechanism

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

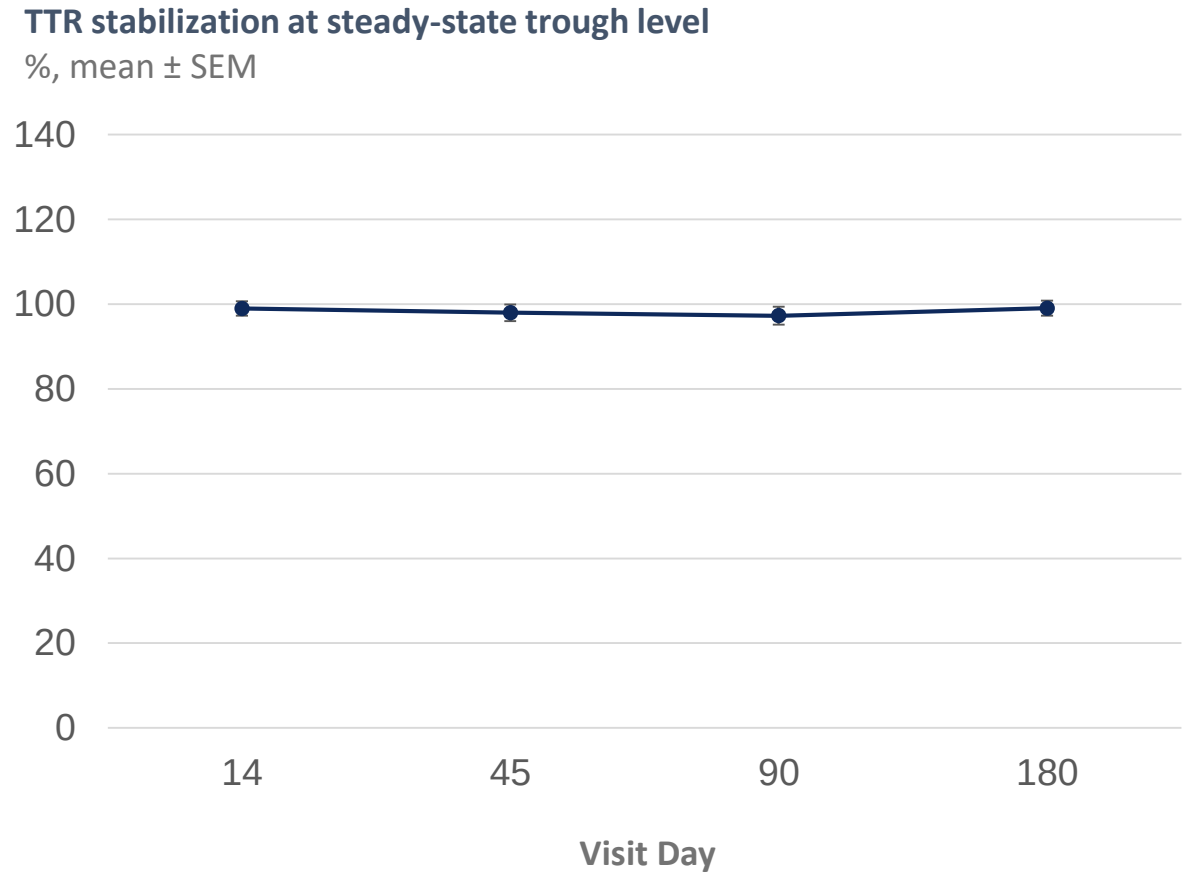
Acoramidis was designed to mimic protective T119M mutation by stabilizing TTR tetramers to slow or halt disease progression

Acoramidis has been well-tolerated and demonstrated near-complete TTR stabilization in pre-clinical, Ph1, and Ph2 studies

Phase 2 safety summary[1]

	Placebo N = 17	Acoramidis (pooled doses) N = 32
Any Adverse Event	**15 (88%)**	**21 (66%)**
Mild	6 (35%)	11 (34%)
Moderate	8 (47%)	9 (28%)
Severe	1 (6%)	1 (3%)
Any Serious Adverse Event	**2 (12%)**	**1 (3%)**
AF and CHF	1 (6%)[1]	0
Leg cellulitis	1 (6%)	0
Dyspnea	0	1 (3%)

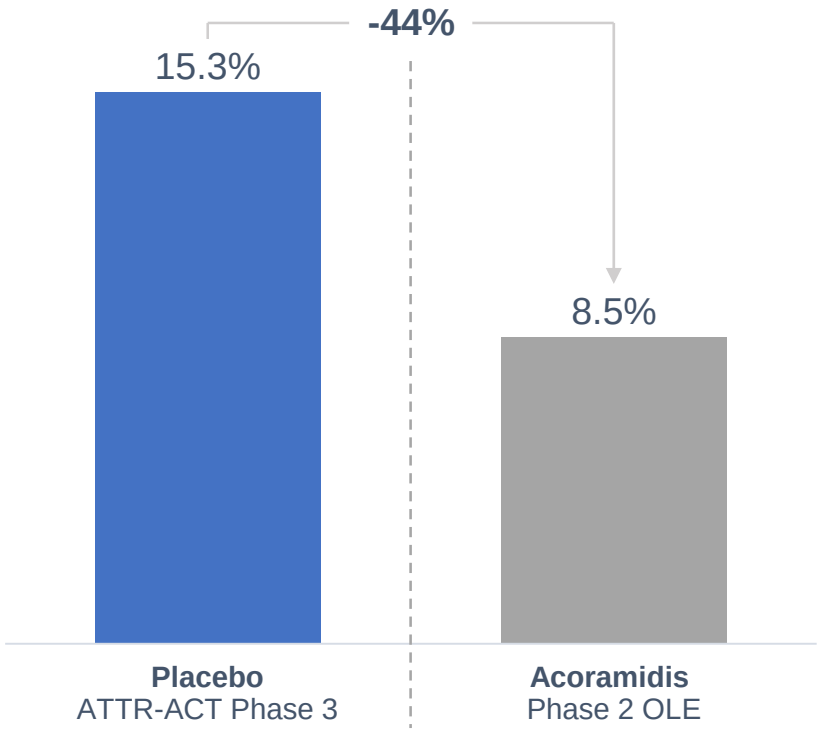
Phase 2 TTR stabilization[2]



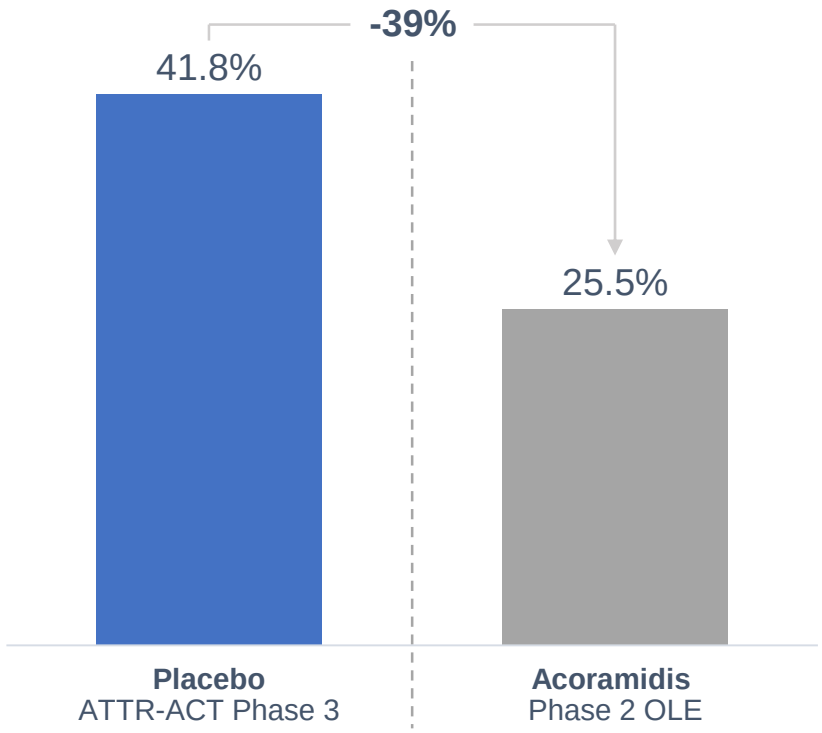
1 Judge, D.P. et al. JACC Vol. 74, No. 3, 2019:285 – 95
2 Judge, D.P. et al. American Heart Association 2019

Deaths and CV hospitalizations reported in acoramidis Phase 2 OLE were lower than in placebo-treated ATTR-ACT participants

All-cause mortality at 15 months
Participants died or receiving transplant (%)

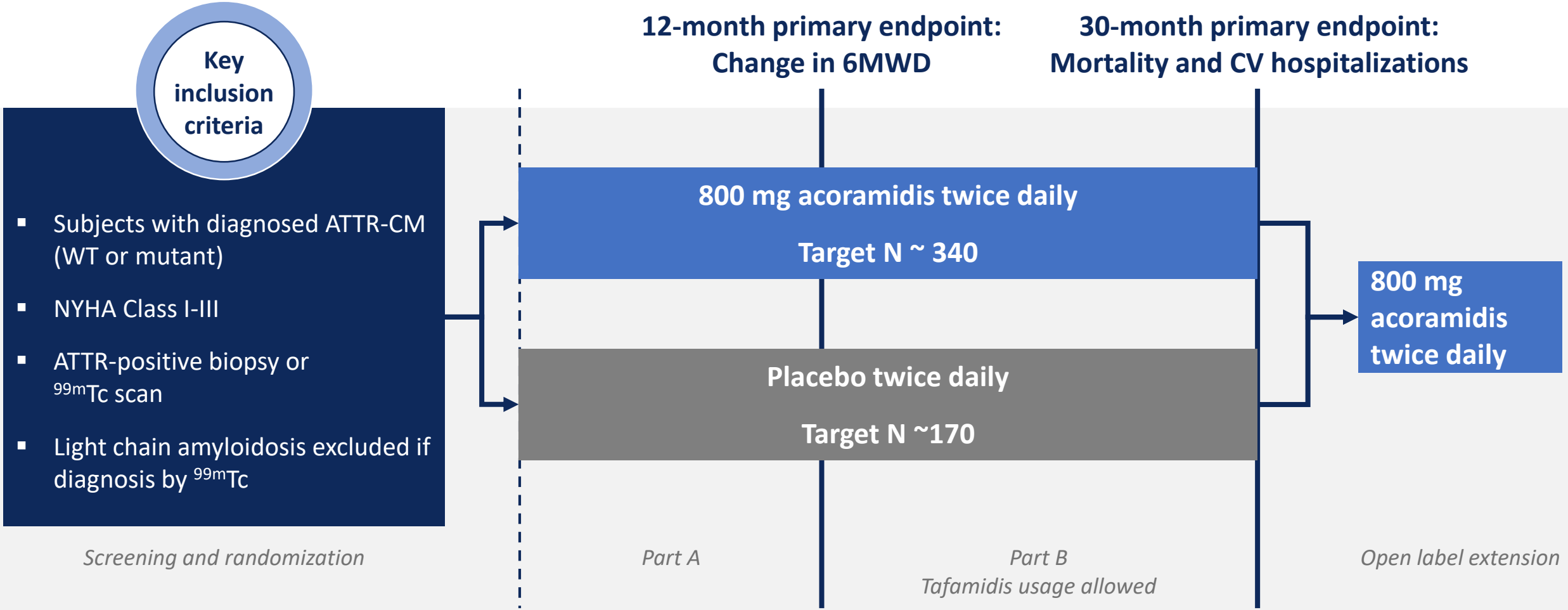


Cardiovascular hospitalizations at 15 months
Participants with ≥1 CV hospitalization (%)



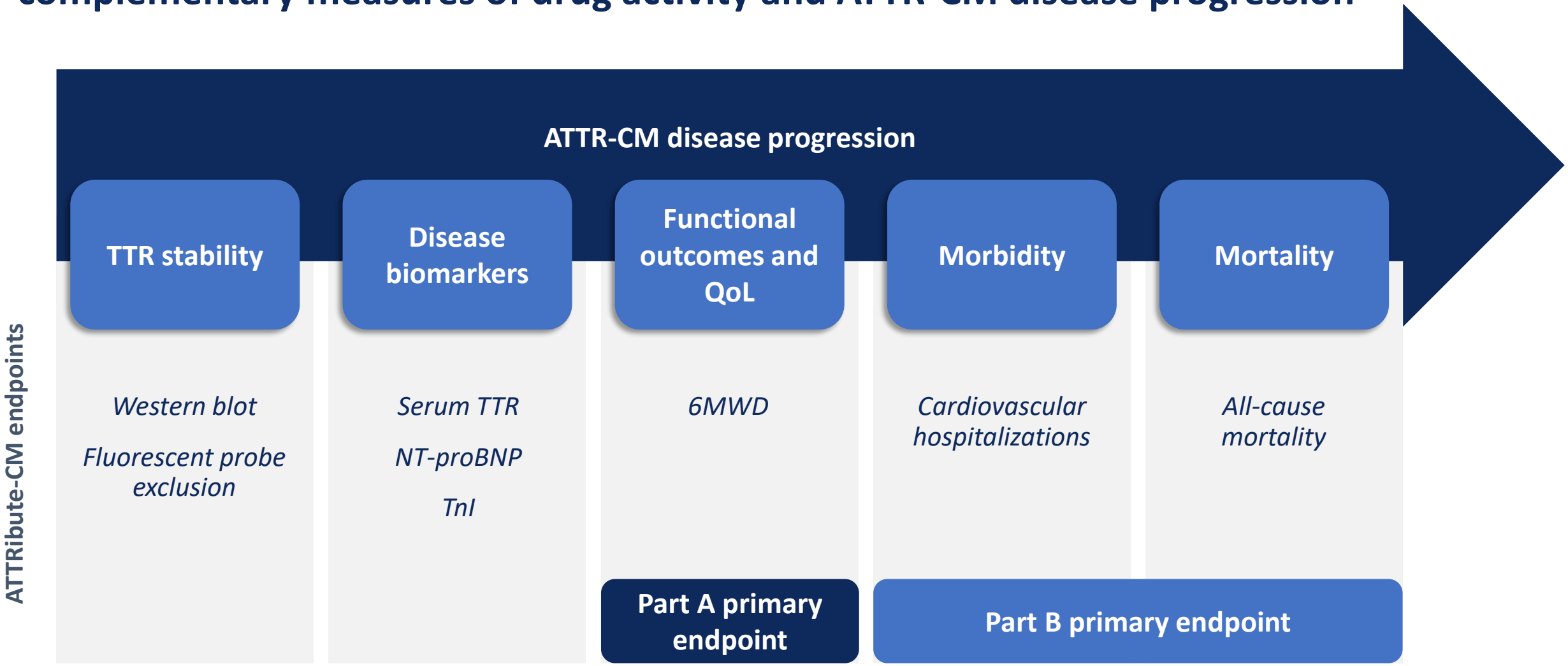
1 Based on routine adverse event reporting
Note: These data are based on a cross-trial comparison and not a randomized clinical trial. As a result, the values shown may not be directly comparable
Source: Judge, DP et al. American Heart Association Scientific Sessions 2019

ATTRibute-CM will provide 12-month functional outcome data and 30-month mortality and CV hospitalization data



6MWD = Six-minute walk distance; NYHA = New York Heart Association;
^{99m}Tc = Technetium labeled pyrophosphate (PYP) or bisphosphonate (e.g., DPD);
CV = cardiovascular-related

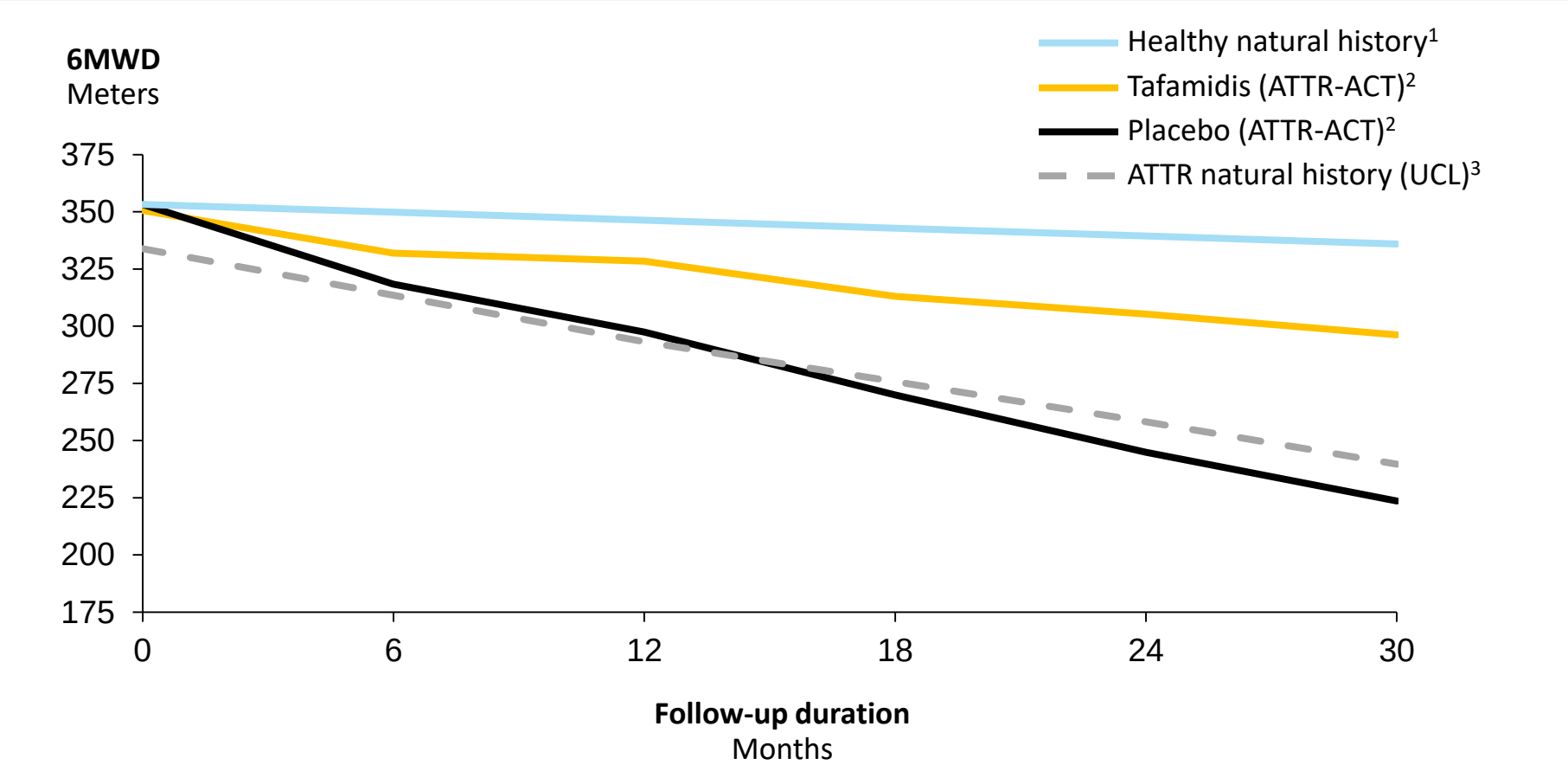
ATTRibute-CM is designed to evaluate safety and efficacy of acoramidis across complementary measures of drug activity and ATTR-CM disease progression



NT-proBNP = N-terminal pro b-type natriuretic peptide; TnI = Troponin I; 6MWD = Six-minute walk distance
QoL = Quality of life

Rapid functional decline in untreated ATTR-CM patients provides opportunity to demonstrate robust clinical benefit

Summary of 6MWD data in ATTR-CM and healthy cohorts

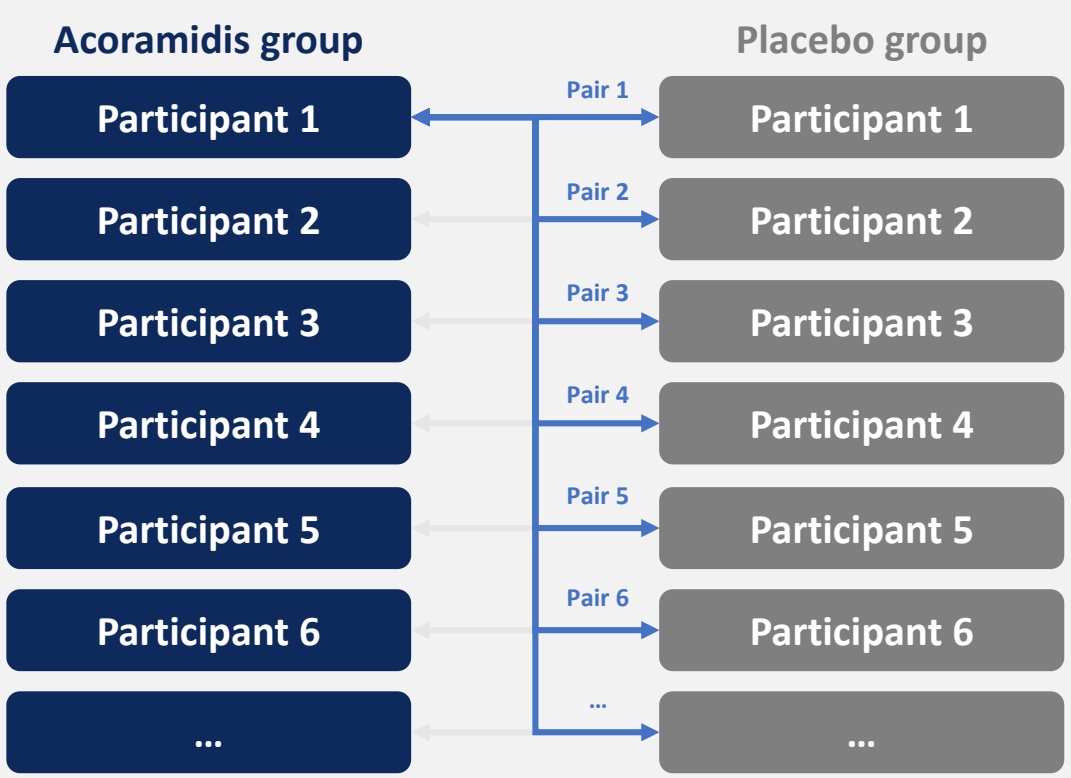


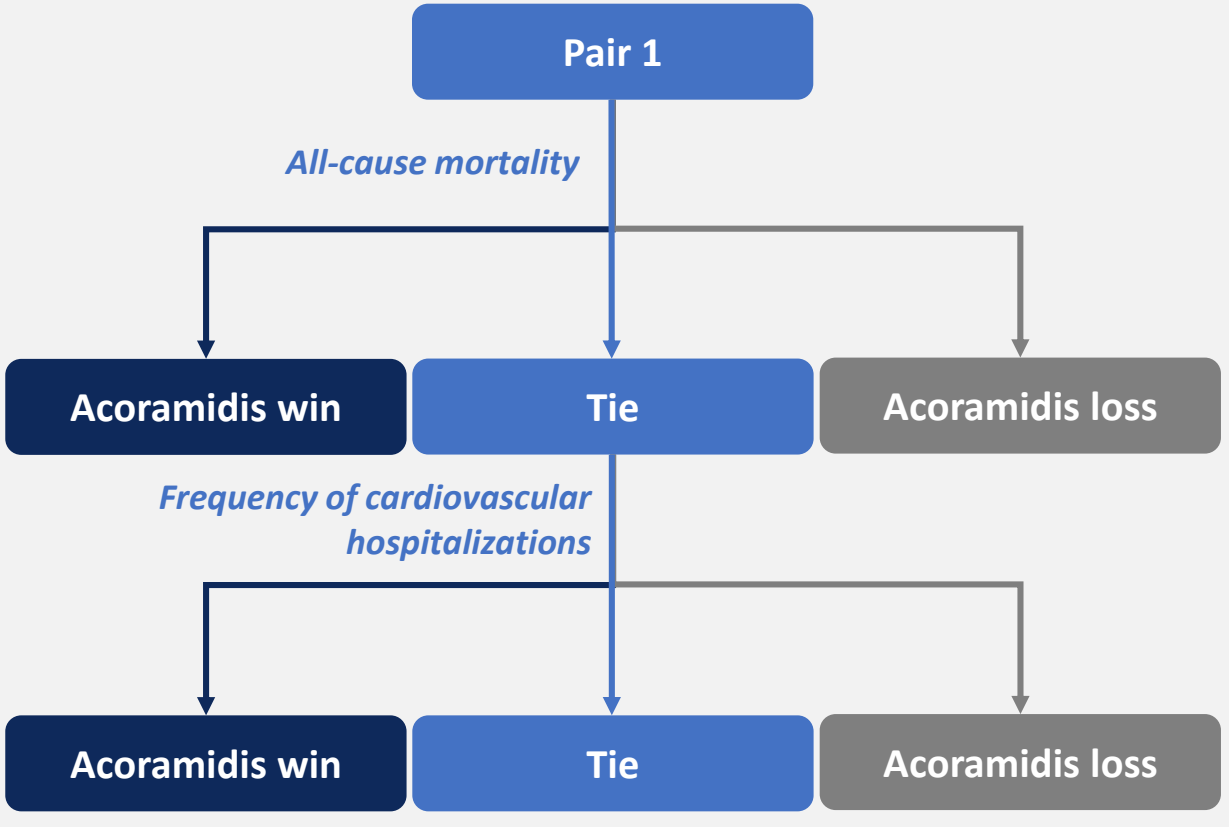
Optimal profile for acoramidis would markedly slow or halt decline in 6MWD in trial participants

1. Enright, P.L. et al. Chest 2003. N = 3333 healthy elderly adults, baseline set to match ATTR-ACT placebo group
2. Maurer, M.S. et al. NEJM 2018. N = 264 (tafamidis), N = 177 (placebo) ATTR-CM trial participants
3. Lane, T.L. et al. Circulation 2019. N = 1034 ATTR-CM patients

Part B endpoint will hierarchically compare mortality and cardiovascular hospitalizations between all pairs of trial participants

Schematic illustration of win ratio analysis[1]

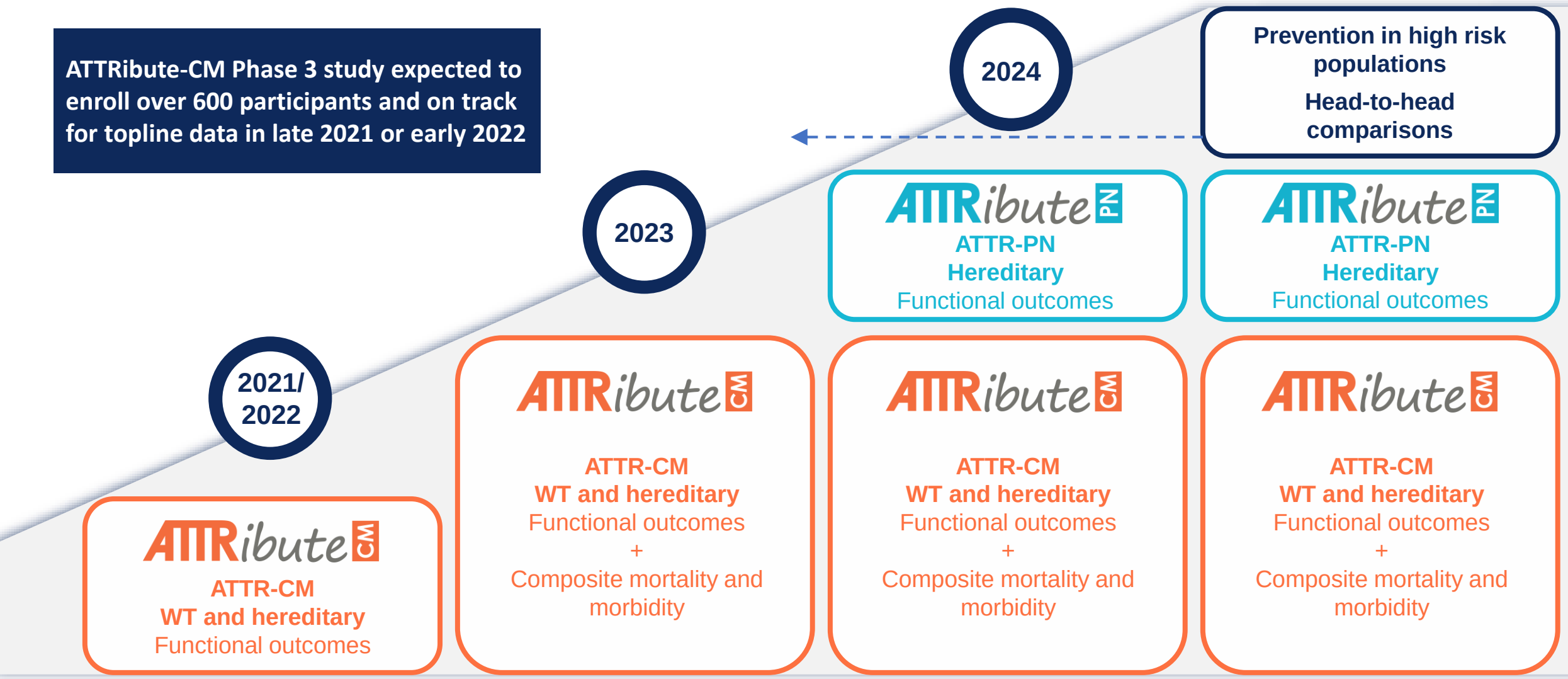




1 Primary analysis of ATTRibute-CM will use a modified win ratio analysis (Finkelstein-Schoenfeld)

Ongoing and planned studies of acoramidis aim to continually expand clinical evidence and addressable patient population

ATTRibute-CM Phase 3 study expected to enroll over 600 participants and on track for topline data in late 2021 or early 2022



Claudia,
child with achondroplasia

Low-dose FGFR inhibitor (infigratinib) for achondroplasia

Achondroplasia overview

Prevalence

55,000 (US+EU) –
one of the most common genetic conditions

Genetic driver

FGFR3 activation

Pathophysiology

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

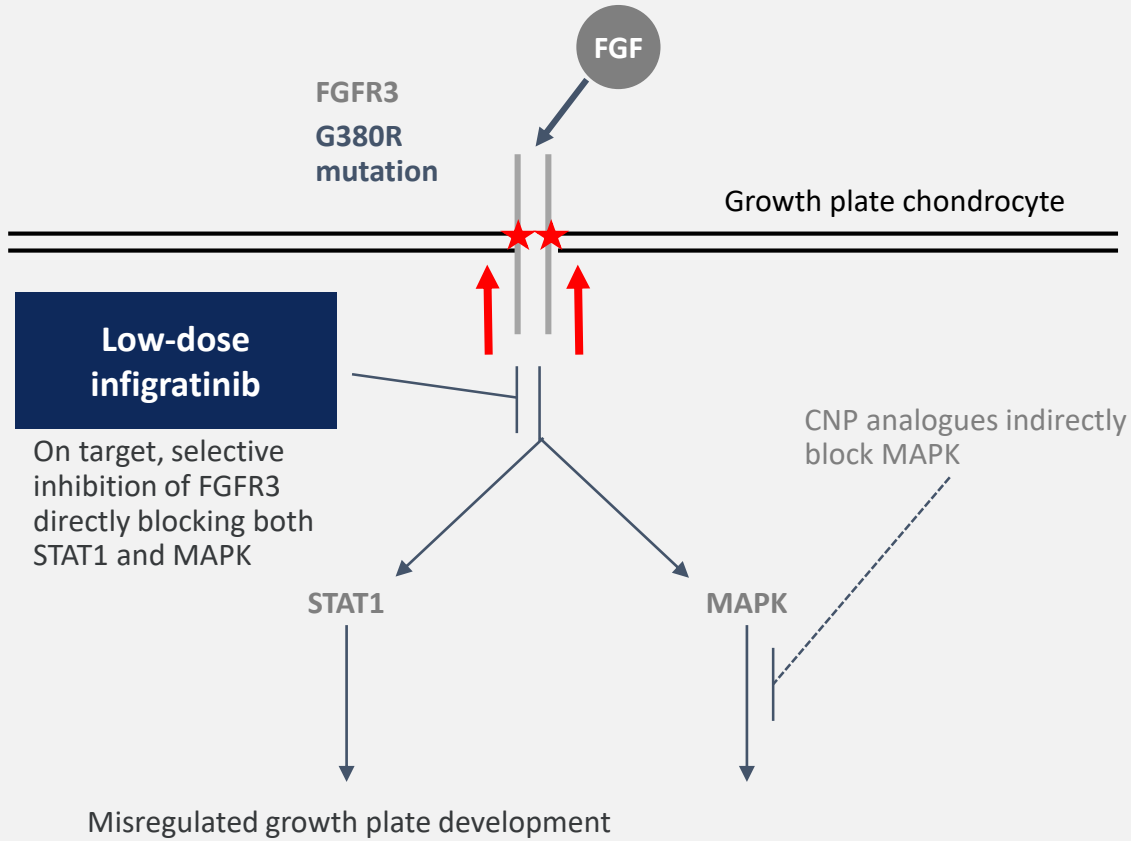
Features of a potential best-in-class medicine for achondroplasia

Direct targeting of FGFR3 and normalization of both STAT1 and MAPK signaling pathways

Potential to address all drivers of symptoms, including cranial, spinal and stature issues

Oral dosing, the most convenient solution for children with achondroplasia and their families

Potential best-in-class approach targeting achondroplasia directly at its genetic source



ACH FGFR3 gain-of-function mutation causes:

- 2-3x over-activation of the receptor
- Up-regulation of downstream pathways STAT1 and MAPK
- Aberrant growth plate development, which causes cranial, spinal, and stature symptoms

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

Low-dose infigratinib improves all the key drivers of clinical symptomology in validated ACH mouse model

FGFR3 WT
No treatment

FGFR3$^{Y367C/+}$
No treatment

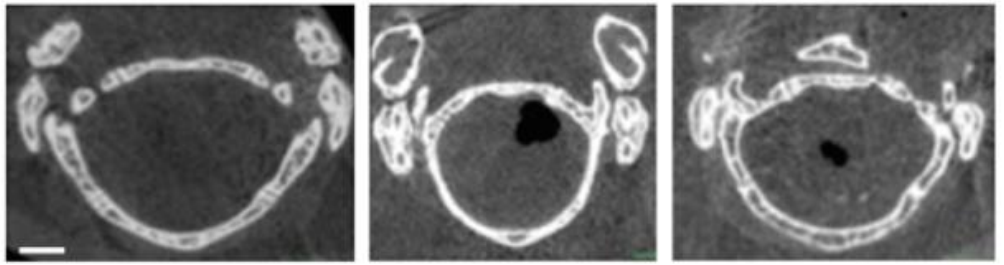
FGFR3$^{Y367C/+}$
Infigratinib tx

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

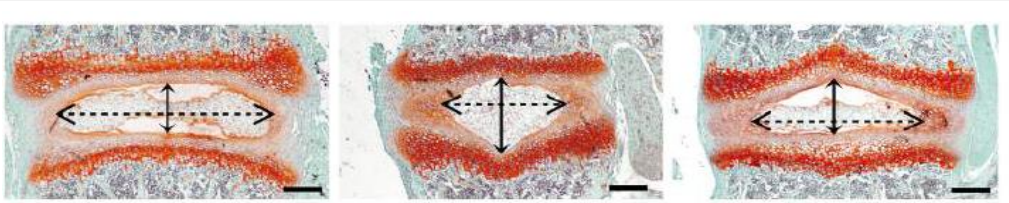


2 Disorders of the spine

12% increase in L4-L6 length

73% increase in disc width

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

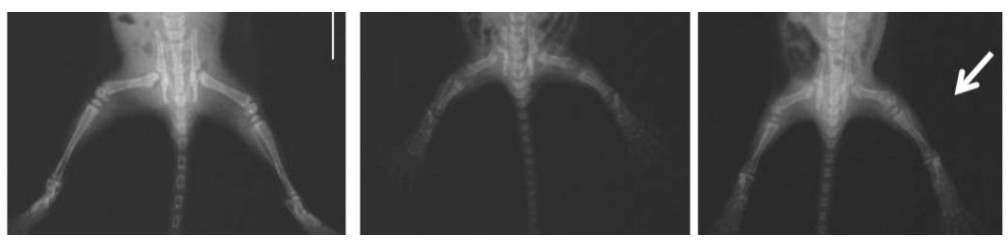


3 Disproportionate short stature

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 dos

Low-dose infigratinib showed potential best in-class preclinical profile in validated achondroplasia mouse model

Company/ Asset	MOA	Route	Status	Mouse model	Tibia length	Femur	Foramen magnum area	L4-L6 height
bridgebio Infigratinib	**Selective FGFR1-3i**	**Oral**	**Ph2**	**FGFR3^{Y367C}**	32.6%	20.9%	17.0%	12.1%
BIOMARIN Vosoritide (BMN111)	CNP analogue	Daily SQ	Pivotal (NDA filed)	FGFR3$^{Y367C/+}$	6.6%	5.2%	**No known publicly available data**	3.3%
ascendis pharma TransCon CNP[1]	CNP analogue	Weekly SQ	Ph2	FGFR3$^{Y367C/+}$	12.3%			
Pfizer Reifercept (TA-46)	FGFR3 decoy	Weekly SQ	Ph1	FGFR3^{ACH}	8.6%	6.2%		

Preclinical data from infigratinib and other investigational achondroplasia therapies

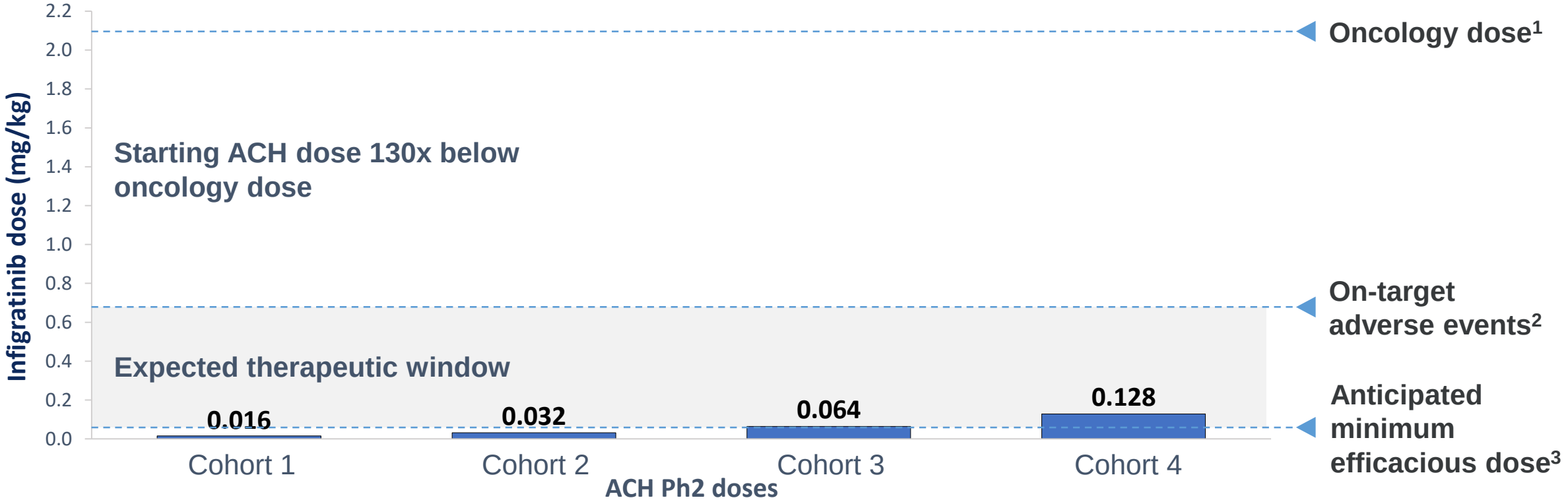
Percent increase compared to non-treated mouse

Source: Komla-Ebri et al. J Clin Inv 2016, 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 FGFR3$^{Y367C/+}$, FGFR3$^{ACH/+}$ mouse as noted in "Mouse model" columns
Infigratinib treatment with 2mg/kg subcutaneous dose [1]Based on vosoritide continuous infusion; *Value estimated using DigitizeIt.

We have a wide anticipated therapeutic index in achondroplasia

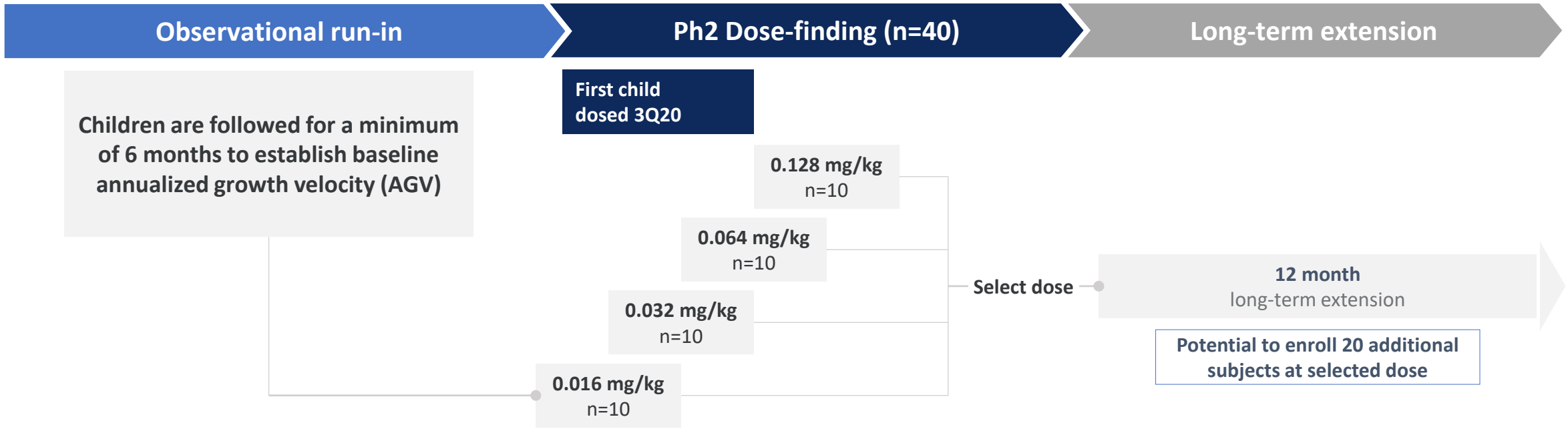
Infigratinib has been tested in >700 humans in our oncology program, providing significant data on PK, tolerability and safety

Most common and dose-limiting side effect is phosphorus elevation (on-target through FGFR1 inhibition), which occurs significantly above our planned achondroplasia doses



[1]Based on 125mg dose and 60kg adult; [2]Based on estimated TD_{50} at 40mg and 60kg adult; [3]Based on PK modeling and allometric scaling from animal models

The PROPEL clinical program is enrolling with data expected in 2021



Key inclusion criteria

- Children 2.5 – 10 years old
- Clinical and molecular ACH diagnosis

Primary objectives

- Baseline annualized growth velocity (AGV)

Primary objectives

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

Primary objectives

- Long-term safety and efficacy

Pipeline

BBP-631: AAV5 for CAH (IND-enabling)
IND anticipated in 2020

BBP-812: AAV9 for Canavan Disease
IND anticipated in 2020

BBP-815: AAV for TMC1 hearing loss

Multiple undisclosed discovery programs

BridgeBio's gene therapy programs and capabilities

- Collaborations with leading gene therapy pioneers
- In-house research vector manufacturing and optimization
- Best-in-class CMC, process development, and analytical development team
- Dedicated clinical/commercial manufacturing space at Catalent
- Leading clinical, non-clinical and regulatory team, with significant gene therapy experience

Maris,
child with CAH

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

Program overview

Prevalence

75,000 (US+EU) – One of the largest known AAV gene therapy markets

Genetic driver

21-hydroxylase inactivation

Pathophysiology

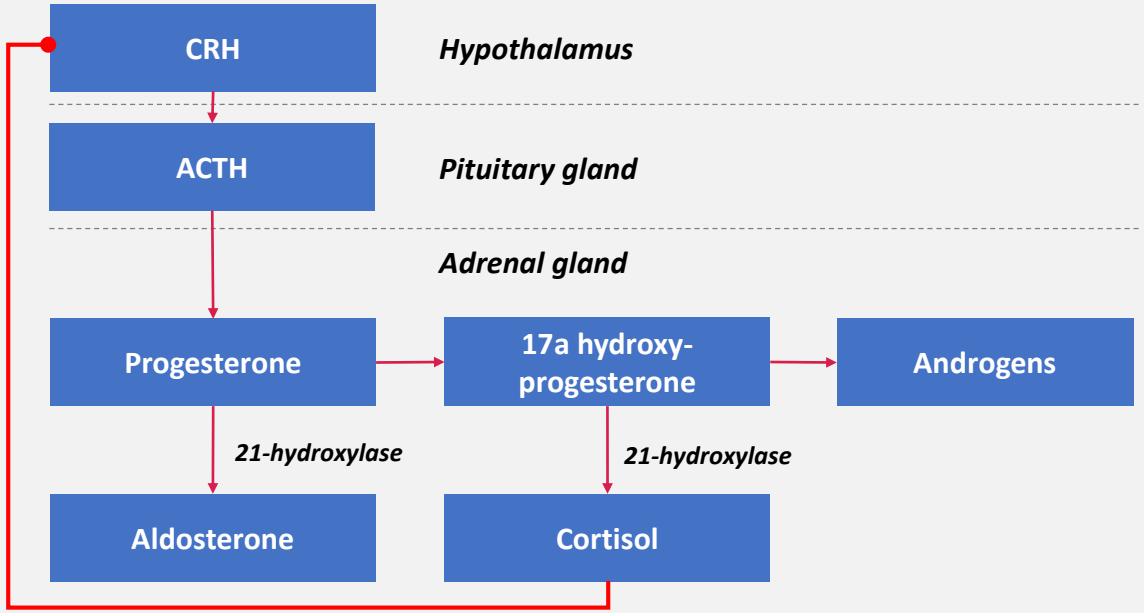
Inability to produce cortisol causes need for supraphysiologic doses of synthetic steroids, 3x increase in mortality risk, hirsutism, Cushingoid symptoms

We believe CAH is an ideal indication for AAV gene therapy:

- **Low threshold to correct phenotype**, validated by human clinical genetics (~5-10% of WT enzyme activity)
- **Only approach designed to induce endogenous cortisol and mineralocorticoid production**, potentially allowing steroid withdrawal
- **Durable transgene delivery to the adrenal gland of NHPs** with IV dosing of our construct
- **Preliminary Ph1/2 data anticipated in 2021** with endogenous cortisol production as a key endpoint

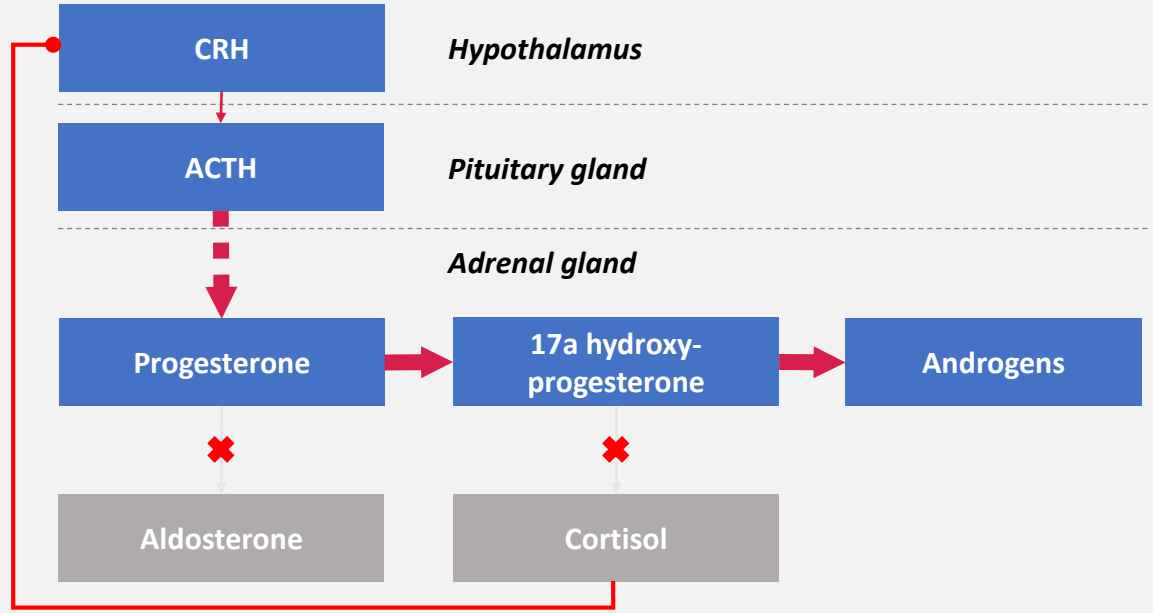
Gene therapy is the only modality designed to treat CAH at its source and allow for production of endogenous cortisol

Healthy Hypothalamic-Pituitary-Adrenal Axis



In a functional HPA system, cortisol and aldosterone are produced as needed by the body. Cortisol serves as a “brake” on the CRF/ACTH system

Hormonal dysregulation with 21OHD; no cortisol “brake” on ACTH, shunting of 17OHP to androgens

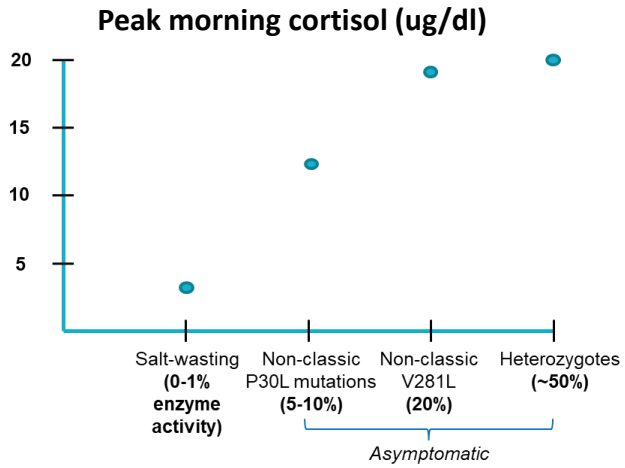


In CAH, cortisol and aldosterone are not able to be produced. The lack of a “cortisol brake” results in buildup of progesterone and 17OHP, leading to an excess of androgen production

CAH patients have 3-4X higher mortality than the general population, and suffer significant morbidity ranging across cardiovascular and metabolic disease, bone disease, infertility, chronic fatigue, and other disorders.

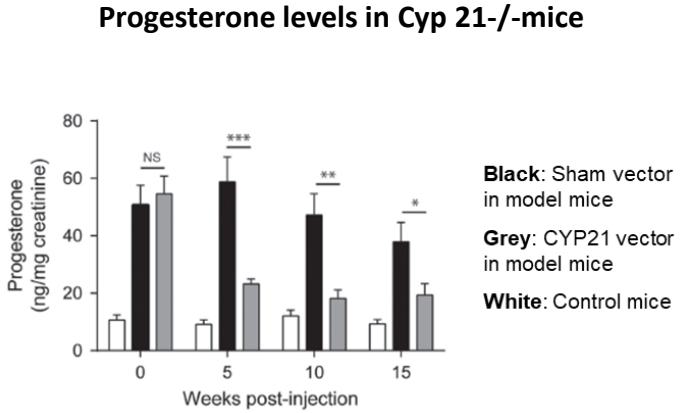
CAH: NHP study showed durable transgene expression; 5-10% of WT enzyme may be sufficient for clinical impact

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



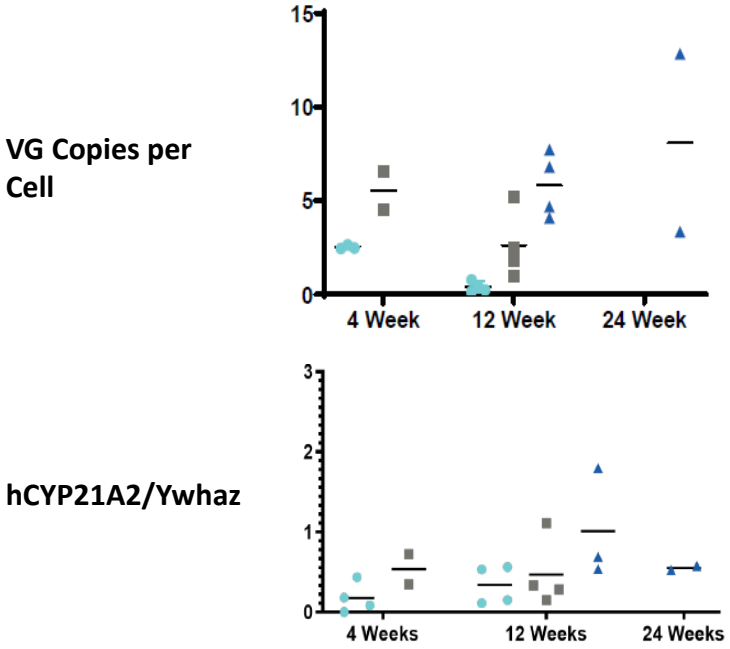
- Due to the high enzymatic efficiency/selectivity of 21-OHase, only a small amount of enzyme is required to rescue the phenotype

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



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

NHP studies show sustained VGC and RNA out to 6 months

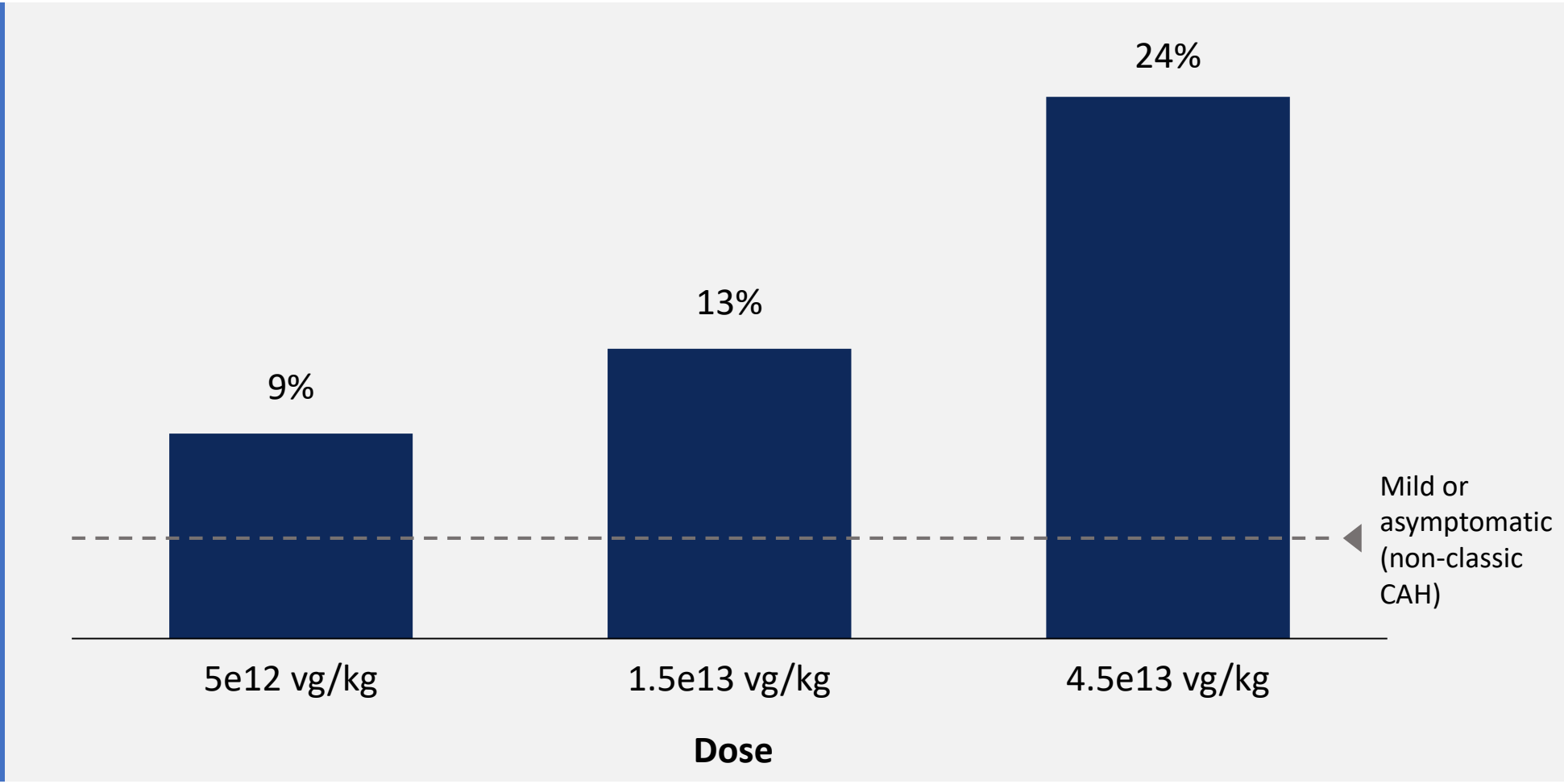


- Transgene expression is dose-dependent and stable out at 24 wks
- We can durably transduce the NHP adrenal gland with our construct at >20x the vector required to correct the CAH phenotype in mice

Source: Perdomini, Gene Therapy 2017; ESGCT 2019

NHP protein data using mass spec methods suggests potentially therapeutic levels of 21-hydroxylase enzyme

- We have developed mass-spec methods to quantify protein expression by identifying differential peptides between human and NHP 21-OH
- These data suggest dose-dependent enzyme expression in the adrenal cortex from 9%-24% of WT levels
- Genotype-phenotype relationship suggests as little as 5% of WT enzyme activity is associated with the mild/asymptomatic non-classic form of CAH



Source: Data on file

Encaleret for disorders of calcium homeostasis, including autosomal dominant hypocalcemia type 1 (ADH1)

Alexis and Jackson
ADH1 patients

Targets hypocalcemia/hypercalciuria by selectively antagonizing the calcium-sensing receptor (CaSR)

- Opportunity identified in collaboration with experts at the NIH

Prior clinical experience enables accelerated development

- Well tolerated in >1,200 human subjects excepting dose-dependent increases in serum calcium (target effect in ADH1 patients)
- Phase 2 study in ADH1 planned to initiate in 2020 with proof-of-concept data anticipated in 2021

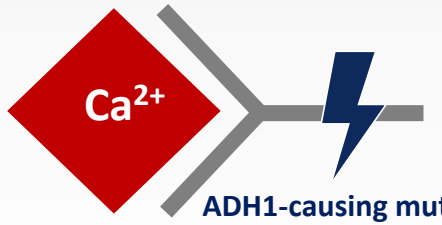
Potential 1st in class CaSR antagonist with differentiated profile for ADH1 and hypoparathyroidism

- Initial development in genetically-defined population of ADH1, driven by CaSR activating mutations (~12K carriers in US)
- Potential for expansion into post-surgical chronic hypoparathyroidism (~200K patients in US & EU)

Encaleret is designed to treat ADH1 at its source

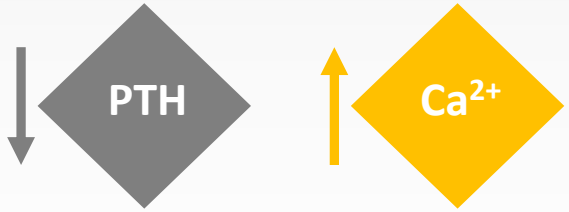
ADH1 disease mechanism

CaSR senses and regulates serum Ca levels

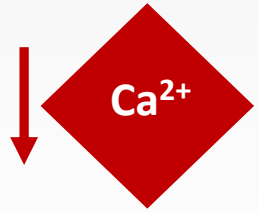


ADH1-causing mutations hyperactivate CaSR

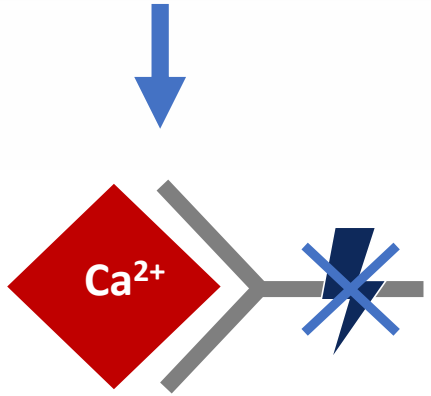
Hyperactive CaSR depresses PTH secretion and increases urinary Ca excretion



Serum Ca levels fall, requiring supplementation to prevent severe hypocalcemia



Therapeutic hypothesis



Encaleret is CaSR antagonist designed to stimulate PTH secretion, stabilize urinary Ca excretion, and increase serum Ca levels

The calcium sensing receptor (CaSR) primarily acts to regulate parathyroid hormone levels and renal calcium reabsorption

Illustration of parathyroid cell

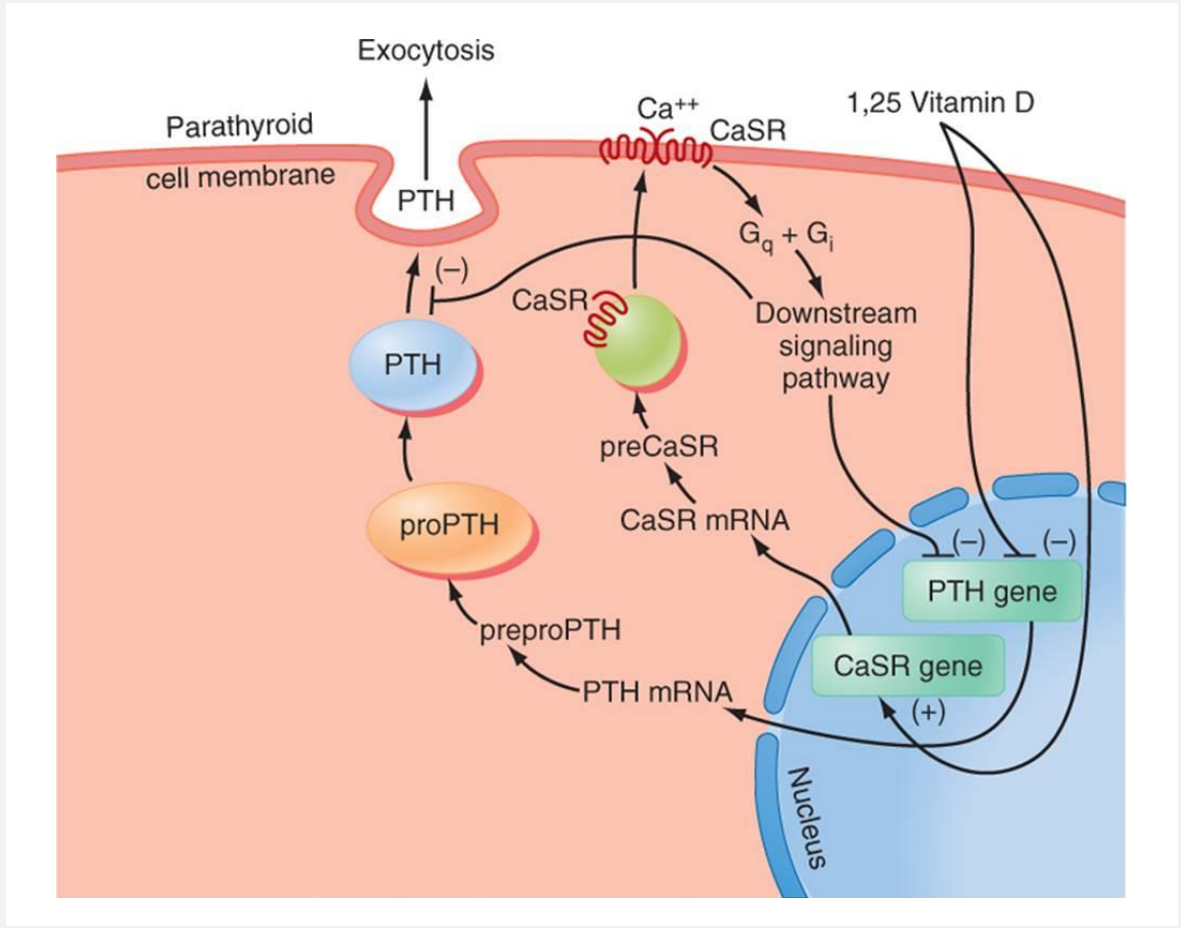
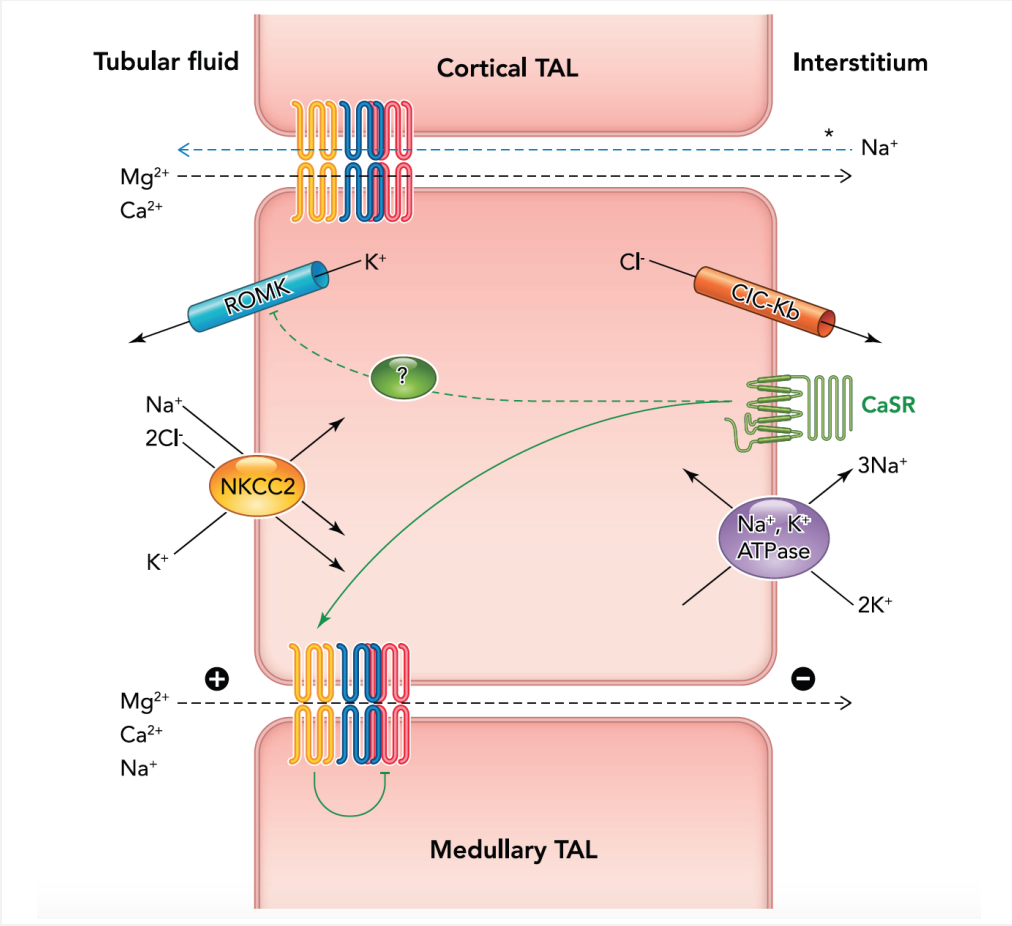


Illustration of renal tubule



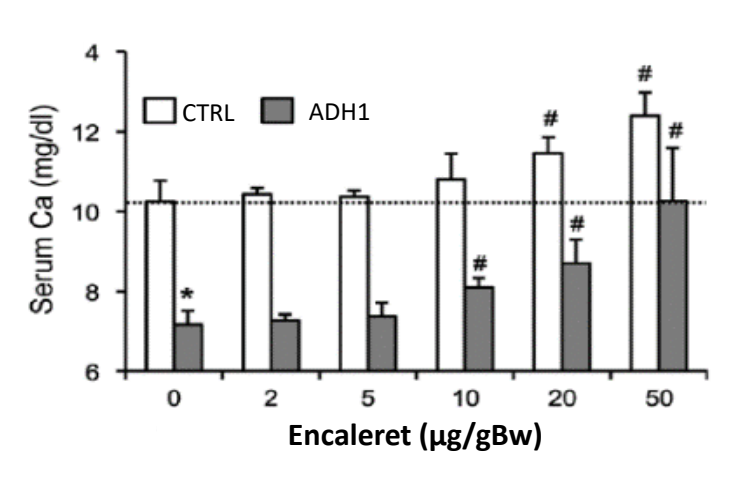
Source: 1 Berne and Levy Physiology, 6th ed. Chapter 39; 2 Toka, H.R., et al. Physiology. 2015.

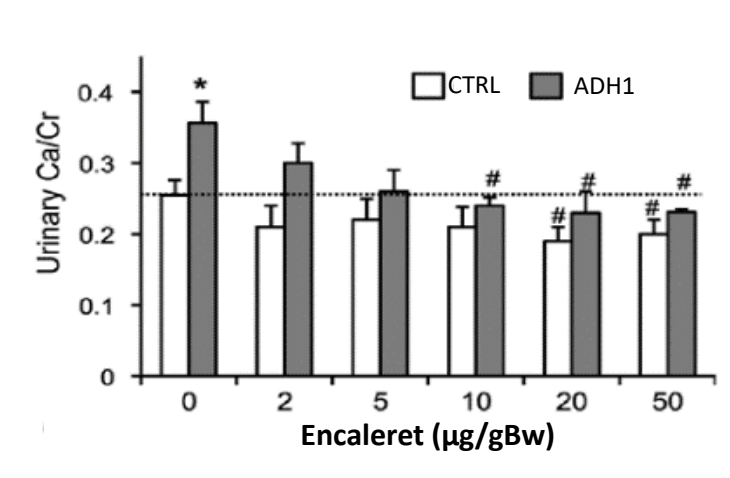
Encaleret is designed to target ADH1 at its source by normalizing hyper-active calcium sensing receptor

Rationale for studying CaSR inhibitor in ADH1

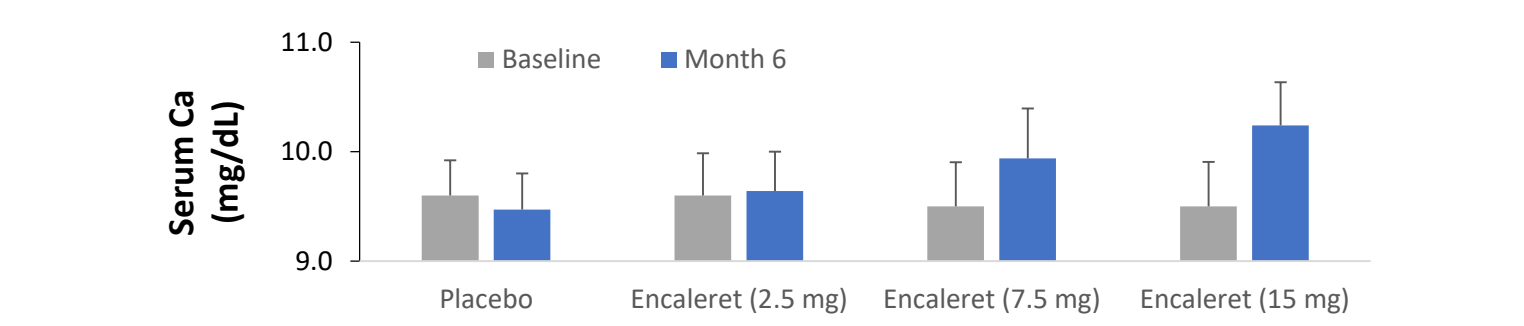
- ADH1 is caused by activating mutations in the CaSR leading to hypocalcemia and hypercalciuria
- Prior generation CaSR inhibitor partially addressed ADH1 phenotype despite limited exposure[1]

Encaleret normalized serum and urine calcium in a mouse model of ADH1[2]



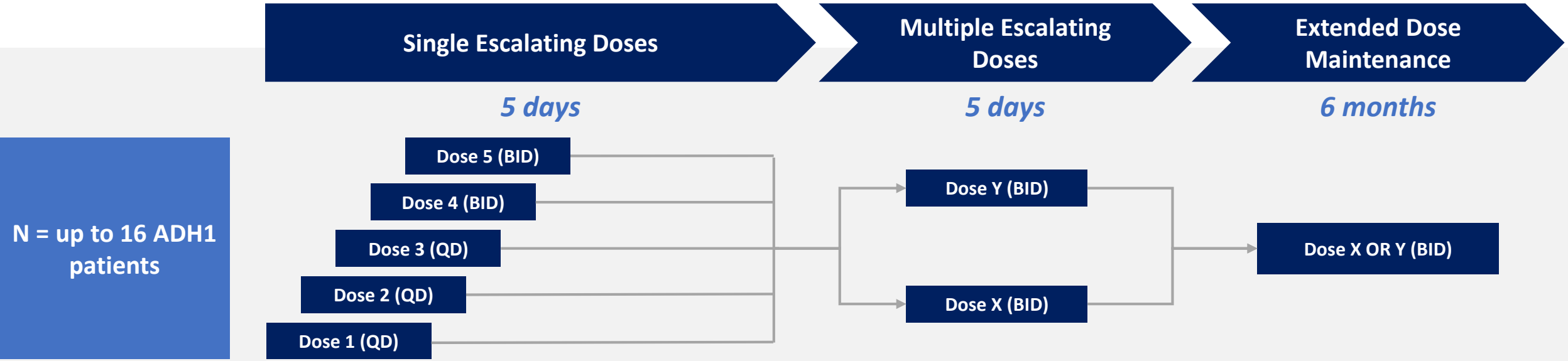


Encaleret increased serum calcium in clinical trials in patients with osteoporosis[3]



Source: 1 Roberts, M.S., et al. J Bone & Min 2019; 2 Dong B., et al. J Bone & Min 2015; 3 Data on file

Phase 2, open-label dose-ranging study will evaluate safety, tolerability, and efficacy of encaleret in ADH1



Top-line, proof-of-concept results of encaleret in ADH1 are anticipated in 2021

1 Pharmacodynamic measurements to be collected through duration of study

Basia, pancreatic cancer patient (>90% KRAS-driven)

BridgeBio oncology research

World-class oncology team drives our discovery and development

Eli Wallace
CSO Oncology Research

ARRAY BIOPHARMA | Peloton Therapeutics

Pedro Beltran
SVP Oncology

AMGEN | UNITY BIOTECHNOLOGY

Frank McCormick
Chairman of Oncology

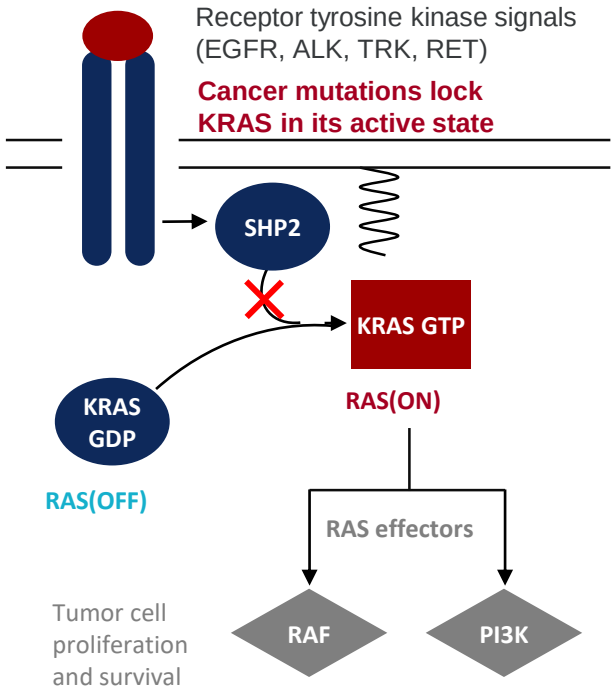
ONYX PHARMACEUTICALS | UCSF

Richard Scheller
Chairman of R&D

Genentech | 23andMe

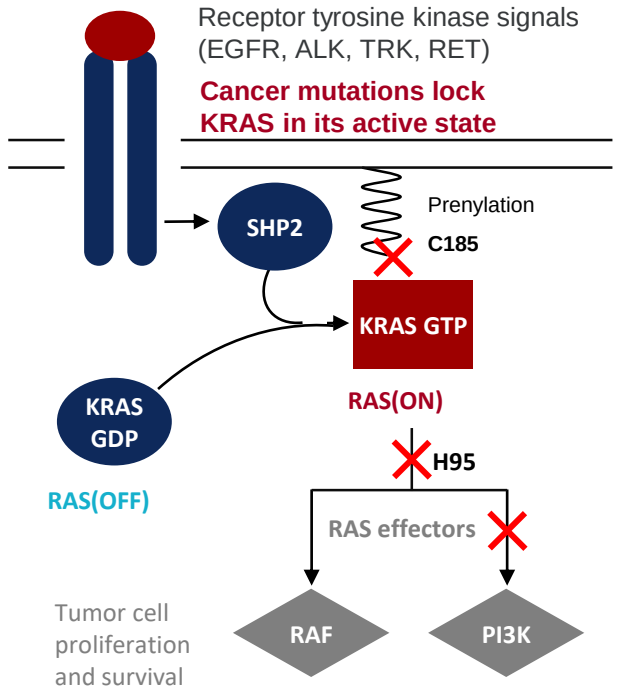
Three disclosed oncology research targets

SHP2 (BBP-398)



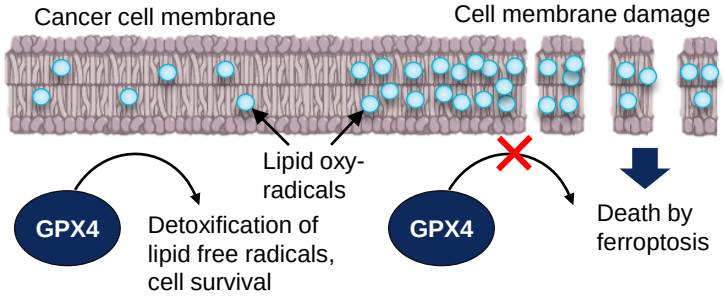
- Potential best in class oral compound
  - Optimized safety, PK and PD profile
  - Maximizes combination therapy potential
- IND cleared

KRAS



- Multiple unexploited sites
- Comprehensive pan-mutant targeting approaches

GPX4



- Potential first in class compound for novel cancer target
- In vivo monotherapy activity and combo potential

Partnerships afford us exceptional collaborators and resources

NIH NATIONAL CANCER INSTITUTE

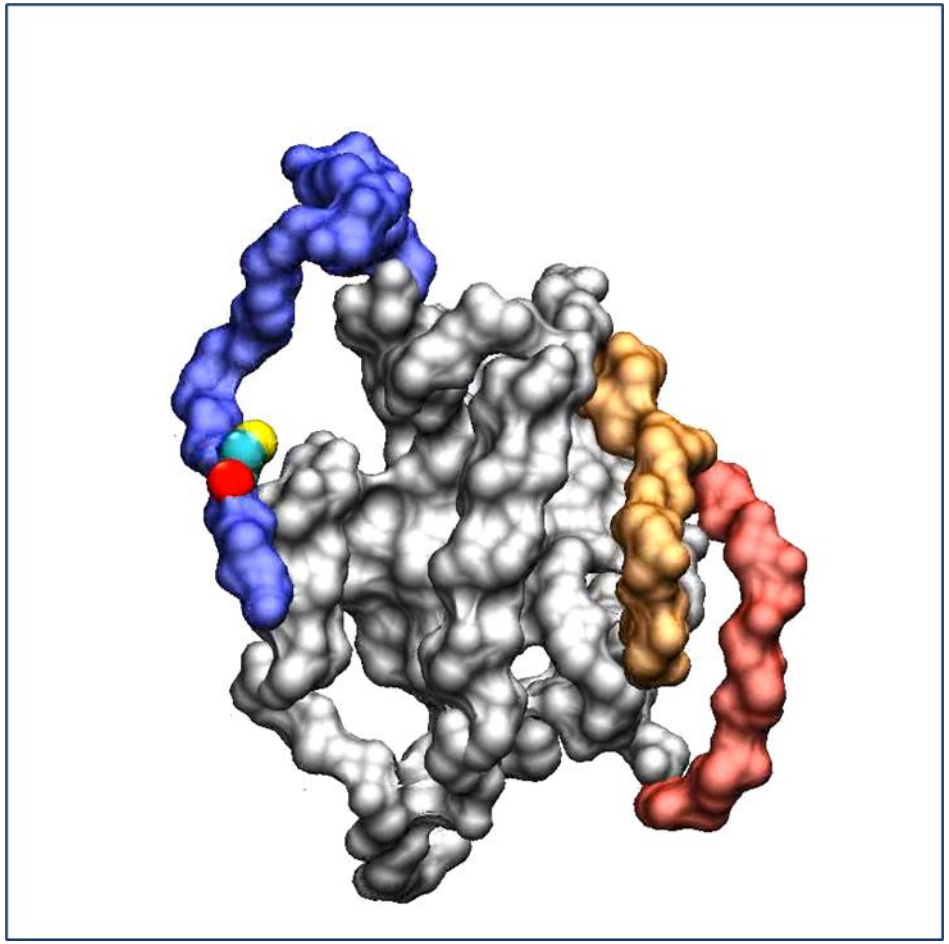
- Partnership with the National RAS Initiative, including 60 of the world's **foremost academic RAS researchers**
- Cutting edge RAS **structural biology expertise**
- Utilization of **cutting-edge instrumentation and techniques**, as well as the **expertise** to lead experiments

Lawrence Livermore National Laboratory

- Home to Sierra: the **world's 3rd fastest computing system**
- Enables **multi-microsecond molecular dynamics simulations** of protein complexes, and highly efficient *in silico* **docking simulations**
- This computing power, combined with RAS structural biology expertise at the NCI, delivers **unique insights that fuel our drug design**

Crystal structure enables a static understanding of the target …

KRAS4b model based on crystal



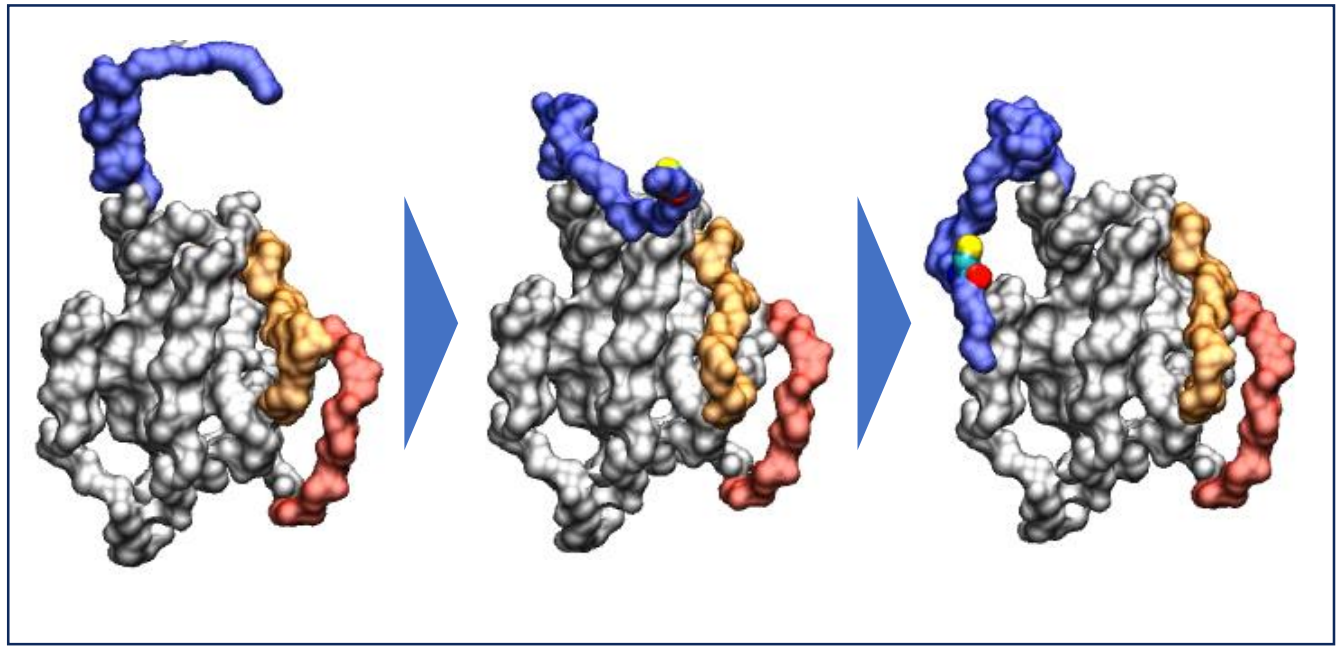
G-domain
G-domain switch I
G-domain switch II
Hypervariable region

One therapeutic approach is to inhibit KRAS4b **membrane localization** by targeting **hypervariable region**

Static model reveals only a **subset of potential binding sites** for pharmacological compounds

… whereas molecular dynamics simulation reveals transient conformations and interactions

KRAS4b simulation



G-domain
G-domain switch I
G-domain switch II
Hypervariable region

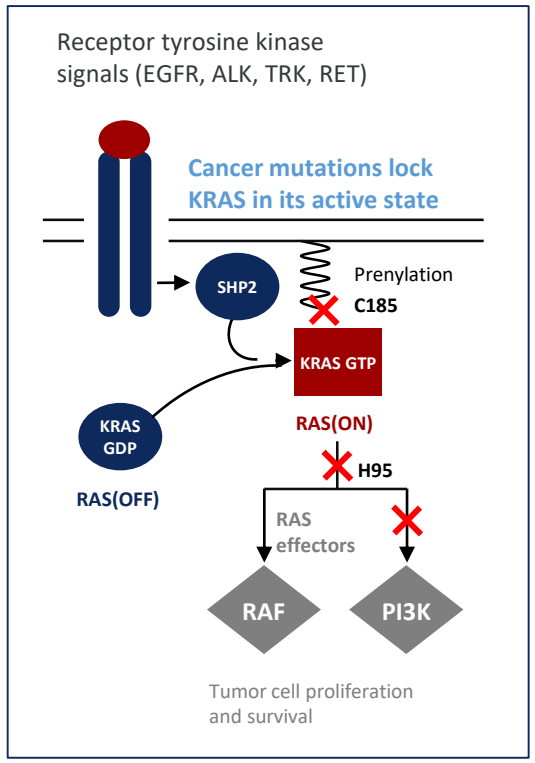
Reveals possible KRAS4b **HVR transient localization to G-domain**

Elucidates potential transient druggable pocket where **compounds could react covalently with C185**

Enables *in silico* SAR to **inhibit KRAS4b membrane localization**

KRAS: multiple shots on goal with our pan-mutant inhibitor programs – each with a unique MOA targeting a novel pocket

KRAS pathway in cancer

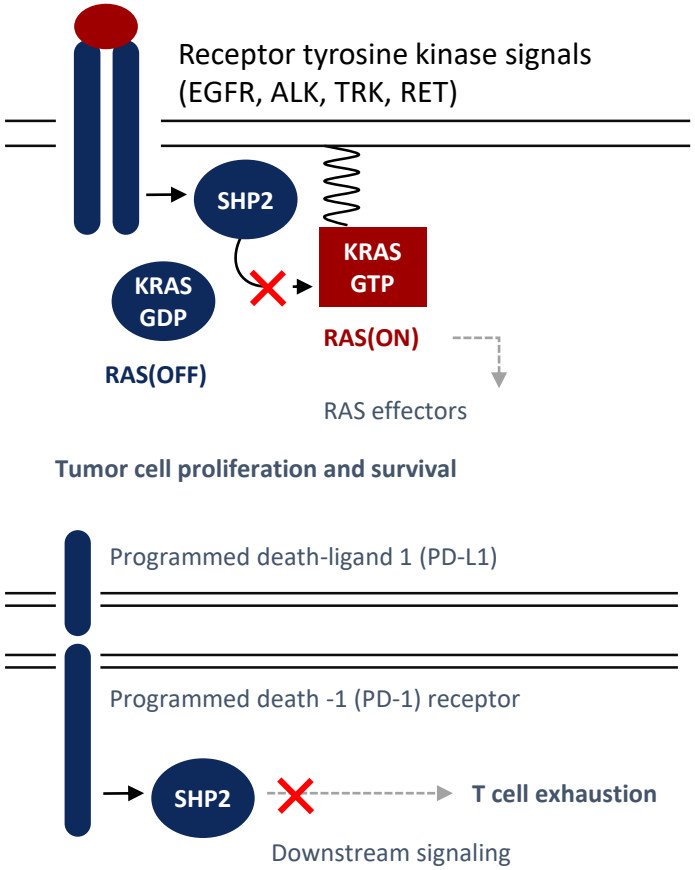


Program	MOA	Targets KRAS GTP	Pan-mutant	Crystal structure	Molecular Dynamics
Program 1: H95 targeting	▪ Directly binds activated KRAS through H95 ▪ Inhibits KRAS from signaling through effectors	✓	✓	✓	✓
Program 2: PI3K effector blocking	▪ Blocks specific interaction between KRAS and PI3Ka ▪ Blocks PI3K / AKT effector signaling	✓	✓	✓	✓
Program 3: C185 targeting	▪ Blocks KRAS from tethering ▪ Blocks conversion of inactive KRAS GDP to active KRAS GTP	✓	✓		✓

Our programs are designed to address all KRAS driver mutations, which occur in >30% of all cancers

SHP2: Our compound shows best-in-class potential and is entering the clinic in 2020

Our SHP2i blocks downstream MAPK signaling and abrogates T cell exhaustion



We believe BBP-398 has the ideal properties for combination with a multitude of other therapeutic classes

Human half life: 10 hours[1]

- Allows for recovery above EC50 and reduced MAPK-driven tox

Potentially differentiated safety profile for combination therapy

- hERG IC50 (µM)*: >100: No QT prolongation

SHP2i combination potential

US + EU incidence, '000s

Supporting evidence[2]

Peclin data:

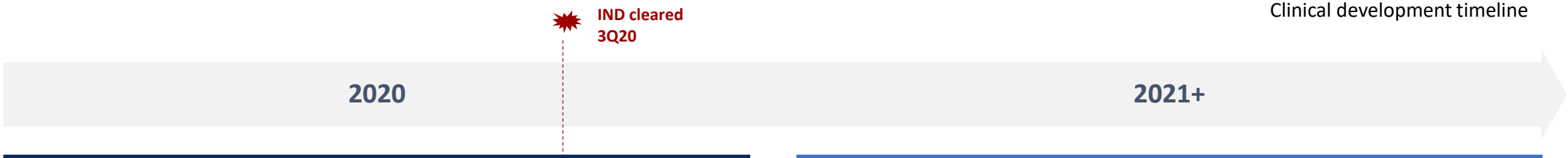
~1 million patients annually

1 Predicted human PK based on preclinical in vivo data 2 Preclinical data of combination efficacy with SHP2i

SOURCE: US incidence estimated from SEER, TCGA and Kiuru & Busam "The NF1 gene in tumor syndromes and melanoma"; all scaled for WW incidence

SHP2: BBP-398 monotherapy study initiating in 2020; combo trials to follow

Clinical development timeline



Mono therapy

- **Monotherapy FPI expected 2020**
- Dose escalation followed by dose expansion
- Starting dose 80mg

Combo Therapy

- **Partnered with Perceptive-backed LianBio in China for initial combo therapy trials**
- Dose escalation followed by dose expansion
- Priority combinations include osimertinib, and G12Ci in NSCLC

Initial clinical combinations of focus based on SHP2i preclinical data

	SHP2i Combination Partner	Tumor growth inhibition
KRAS G12Ci	AMG 510	**~130%**
EGFRi	Osimertinib	**~125%**
PD-1	Anti-mouse PD-1	**~90%**
MEK	Trametinib	**~80%**
CDK4/6 and MEK	Trametinib + palbociclib	**~110%**

Multiple catalysts anticipated through year-end 2021

ESTIMATED

2020

1H

- ☑ New program announcements
- ☑ FGFRi for cancer: FPI Ph3 adjuvant urothelial carcinoma study
- ☑ FGFRi for cancer: FPI Ph2 FGFR fusion tumor agnostic Ph2 study

2H

- ☑ Low-dose FGFRi for achondroplasia: Begin dosing Ph2
- ☑ New IND filings
- ☑ cPMP for MoCD type A: Complete NDA submission
- ☑ CaSR antagonist for ADH1: FPI in Ph2 study
- ☐ FGFRi for cancer: 2L CCA NDA filing

2021

FY

- ☐ TTR stabilizer for ATTR: Ph3 part A data late-2021 / early-2022
- ☐ Low-dose FGFRi for achondroplasia: Ph2 PoC data
- ☐ CAH gene therapy: Ph1/2 PoC data
- ☐ CaSR antagonist for ADH1: Ph2 POC data
- ☐ Topical SMOi for Gorlin: Topline Ph3 data
- ☐ FGFRi for cancer: 2L CCA approval and launch
- ☐ cPMP for MoCD type A: Approval and launch
- ☐ Recombinant COL7 for RDEB: Topline Ph1/2 data

$711mn in cash and equivalents as of September 2020 expected to provide runway into 2022