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# COMPANY PRESENTATION

**September 2020**



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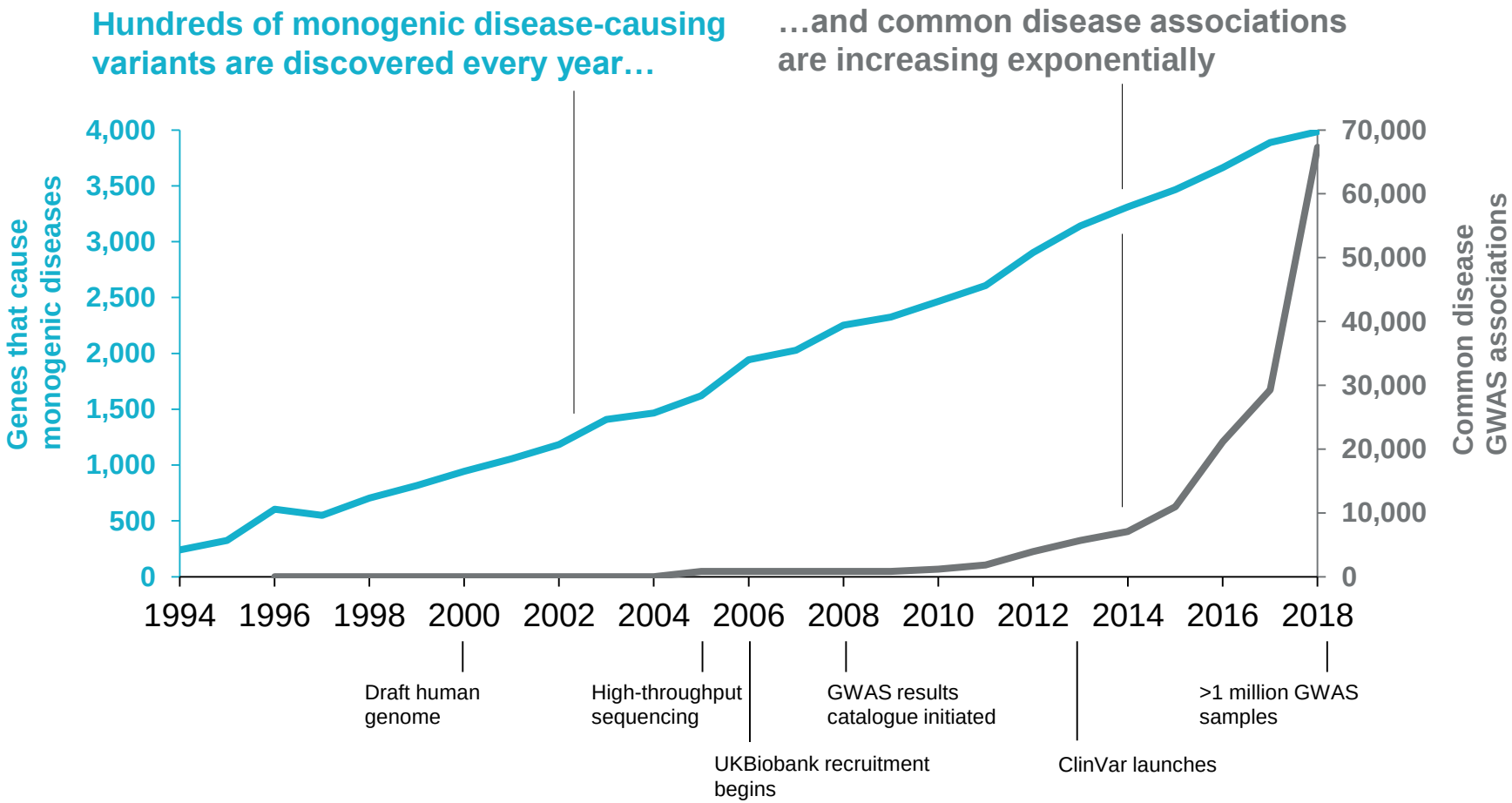
# We are at Day 1 in the era of genetic medicine




**BridgeBio is focused on translating breakthroughs in human genetics into meaningful medicines for patients**

Source: Claussnitzer *et al.*, *Nature* 2020



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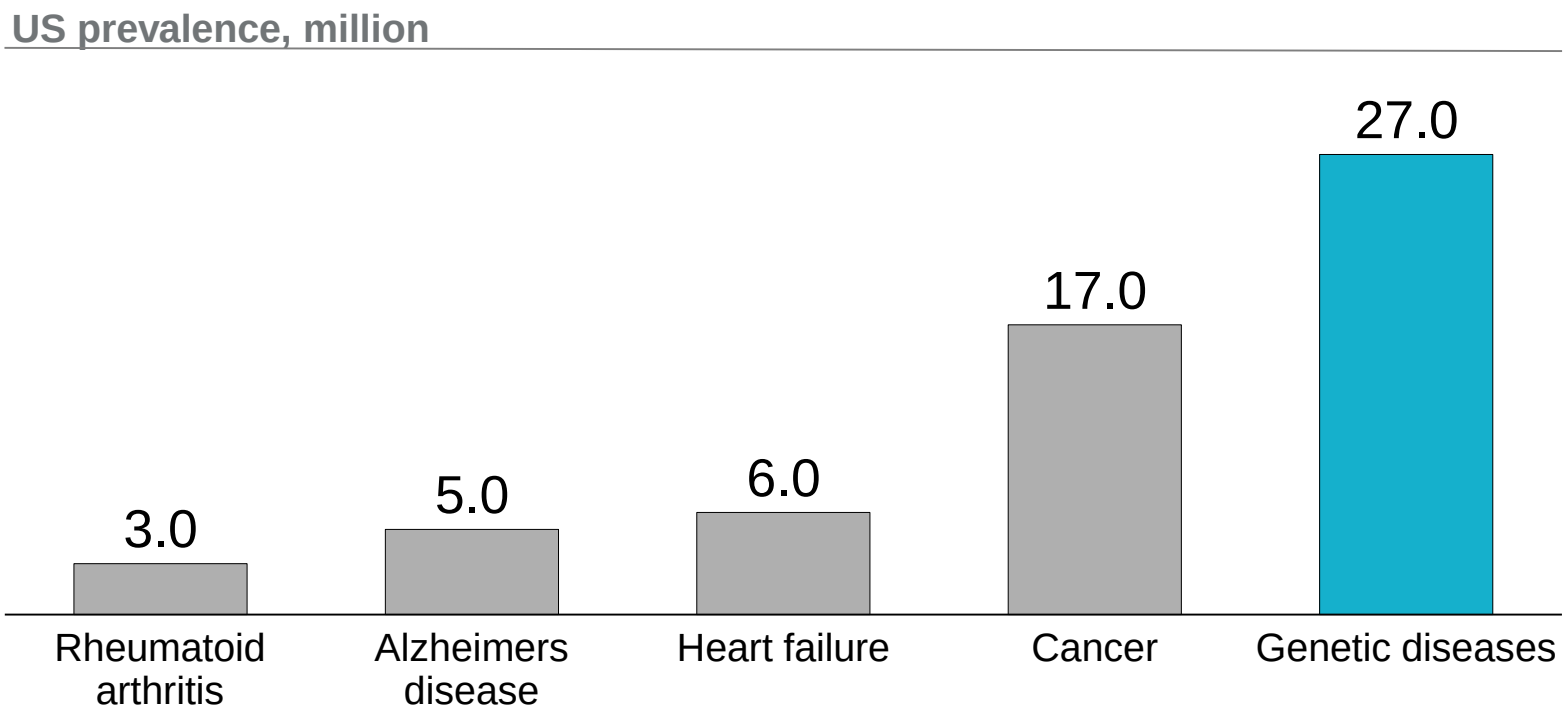
# A vast opportunity to help patients

**~27 million**
Americans are living with a genetic diseases

**50%**
Of people affected are children

**Only 5%**
Of these diseases have an approved therapy




Source: Global Genes, American Cancer Society, American Heart Association, Alzheimer's Association, Arthritis Foundation

# We are building a leading genetic disease company

## Core attributes…

1. **Distinctive early stage asset selection**
2. **Experienced, product-focused R&D team**
3. **Efficient corporate structure**
4. **The willingness and scale to fail**
5. **Focus at the level of individual diseases and assets**

## …applied many times…

eidos a bridgebio company

pellepharm a bridgebio company

MYOKARDIA

GBT

***+ 18 BridgeBio programs***

## …has yielded a pipeline poised to deliver over the next 12-24 months

- **Major catalysts from four core value drivers, three of which are in $1B+ markets**
- **Two NDA submissions expected in 2020**
- **A distinctive early stage targeted oncology pipeline**
  - SHP2
  - KRAS
  - GPX4
- **Multiple INDs submitted in 2020**
- **>10 INDs filed over 5 years**

# BridgeBio is led by a world-class team of experienced drug developers

## We rely on some of the top R&D minds in this industry to select assets…

| | | |
|---|---|---|
| **Charles Homcy, MD**<br>Chairman of Pharmaceuticals | PORTOLA PHARMACEUTICALS, MyoKardia, GBT, Takeda MILLENNIUM THE TAKEDA ONCOLOGY COMPANY | VELCADE (bortezomib) FOR INJECTION, Andexxa (Coagulation Factor Xa (Recombinant), inactivated - zhzo), Oxbryta (voxelotor) |
| **Frank McCormick, PhD, FRS**<br>Chairman of Oncology | Cetus, ONYX PHARMACEUTICALS, UCSF | Nexavar (sorafenib) tablets, Kyprolis (carfilzomib) for injection |
| **Richard Scheller, PhD**<br>Chairman of R&D | Genentech, 23andMe | TECENTRIQ atezolizumab, PERJETA pertuzumab for injection, Kadcyla trastuzumab emtansine, OCREVUS ocrelizumab, VENCLEXTA venetoclax tablets |

## …and put them in the hands of one of the most productive groups of R&D operators in the industry

| | | |
|---|---|---|
| **Uma Sinha, PhD**<br>Chief Scientific Officer | GBT, PORTOLA PHARMACEUTICALS, Takeda MILLENNIUM THE TAKEDA ONCOLOGY COMPANY | (eptifibatide) Injection INTEGRILIN, Andexxa (Coagulation Factor Xa (Recombinant), inactivated - zhzo), Oxbryta (voxelotor) |
| **Eli Wallace, PhD**<br>Chief Scientific Officer in Residence, Oncology | ARRAY BIOPHARMA, Peloton Therapeutics | MEKTOVI (binimetinib) 15 mg tablets, TUKYSA tucatinib 50 mg \| 150 mg tablets, Koselugo (selumetinib) 10 mg & 25 mg capsules<br>PT2997 (HIF2αi, Ph3) |
| **Robert Zamboni, PhD**<br>Chemistry | MERCK FROSST | SINGULAIR (montelukast, MSD), ARCOXIA (etoricoxib), VIOXX (rofecoxib, MSD) |

**Together, our R&D team is responsible for 100+ INDs and 20+ approved products**



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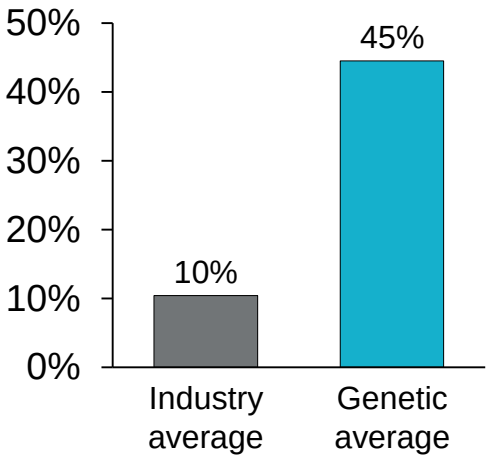
# We believe genetic disease drug discovery is lower risk, faster, with potentially higher returns than traditional drug discovery

**>4x** Higher cumulative probability of success

**>65%** Faster time to Phase 3*

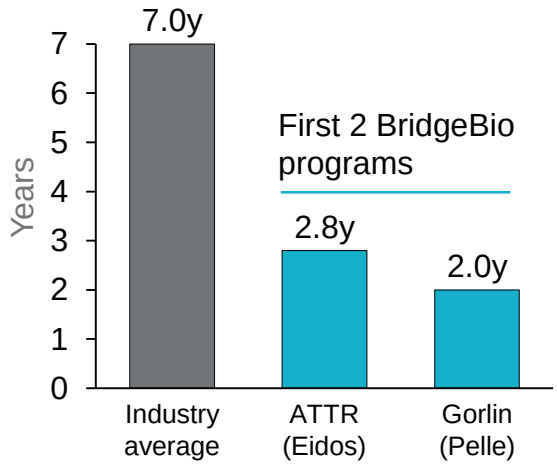
**>8x** Better return on investment*

**Probability of success from Ph1 to launch**



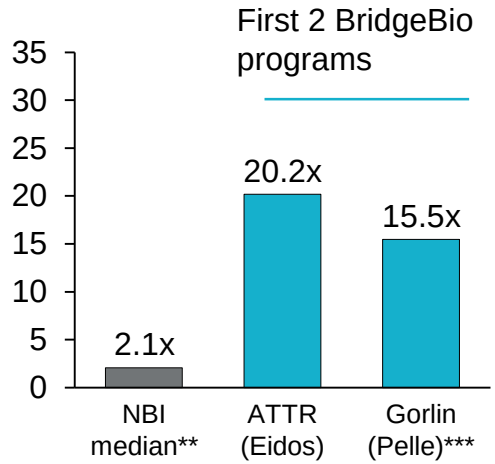

Sources: Hay et al., Nature Biotechnology, "Clinical Development Success Rates for Investigational Drugs", 2014

**Time from lead optimization to Ph3**




Sources: Paul et al., Nat Rev Drug Disc, "How to improve R&D productivity: the pharmaceutical industry's grand challenge.", 2010

**Total return on investment**
[Enerprise value]/[APIC - cash on hand]*




*As of 2/28/2020 close
**Includes all NBI constituents with market value <$20bn
***Calculated as total consideration from LEO Pharma transaction divided by total burn to date
Sources: FactSet

**Targeting genetic disease has higher average probability of success and BridgeBio has demonstrated higher ROI and shorter development time in its first 2 programs**

*For first two BridgeBio programs



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# Assessing BridgeBio

| | Criteria | Relevance |
|---|---|---|
| 1 | High probability of success | • Historically higher probability of success for genetic disease drugs<br>• BridgeBio's early programs have outperformed historical probabilities |
| 2 | Number of programs | • We find great science and unlock its potential for patients<br>• Always searching for the next PellePharm or Eidos<br>• Scale allows for objective assessment and failure |
| 3 | Capital efficiency | • Generate value by making each program ROI-positive<br>• Driven by judicious use of capital at the high-risk preclinical stages |

# BridgeBio since IPO (1 of 2)

***From cutting edge . . .***  ***. . . to cutting edge + rock solid***

| ***Achievement:*** | ***Examples:*** |
|---|---|
| ▪ Development strategy successes | ▪ Adjuvant urothelial (first in class in potential $1B+ market), Clinical Advisory Board (Robert Harrington, David Solit, and others) |
| ▪ Continued clinical execution | ▪ Six new clinical trials initiated (16 total), >350 trial sites across 25 countries |
| ▪ Late-stage regulatory submissions | ▪ NDA for MOCD Type A submitted, ODD & Fast Track received for 2L CCA program |
| ▪ Increasing discovery productivity | ▪ 7 INDs filed |
| ▪ New high-quality programs | ▪ 8 new programs, including LGMD2i and ADH1, both in the clinic |

***Bedrock in place to build leading genetic disease company in next 12-24 months***

# BridgeBio since IPO (2 of 2)

***From cutting edge . . .***  ***. . . to cutting edge + rock solid***

| ***Achievement:*** | ***Examples:*** |
|---|---|
| ▪ Quick program kills | ▪ Multiple programs terminated, with average spend less than $5M |
| ▪ Continued access to capital | ▪ $550M raised through convertible bond placement |
| ▪ Doubling of the organization | ▪ From ~200 employees to 364. Added CAO, COO, top scientists, commercial expertise at BOD and company level |
| ▪ Strong data | ▪ DEB clinical data, TTR clinical data, CAH and Canavan pre-clinical data, achon pre-clinical data, TIO data |
| ▪ Dedication to patients | ▪ Portfolio-wide support of advocacy and COVID-centric reach-out to help outside therapeutic programs |

***Bedrock in place to build leading genetic disease company in next 12-24 months***

# 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



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# Discover: Three defining features of a BridgeBio program

| Feature | Benefit |
| --- | --- |
| Monogenic diseases where molecular pathophysiology is well-understood | ▪ Reduced target risk<br>▪ Rational drug design and development |
| Diseases we can target directly at their source | ▪ Direct and potentially complete correction of disease-causing biology |
| First or best-in-class potential for high unmet need diseases | ▪ High potential benefit to patients<br>▪ Significant value to health system |

# Capabilities to discover new genetic disease targets at scale

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

### Computational genomics

- De novo target discovery
- Target validation
- Indication expansion

### Systematic disease mapping

- Prioritization and manual annotation of the 7K known genetic diseases

### Broad network of academic partners

- 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™

Stanford University



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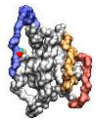
# Create: We select the optimal therapeutic modality to target each disease at its source

## Pipeline leverages 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
- Manufacturing and 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

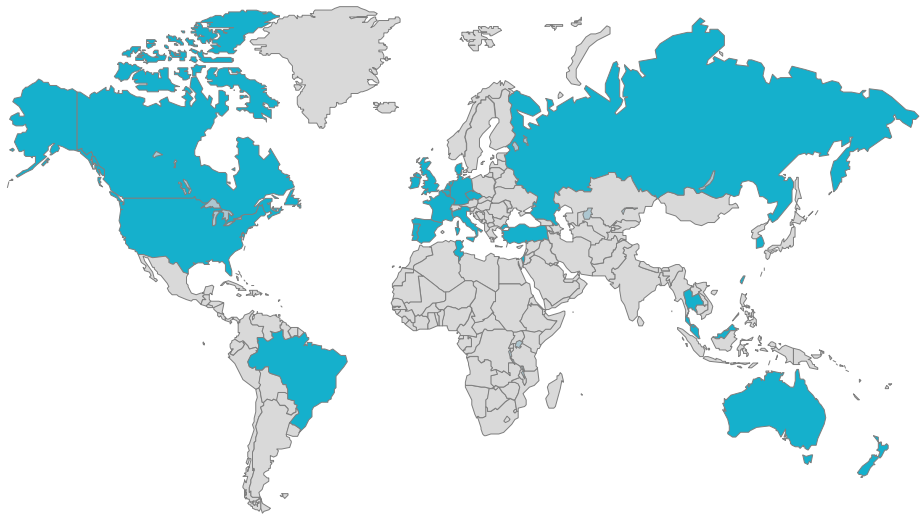
- Target mapping with functional genomics
- Activity screening assay development
- Novel backbone and base chemistry

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

# Test: our global clinical development footprint

- **15 ongoing trials** across 5 different therapeutic areas, 350 trial sites, and 27 countries
- **Expert, dedicated R&D teams** in each therapeutic area
- **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

## Countries with BridgeBio trial sites





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# Deliver: We are developing the 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
- **Patient services** (HUB services) to assist the most patients
- **Commercial partners in strategic geographies:**

*FGFRi and SHP2i in China:* LianBio

*TTR in Japan:* Alexion

# 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**

**15**
Clinical trials across the globe

## Deliver
**Our products to patients through commercial infrastructure**

**2**
Product launches in 2021



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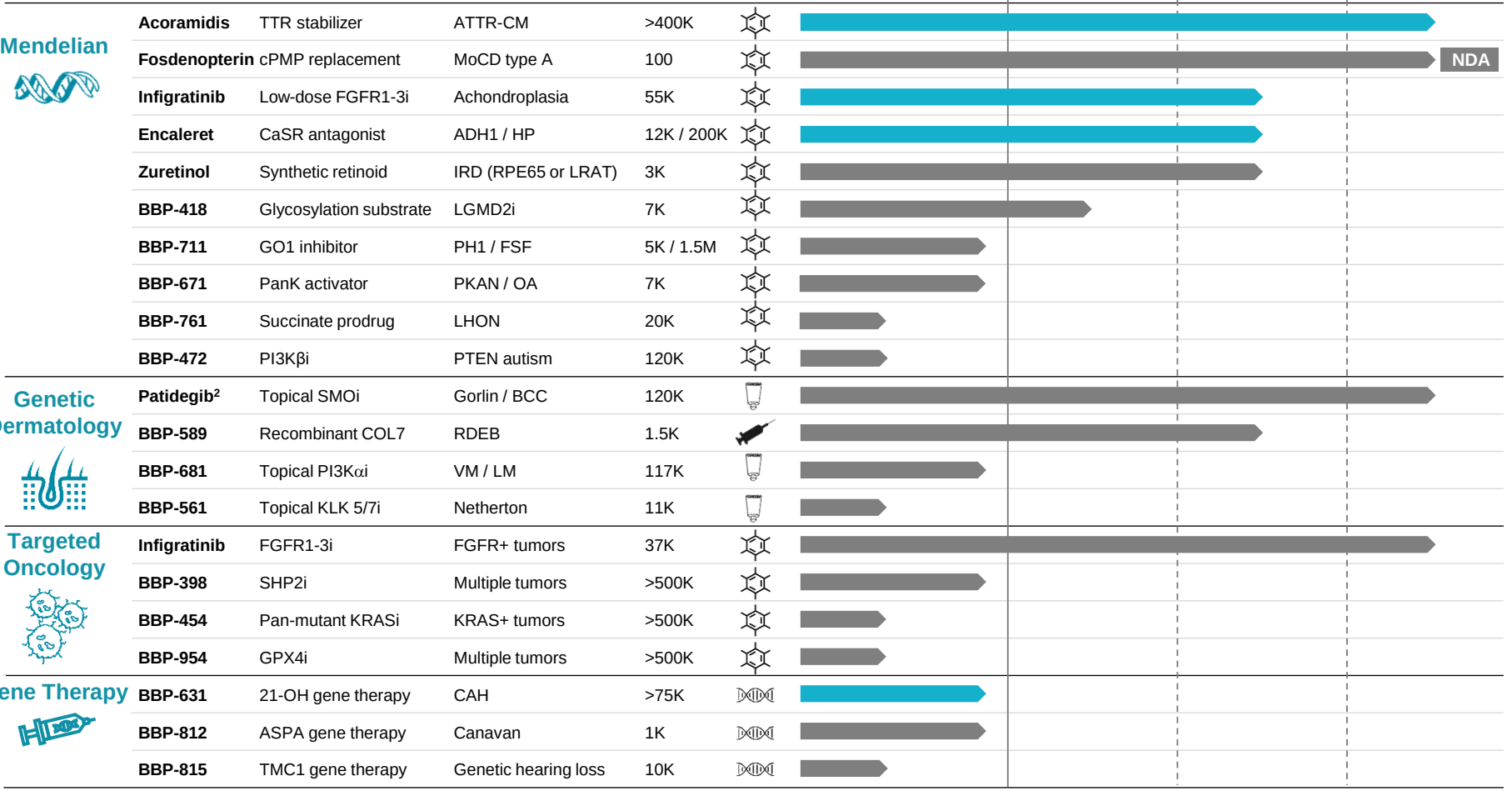
# Our pipeline of 20+ development programs spans multiple therapeutic areas and drug modalities

Small molecule | Topical small molecule | Biologics | Gene therapy

= Core value drivers over the next 12-24 months

| Portfolio segment | Program[1] | Drug mechanism | Diseases | Patient pop. (US+EU) | Modality |
|---|---|---|---|---|---|
| Mendelian | **Acoramidis** | TTR stabilizer | ATTR-CM | >400K | |
| | **Fosdenopterin** | cPMP replacement | MoCD type A | 100 | |
| | **Infigratinib** | Low-dose FGFR1-3i | Achondroplasia | 55K | |
| | **Encaleret** | CaSR antagonist | ADH1 / HP | 12K / 200K | |
| | **Zuretinol** | Synthetic retinoid | IRD (RPE65 or LRAT) | 3K | |
| | **BBP-418** | Glycosylation substrate | LGMD2i | 7K | |
| | **BBP-711** | GO1 inhibitor | PH1 / FSF | 5K / 1.5M | |
| | **BBP-671** | PanK activator | PKAN / OA | 7K | |
| | **BBP-761** | Succinate prodrug | LHON | 20K | |
| | **BBP-472** | PI3Kβi | PTEN autism | 120K | |
| Genetic Dermatology | **Patidegib[2]** | Topical SMOi | Gorlin / BCC | 120K | |
| | **BBP-589** | Recombinant COL7 | RDEB | 1.5K | |
| | **BBP-681** | Topical PI3Kαi | VM / LM | 117K | |
| | **BBP-561** | Topical KLK 5/7i | Netherton | 11K | |
| Targeted Oncology | **Infigratinib** | FGFR1-3i | FGFR+ tumors | 37K | |
| | **BBP-398** | SHP2i | Multiple tumors | >500K | |
| | **BBP-454** | Pan-mutant KRASi | KRAS+ tumors | >500K | |
| | **BBP-954** | GPX4i | Multiple tumors | >500K | |
| Gene Therapy | **BBP-631** | 21-OH gene therapy | CAH | >75K | |
| | **BBP-812** | ASPA gene therapy | Canavan | 1K | |
| | **BBP-815** | TMC1 gene therapy | Genetic hearing loss | 10K | |




[1] Each of our programs is housed in a separate subsidiary; [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.



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# Four core value drivers over the next 12-24 months

| Program | Population (US+EU) | Status | Upcoming event(s) |
|---|---|---|---|
| **Acoramidis: TTR stabilizer for ATTR**<br>▪ Most potent TTR stabilizer; MOA mimics protective genetic variant<br>▪ Data to date suggest potential best-in-class clinical profile | **>400K** | Enrolling ATTR-CM Ph3 | ❑ Topline Ph3 part A data 1H22<br>❑ Topline Ph3 part B data 2023 |
| **Low-dose infigratinib (FGFRi) for achondroplasia**<br>▪ Only agent designed to directly target genetic cause of ACH<br>▪ Differentiated pre-clinical data on cranial and spinal defects | **55K** | Enrolling Ph2 study | ✓ Dose first child<br>❑ Ph2 data 2021 |
| **Gene therapy for congenital adrenal hyperplasia (BBP-631)**<br>▪ One of largest potential gene therapy markets<br>▪ Only approach capable driving endogenous cortisol production | **>75K** | GLP tox ongoing | ❑ File IND<br>❑ Ph1/2 data 2021 |
| **Encaleret: CaSR antagonist for autosomal dominant hypocalcemia type 1 (ADH1)**<br>▪ Directly targets ADH1 genetic driver; potentially first-in-class | **12K** | Ph2-ready | ✓ FPI in Ph2<br>❑ Ph2 data 2021 |



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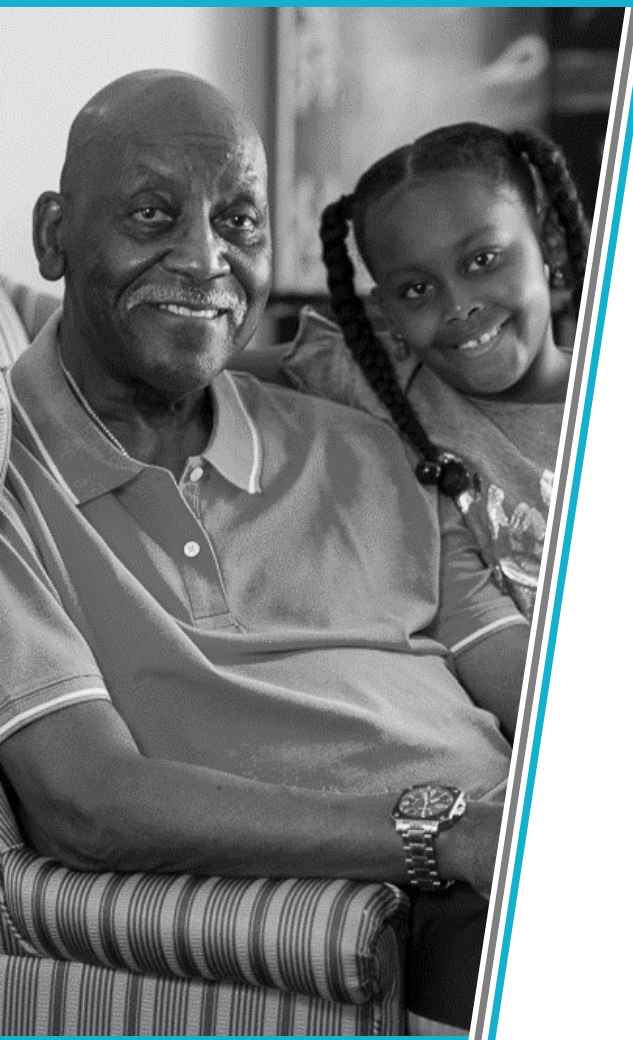
# Acoramidis (formerly AG10) for TTR amyloidosis



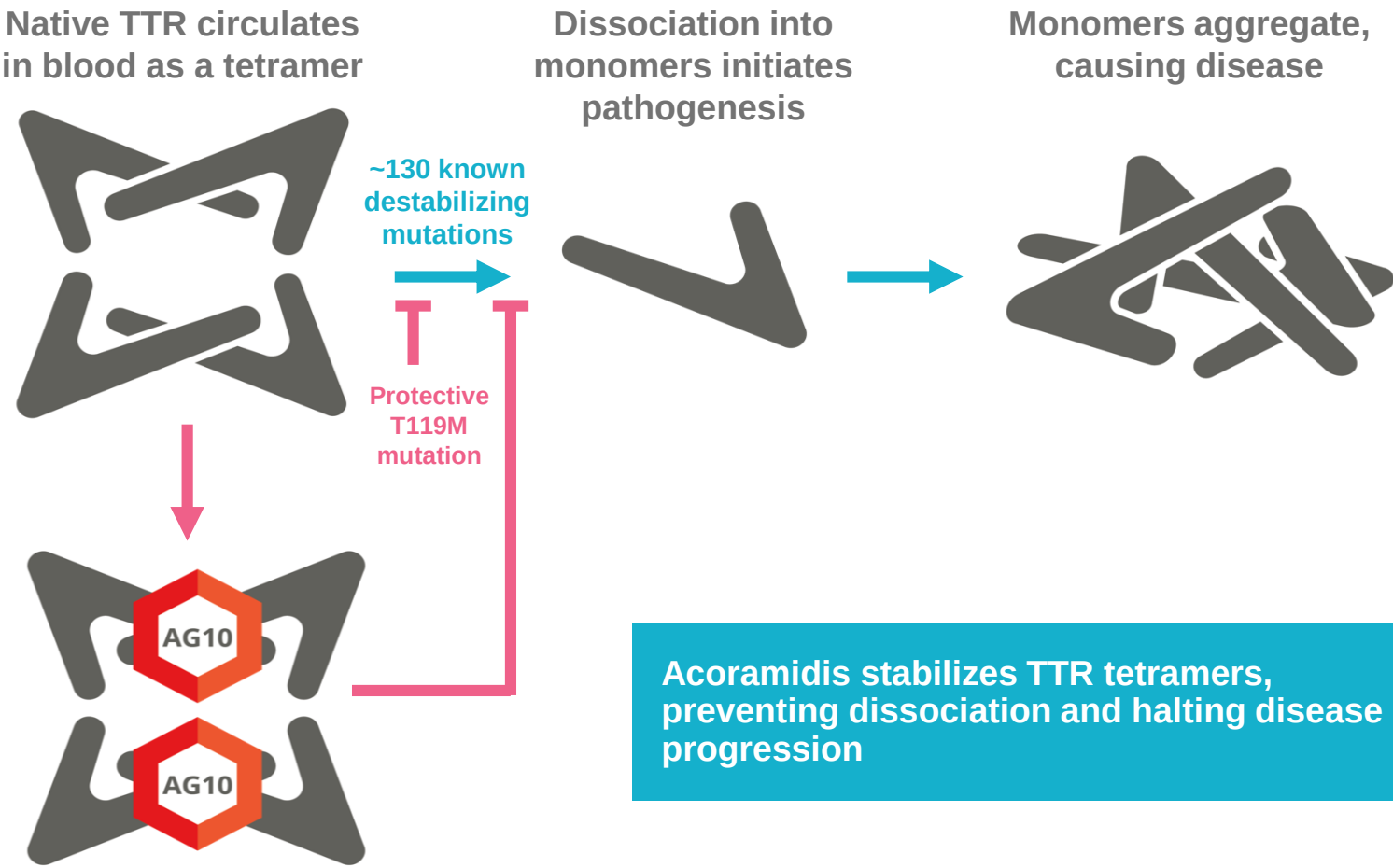
**Art, ATTR-CM patient**

- **Addressing large and growing need in ATTR**, a fatal disease affecting >400K patients
- **Targeting the disease at its source** by stabilizing TTR, a genetic and clinically validated mechanism
- **Advancing acoramidis, a potential best-in-class drug** that mimics naturally occurring rescue mutation
- Phase 2 open label extension study suggests potential to **reduce mortality and cardiovascular hospitalizations** at 15 months
- **Executing Phase 3 study in ATTR-CM** with top-line data expected in 2022

# Acoramidis is designed to treat TTR amyloidosis at its source

**Disease mechanism**

**Therapeutic hypothesis**




**Acoramidis stabilizes TTR tetramers, preventing dissociation and halting disease progression**



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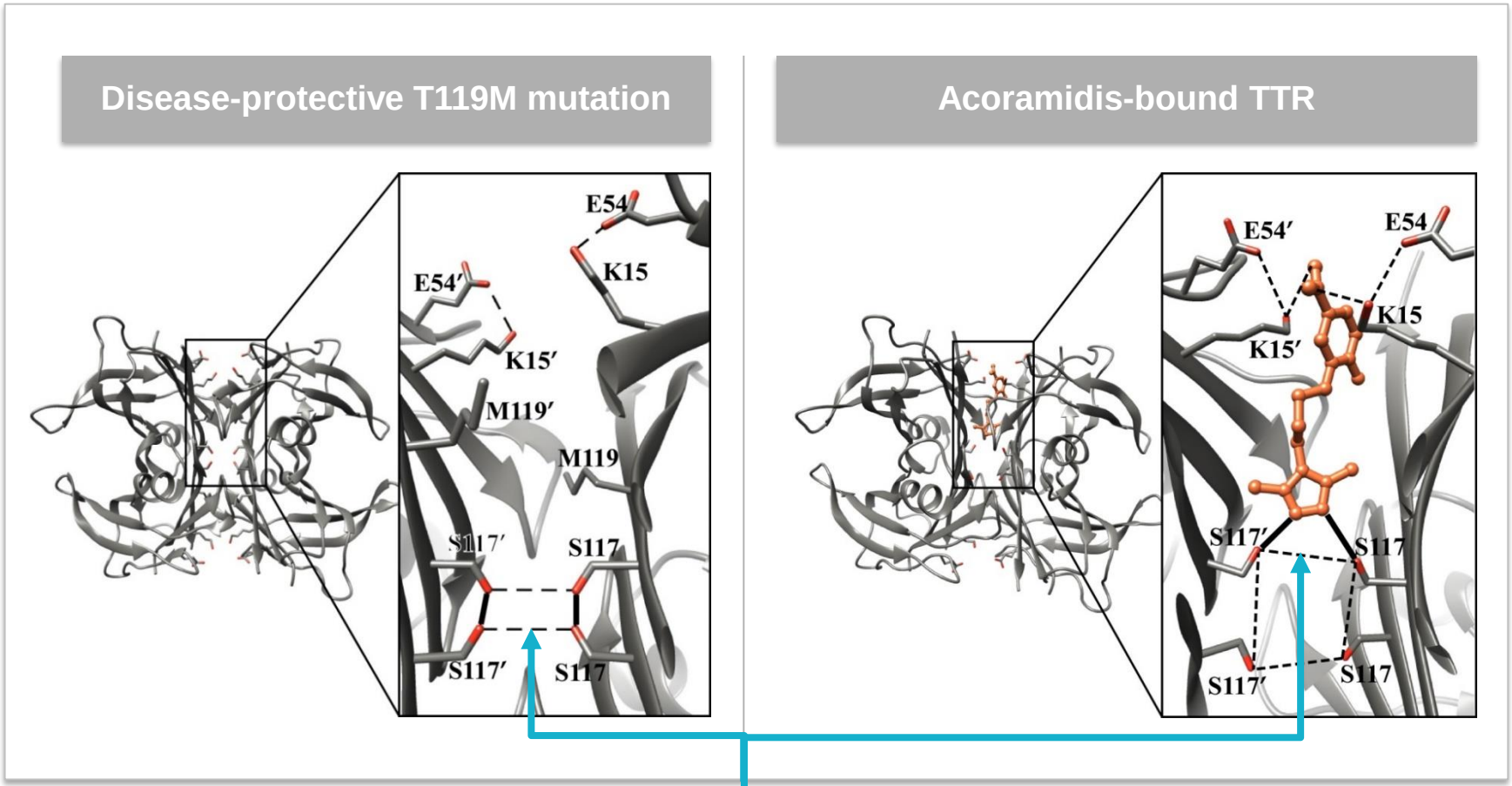
# Acoramidis structurally mimics disease-protective mutation by hyper-stabilizing TTR




**Strong inter-monomer H-bonds observed via X-ray crystallography**
**Unique binding mode vs other stabilizers**



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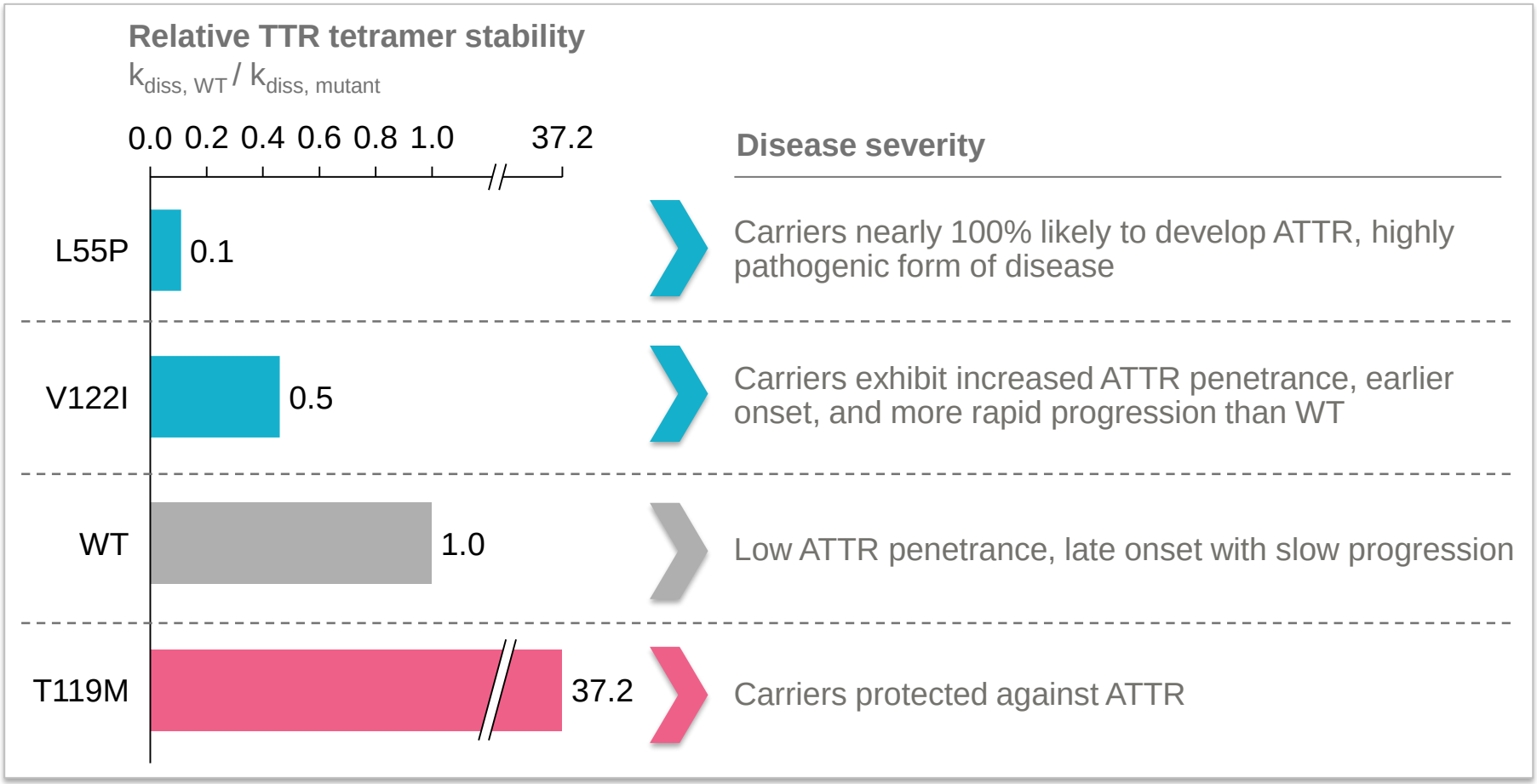
# Human genetics suggest TTR stability is associated with disease severity




- **Greater TTR destabilization correlates with earlier disease onset, increased disease severity**
- **ATTR-protective mutations stabilize TTR tetramer, preventing dissociation**

$k_{diss}$ = dissociation constant
Source: Hammarstrom, P. et al. PNAS 2002, 99:16427-16432



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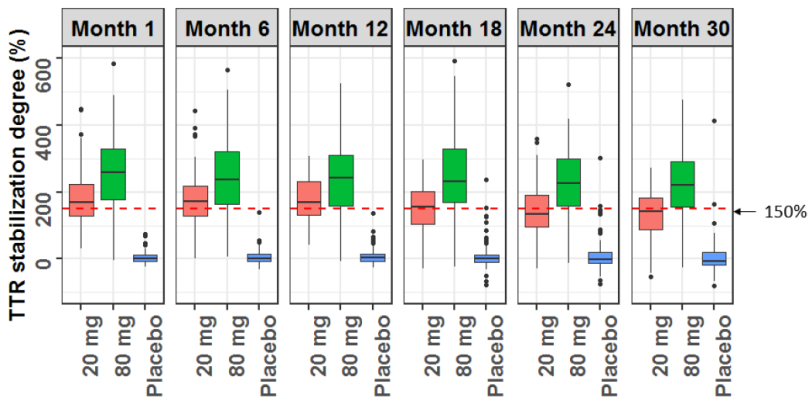
# Higher dose of tafamidis demonstrated increased TTR stabilization and greater clinical benefit in ATTR-ACT + LTE

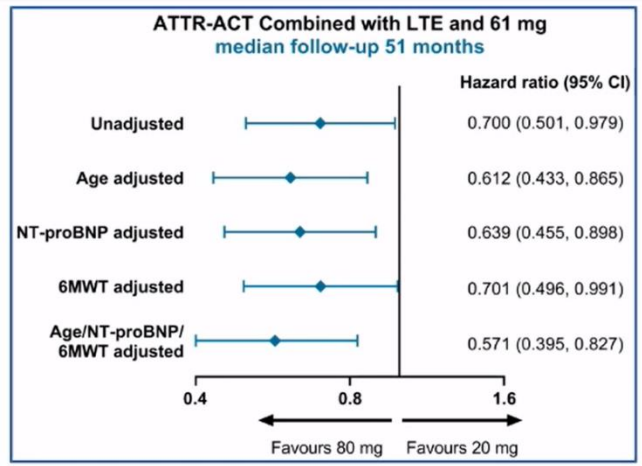
## Phase 3 ATTR-ACT study tested two doses of tafamidis (20 mg & 80 mg) vs. placebo

- In an analysis of ATTR-ACT combined with long-term extension (LTE), benefit of tafamidis 80 mg vs. 20 mg was evident on all-cause mortality[1]
- At baseline, ATTR-ACT participants treated with 80 mg of tafamidis were older and had more severe evidence of disease than those treated with 20 mg of tafamidis[1]
- Participants receiving 80 mg of tafamidis (vs. 20 mg) exhibited greater TTR stabilization[2]

### TTR stabilization[2]




### All-cause mortality[1]

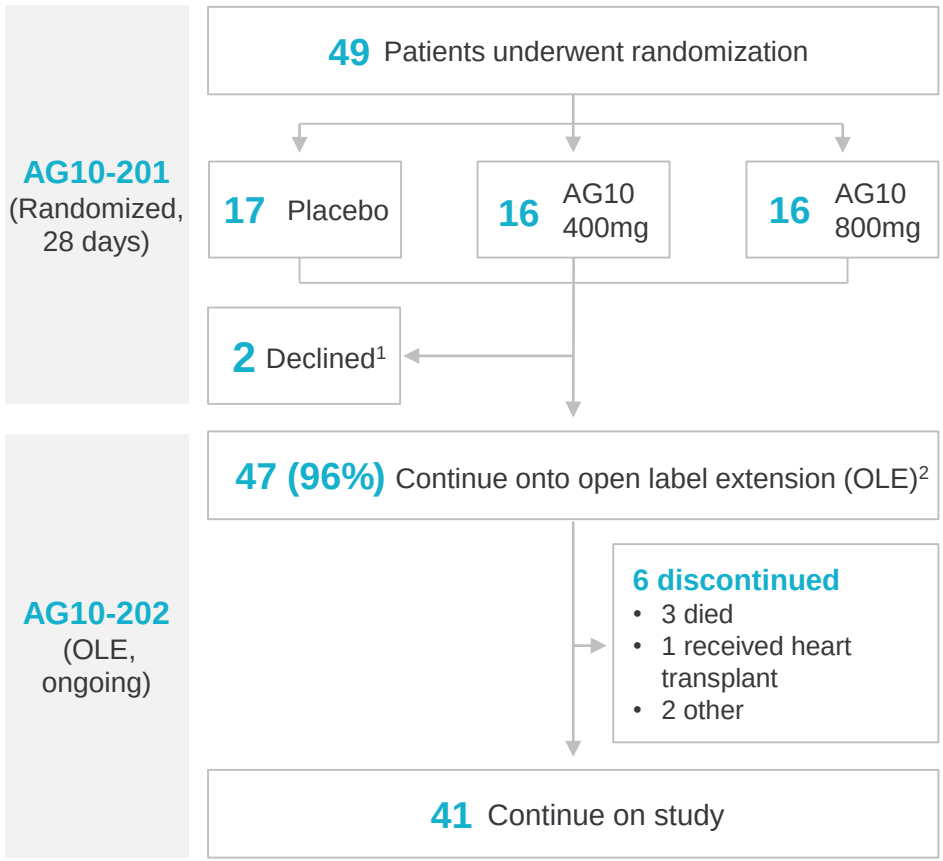



**Increased levels of TTR stabilization may translate to improved clinical outcomes in ATTR-CM**

1 Damy, T., ESC Heart Failure Association Discoveries 2020. "The Tafamidis in Transthyretin Cardiomyopathy Clinical Trial."
2 FDA CDER Clinical Pharmacology and Biopharmaceutics, Clinical Review (Vyndaqel/Vyndamax), 2019; Fourfold increase in tafamidis dose did not lead to a fourfold increase in TTR stabilization due to non-linear pharmacokinetics

# Phase 2 ATTR-CM trial provides randomized 28-day and 15-month open label data

## SCHEMATIC OF AG10 PHASE 2 STUDY




## OUTCOMES

### Primary

**Safety and tolerability**

- Adverse events
- Clinical events and vital signs
- Clinical laboratory parameters

### Secondary and Exploratory

**Pharmacokinetics**

**Pharmacodynamics**

**Echocardiographic parameters**

**Two analyses to date:**

- **Randomized 28-day study[3]**
- **Open label extension analysis as of 8/31/2019, median 65 weeks from AG10-201 (Randomized) initiation, median 53 weeks on AG10[4]**

1 Both declined participation due to geographical constraints regarding study visits
2 Median rollover period of 72 days (range 41-152 days)
3 Judge, D.P. et al. JACC Vol. 74, No. 3, 2019:285 – 95
4 Judge, D.P. et al. American Heart Association 2019



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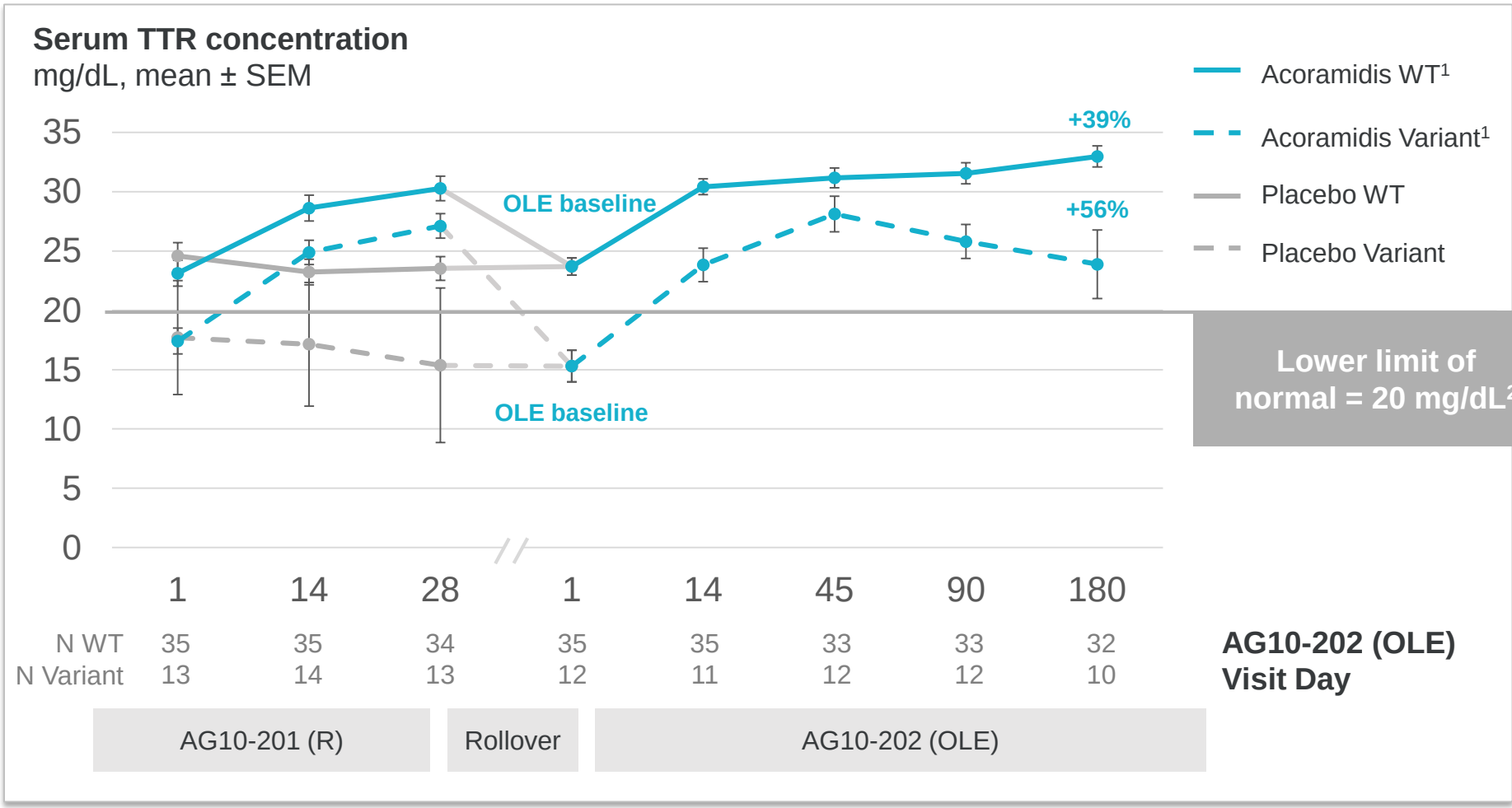
# Serum TTR levels, a prognostic indicator of survival, increased upon acoramidis treatment and were maintained throughout Ph 2 study



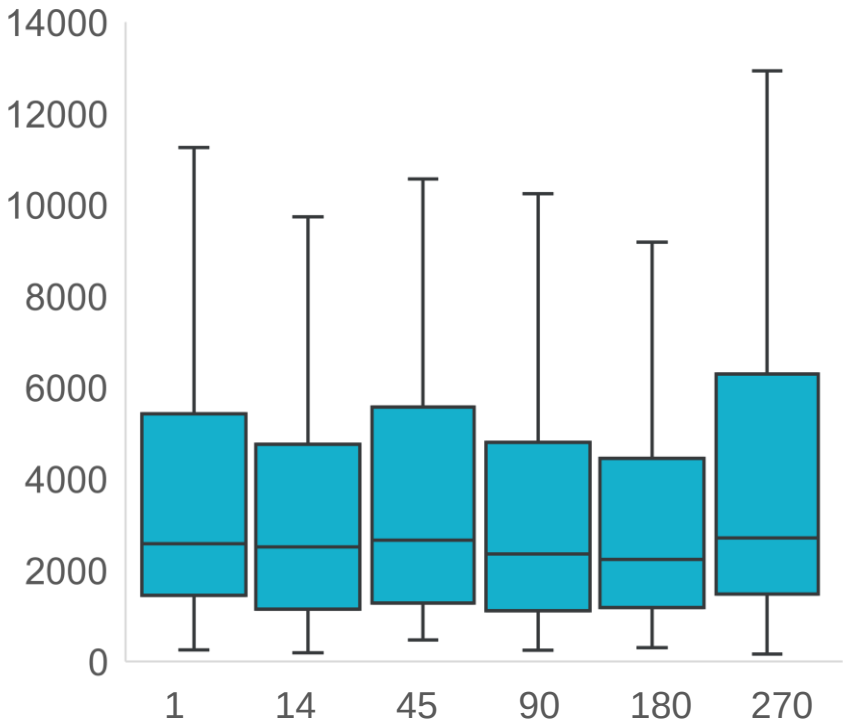

1 400mg and 800mg BID acoramidis groups pooled during randomized portion
2 Defined as the lower limit of the reference interval for the serum prealbumin (TTR) clinical laboratory assay

Source: Judge, DP et al. American Heart Association Scientific Sessions 2019

# Cardiac biomarkers were unchanged in acoramidis-treated participants throughout OLE

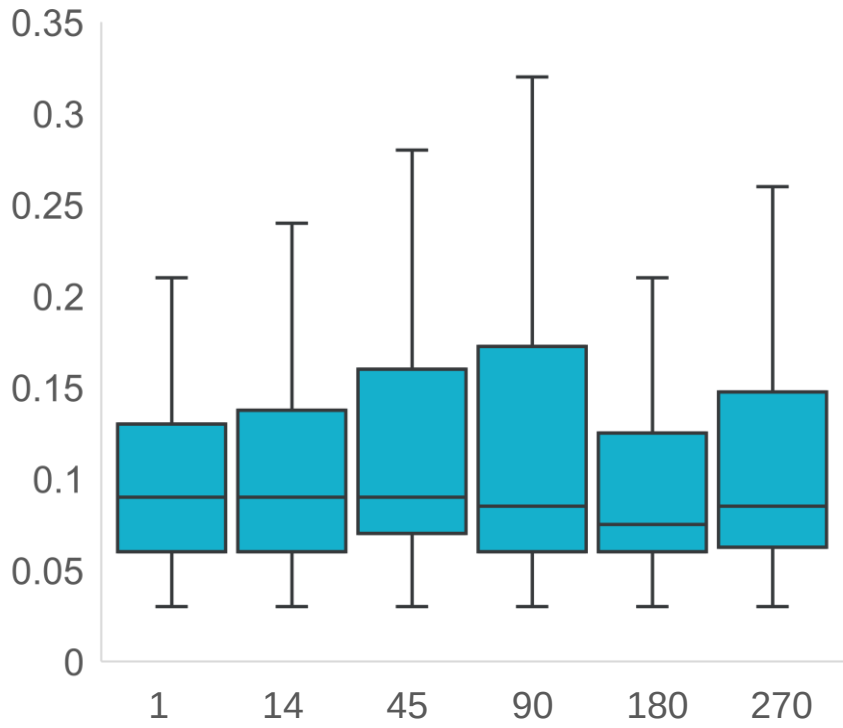
**NT-proBNP**

pg/mL; 95% confidence interval, quartiles, median




**Troponin I**

ng/mL; 95% confidence interval, quartiles, median



# Participants in the acoramidis Ph2 study had similar baseline characteristics as those in the tafamidis Ph3

## Baseline characteristics from ATTR-ACT study and AG10 Phase 2 study

| | ATTR-ACT Ph3 study Tafamidis group[1] | ATTR-ACT Ph3 study Placebo group[1] | Acoramidis Ph2 study All groups[2] |
|---|---|---|---|
| Age, median (range) | 75 (46-88) | 74 (51-89) | 73 (60-86) |
| Male, n (%) | 241 (91%) | 157 (89%) | 45 (92%) |
| ATTRm, n (%) | 63 (24%) | 43 (24%) | 14 (29%) |
| NYHA Class | | | |
| Class I, n (%) | 24 (9%) | 13 (7%) | 0 (0%) |
| Class II, n (%) | 162 (61%) | 101 (57%) | 35 (71%) |
| Class III, n (%) | 78 (30%) | 63 (36%) | 14 (29%) |
| Race | | | |
| White, n (%) | 211 (80%) | 146 (83%) | 35 (71%) |
| Black, n (%) | 37 (14%) | 26 (15%) | 10 (20%) |
| Other, n (%) | 16 (6%) | 5 (3%) | 4 (8%) |

1 Maurer, M.S. et al. N Engl J Med. 2018;379:1007–16
2 Judge, D.P. et al. JACC Vol. 74, No. 3, 2019:285 – 95



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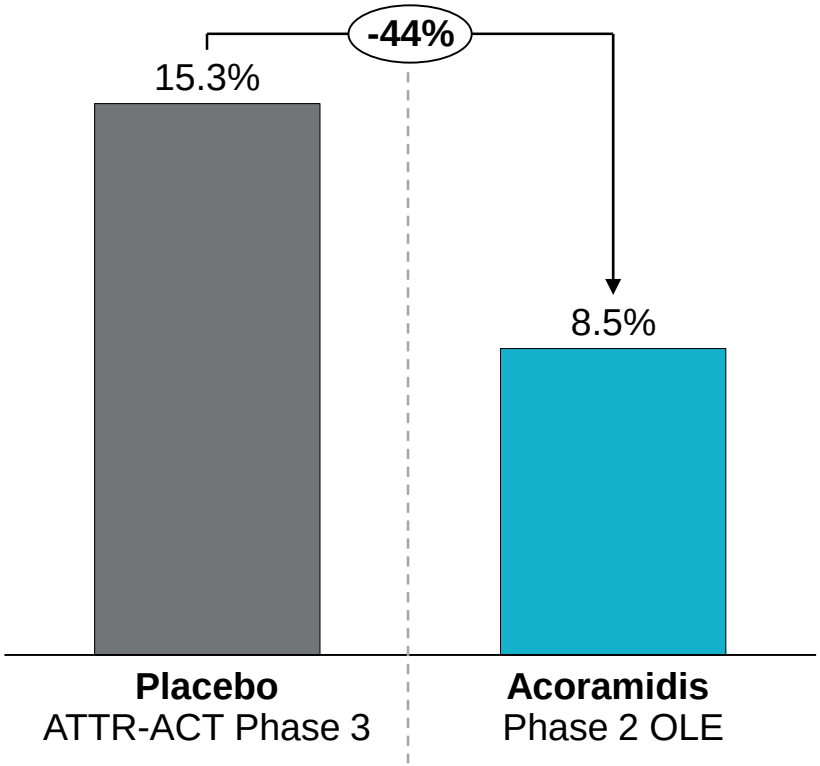
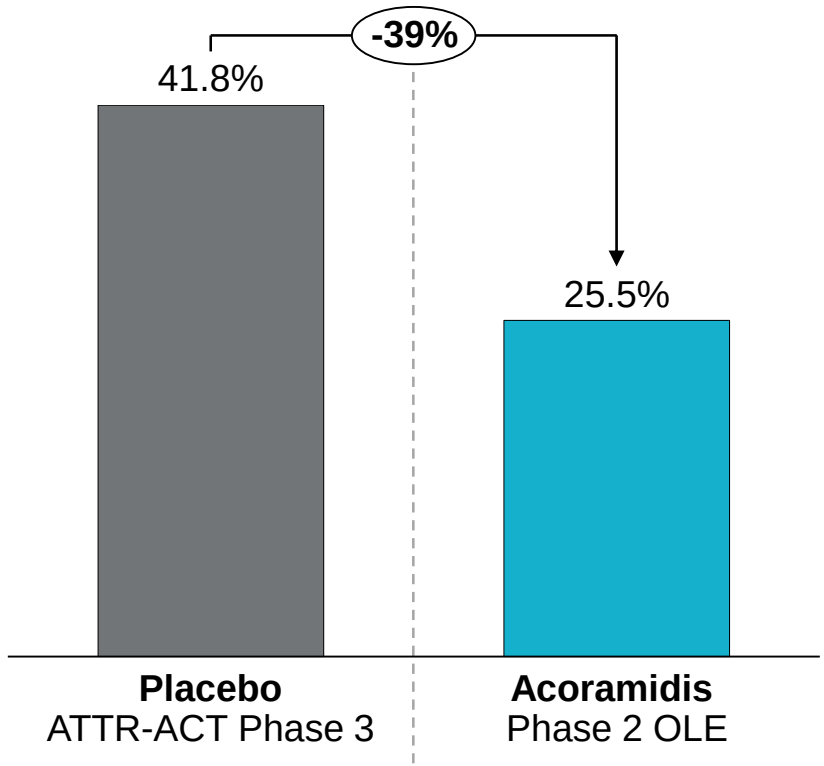
# Deaths and CV hospitalizations reported in acoramidis Phase 2 OLE were lower than in placebo-treated ATTR-ACT participants

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




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




**Phase 3 ATTRibute study expected to complete enrollment in 1H21**

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

# No safety signals of clinical concern identified during open label extension

**Summary of treatment-emergent adverse events**
Number of participants (%)

| Any Adverse Events | 46 (97.9) |
|---|---|
| **Most common Adverse Events (≥ 5)** | |
| Fall | 12 (25.5) |
| Cardiac failure congestive | 7 (14.9) |
| Dyspnoea | 6 (12.8) |
| Acute kidney injury | 6 (12.8) |
| Fluid overload | 5 (10.6) |
| Gout | 5 (10.6) |
| Pneumonia | 5 (10.6) |

**Summary of treatment-emergent severe adverse events**
Number of participants (%)

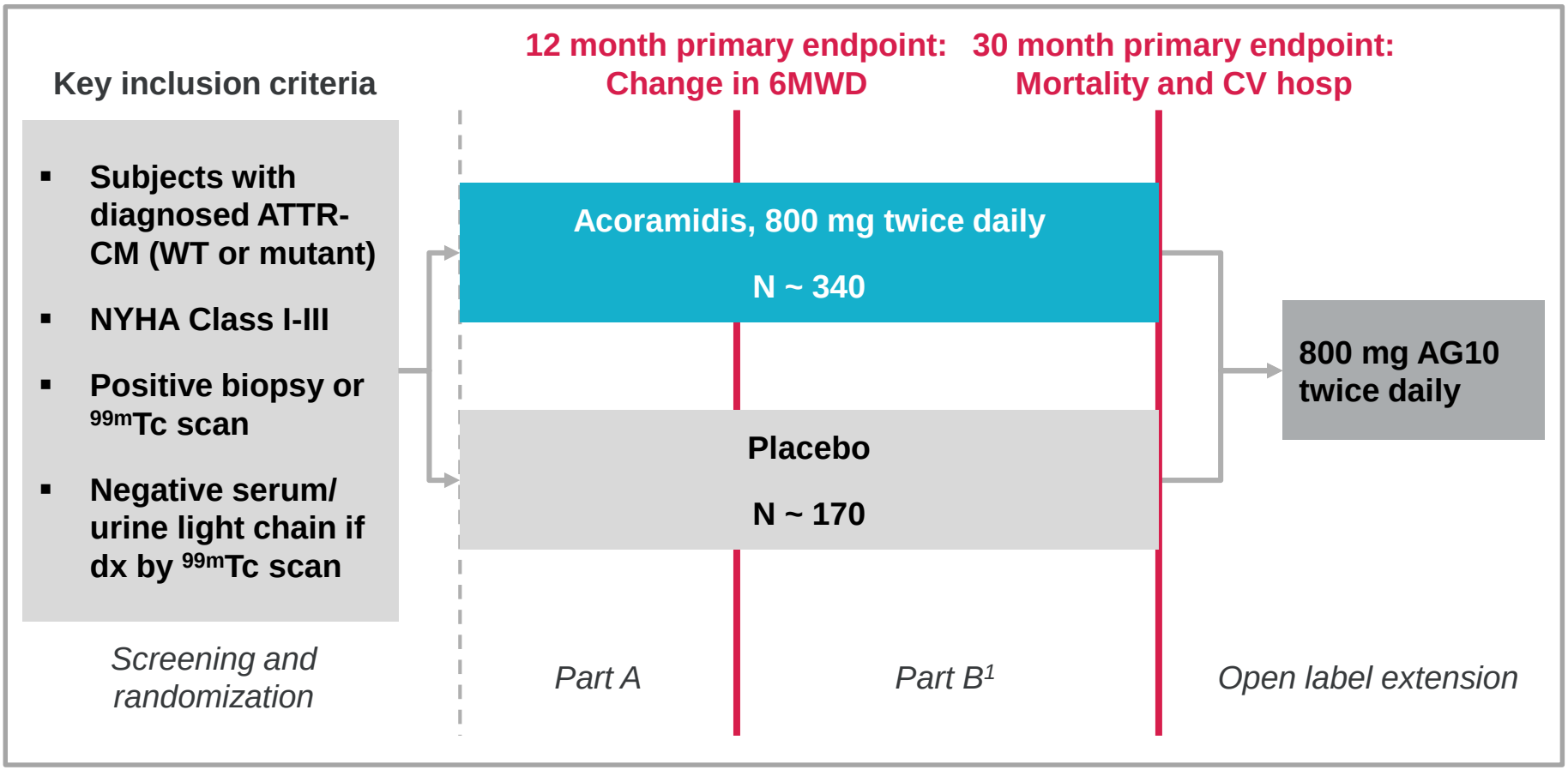
| Any Serious Adverse Events | 19 (40.4) |
|---|---|
| Number of subjects who died | 3 (6.5)[1] |
| Any Cardiovascular Serious Adverse Events | 12 (25.5) |
| **Most common Serious Adverse Events (≥ 2)** | |
| Cardiac failure congestive | 5 (10.6) |
| Acute kidney injury | 4 (8.5) |
| Atrial fibrillation | 2 (4.3) |
| Cardiac failure | 2 (4.3) |
| Fall | 2 (4.3) |
| Dehydration | 2 (4.3) |

**AG10 was generally well tolerated with a pattern of adverse events consistent with underlying disease severity, concurrent illnesses, and age of participants**

1 Includes 2 subjects who had SAEs with an outcome of death (1 disease progression; 1 cervix carcinoma); 1 subject died due to heart failure 86 days after the last dose of study drug
Data reported as of 8/31/2019 in conjunction with annual regulatory reporting and review

# Data from 12-month registration endpoint expected in 1H22

## ATTRibute-CM study schematic




Secondary endpoints include: Kansas City Cardiomyopathy Questionnaire, serum TTR, TTR stabilization

[1]As local standard of care evolves, concomitant use of approved, indicated therapies may be allowed

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

# Low-dose FGFR inhibitor (infigratinib) for achondroplasia

Claudia, child with 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 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

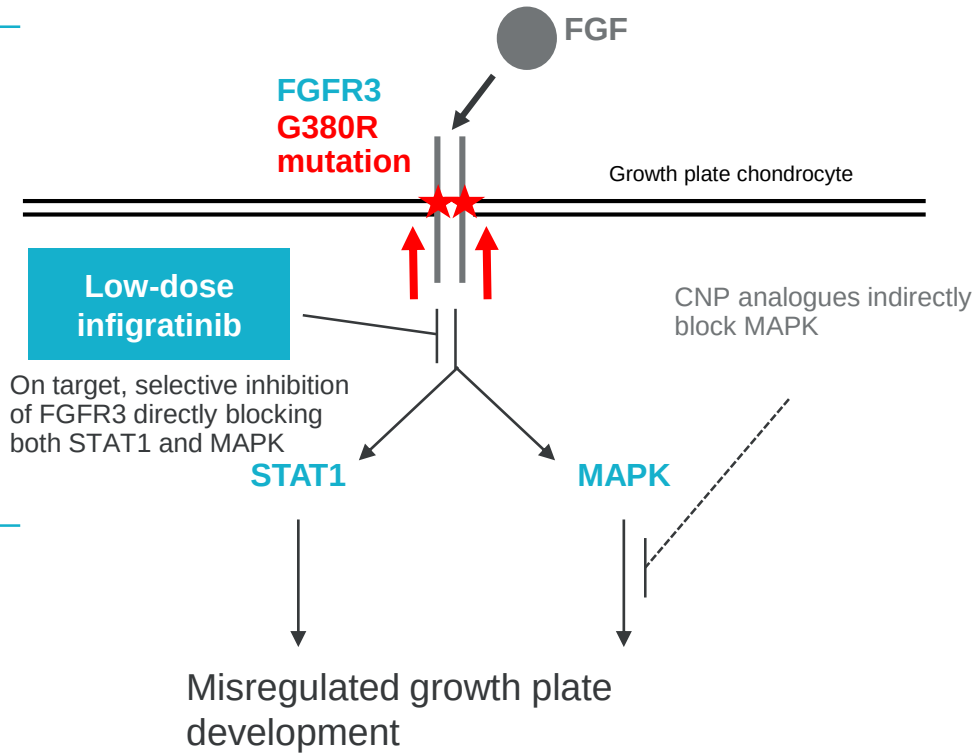
# Potential best-in-class approach to treating achondroplasia directly at its genetic source

## 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 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

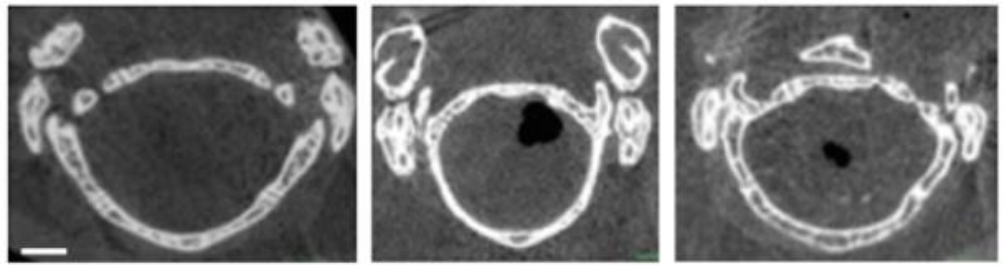
**FGFR3 WT** No treatment | **FGFR3$^{Y367C/+}$** No treatment | **FGFR3$^{Y367C/+}$ Infigratinib tx**

## 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

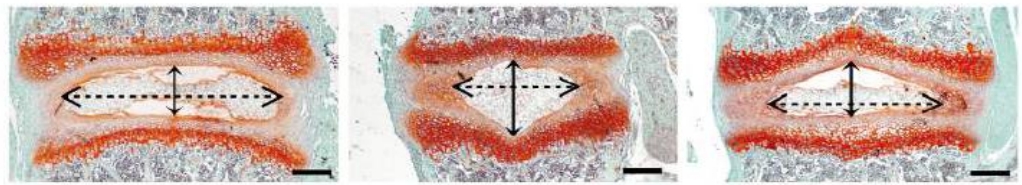


## 2 Disorders of the spine

**12%** increase in L4-L6 length

**73%** increase in disc width

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

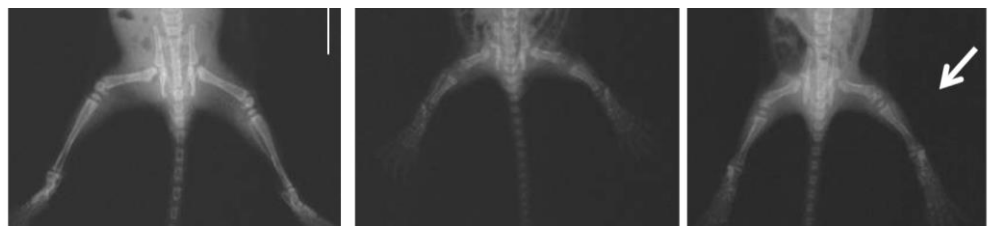


## 3 Disproportionate short stature

**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 FGFR3$^{Y367C/+}$ mouse, infigratinib treatment with 2mg/kg subcutaneous dose



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

## Preclinical data from infigratinib and other investigational achondroplasia therapies

Percent increase compared to non-treated mouse

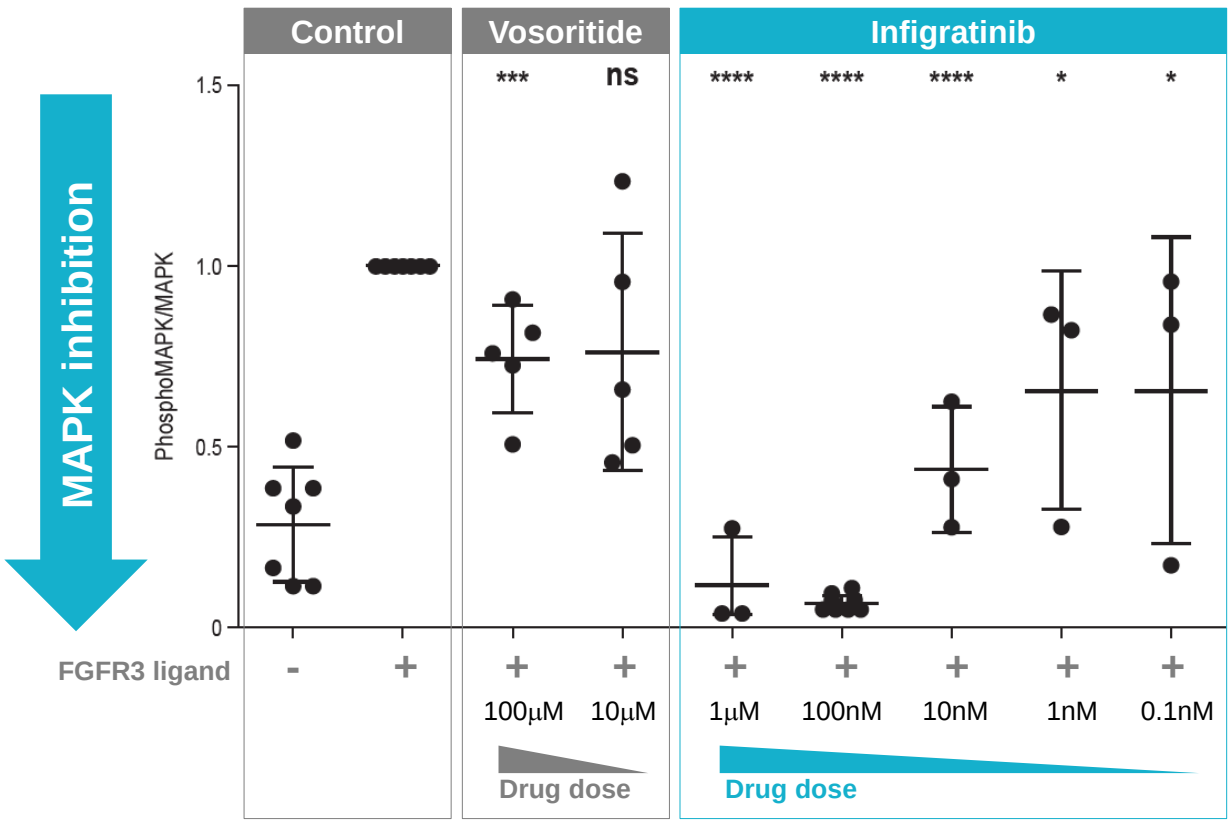
| Company/ Asset | MOA | Route | Status | Mouse model | Tibia length | Femur length | Foramen magnum area | L4-L6 height |
|---|---|---|---|---|---|---|---|---|
| bridgebio Infigratinib | Selective FGFR1-3i | Oral | Ph2 | FGFR3$^{Y367C/+}$ | 33% | 21% | 17% | 12% |
| BIOMARIN Vosoritide (BMN111) | CNP analogue | Daily SQ | Pivotal | FGFR3$^{Y367C/+}$ | 7% | 5% | No known publicly available data | 3% |
| ascendis pharma TransCon CNP[1] | CNP analogue | Weekly SQ | Ph2 | FGFR3$^{Y367C/+}$ | 12%* | | | |
| Pfizer Reifercept (TA-46) | FGFR3 decoy | Weekly SQ | Ph1 | FGFR3$^{ACH/+}$ | 9%* | 7%* | | |

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.

# *In vitro* data suggest infigratinib is a more potent inhibitor of MAPK signaling than vosoritide

## PhosphoMAPK/MAPK ratio in FGF18-conditioned TAN 4-18-chondrocytes

Vosoritide, infigratinib




- **Infigratinib showed significant inhibition of ERK1/2 phosphorylation at all concentrations**
- Vosoritide only showed significant inhibition at higher concentration

Source: Komla-Ebri et al. J Clin Inv 2016, Demuynck B et al. ASHG 2019, Demuynck B et al. ENDO 2020



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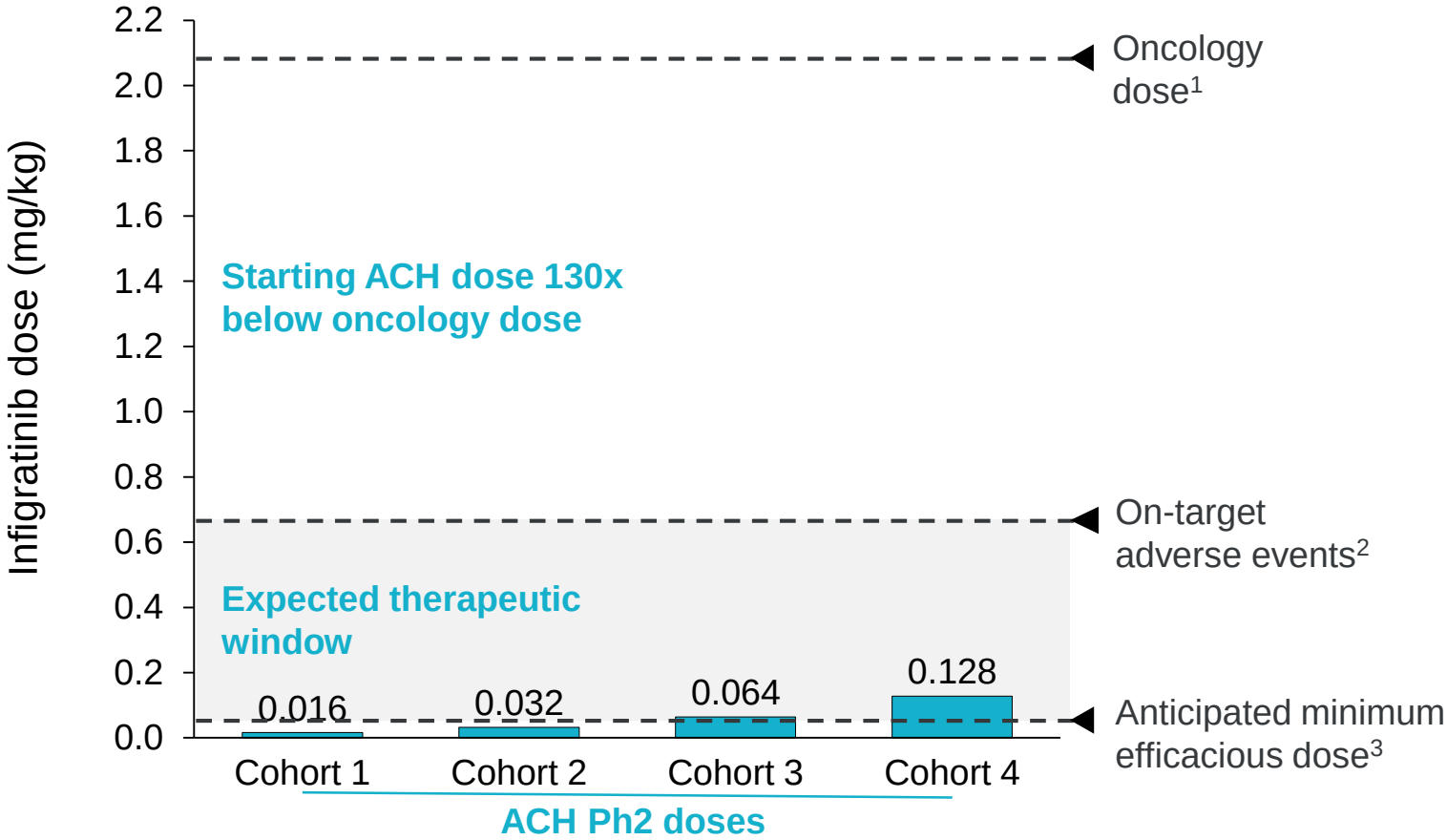
# We have a wide anticipated therapeutic index in achondroplasia

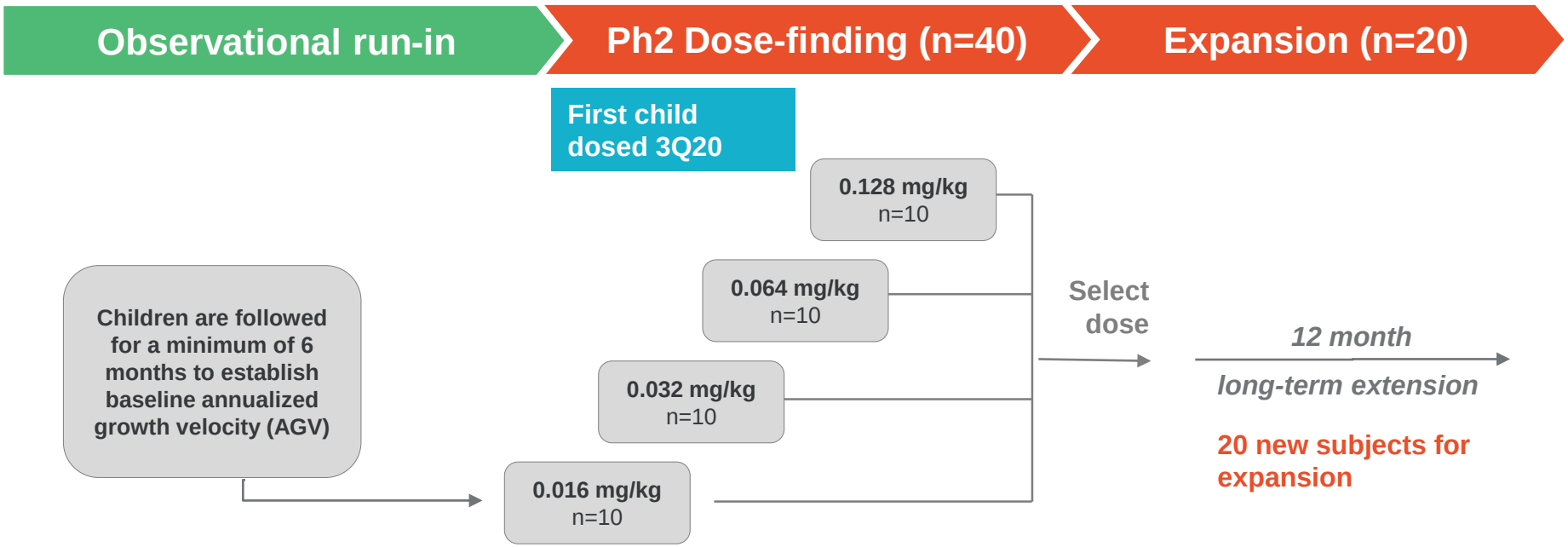
## Infigratinib has been tested in >700 humans in our oncology program, providing significant data on PK, tolerability and safety

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

# Gene therapy for congenital adrenal hyperplasia (CAH)

Maris, child with CAH

## Program overview:

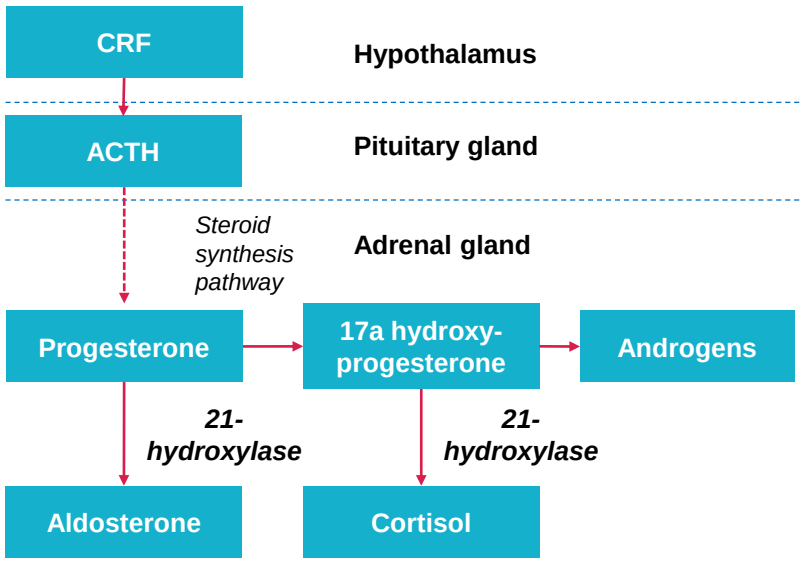
- **Prevalence**: 75,000 (US+EU) – One of the largest known AAV gene therapy markets
- **Genetic driver**: 21-hydroxylase inactivation
- **Pathophysiology**: Inability to produce cortisol causes need for supraphysiologic doses of synthetic steroids, 3x increase mortality risk, hirsutism, Cushingoid symptoms

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

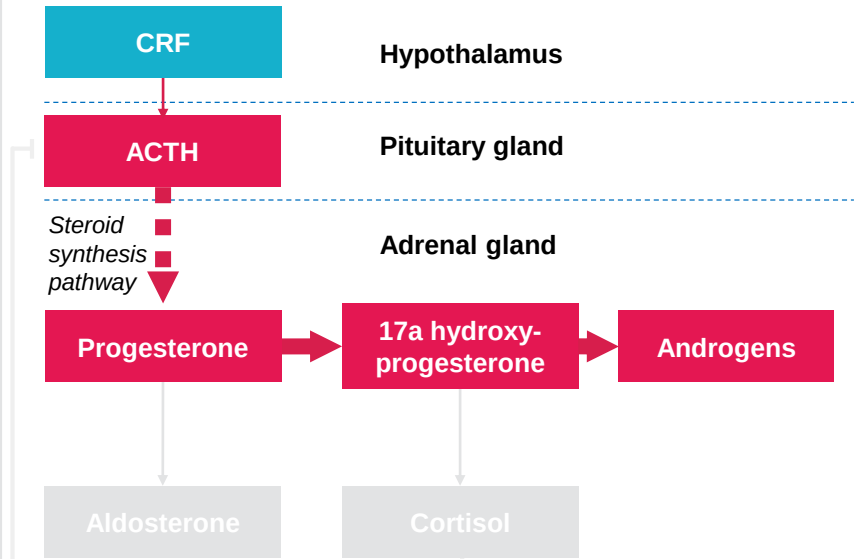
- **Low threshold to correct phenotype**, validated by human clinical genetics
- **Only approach designed to induce endogenous cortisol production**, potentially allowing steroid withdrawal
- **Durable transgene delivery to the adrenal gland of NHP** with IV dosing of our construct
- **Preliminary Ph1/2 data anticipated in 2021**

# Overview of hormone dysregulation in CAH

## Healthy Hypothalamic-Pituitary-Adrenal Axis




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




## HPA Features

- Diurnal rhythm of cortisol release ☑
- Sufficient aldosterone to retain sodium ☑
- Dynamic cortisol response to stress ☑
- Appropriate androgen levels ☑

## Disease Symptoms

- ❑ Sleep dysregulation, chronic fatigue
- ❑ Salt-wasting causing hyponatremia, hyperkalemia
- ❑ Life-threatening adrenal crisis
- ❑ Infertility, hirsutism, adrenal rest tumors



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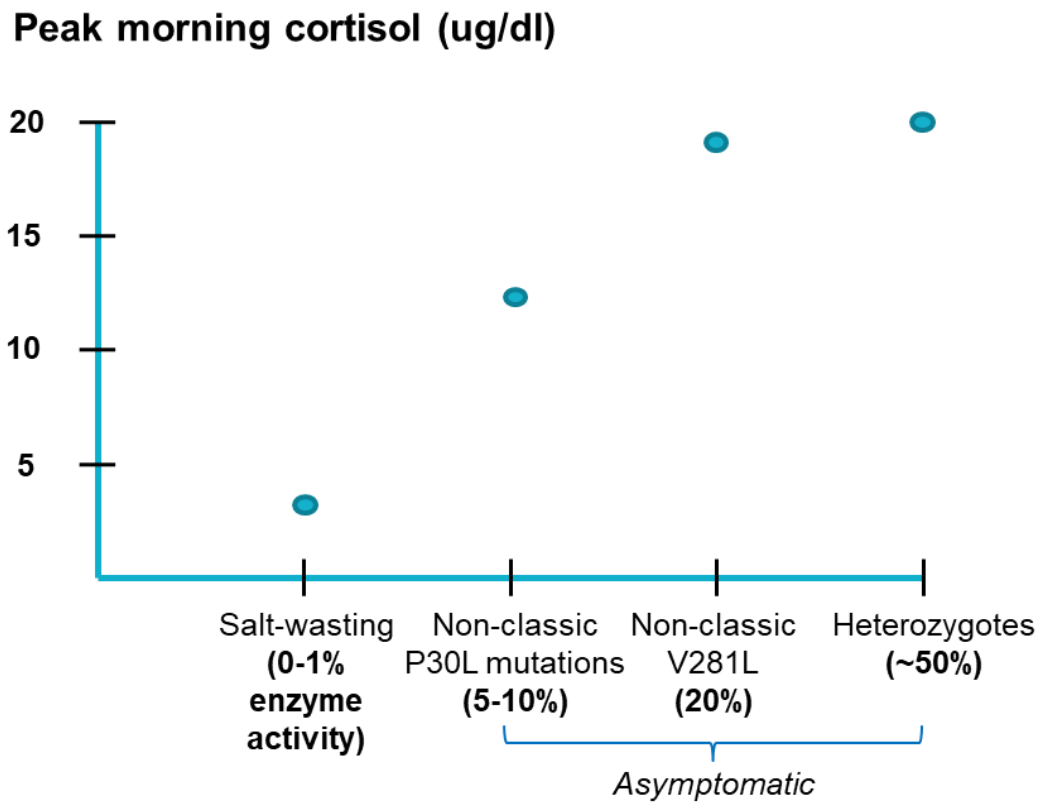
# Genotype-phenotype studies show that >5-10% of enzyme activity results in nonclassical CAH

- **Only a small amount of enzyme is required to rescue the phenotype** due to the high enzymatic efficiency/selectivity of 21-Ohase
- We believe this low threshold creates an ideal situation for AAV gene therapy – restoring as little as 5% of normal enzyme activity could dramatically improve symptoms




Source: KOL advisory boards

# Proof of concept 21OH gene therapy in the definitive mouse model improves body-weight and disease markers

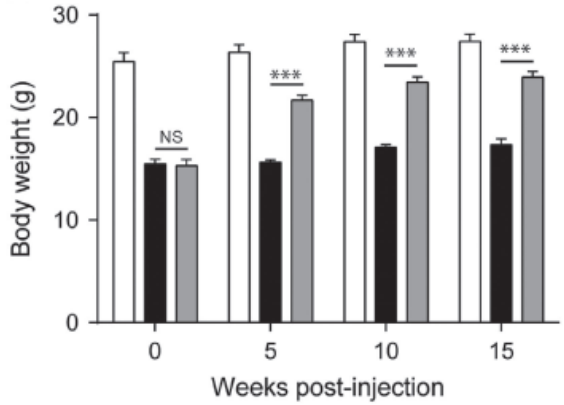
## Mouse Model

- H-$2^{a218}$ ($CYP21^{-/-}$) mouse model
- Deletion is lethal without GC administration; with GC administration, adult mice are still frail
- Increase in biomarkers:
  - Progesterone (21OH substrate) 4x higher
  - Renin 160x higher

## Vector

- AAVrh10 vector
- Human CYP21A2 cDNA
- Hemagglutinin tag
- CAG promoter
- $2x10^{13}$ vg/kg dose

## Substantial recovery of mouse body-weight

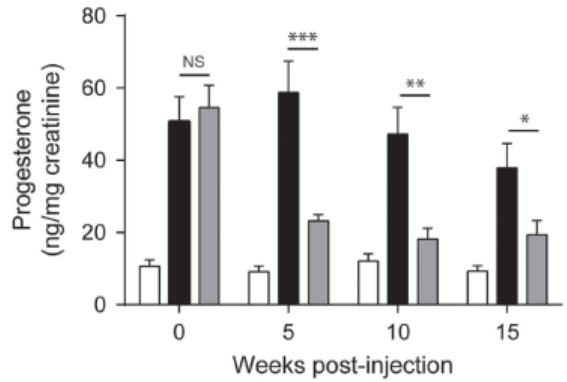



**Black**: Sham vector in model mice

**Grey**: CYP21 vector in model mice

**White**: Control mice

## Correction of progesterone




**At 18 weeks, a VGC of 0.13 was still sufficient for phenotypic restoration**

Source: Perdomini M, Dos santos C, Goumeaux C, Blouin V, Bougnères P. An AAVrh10-CAG-CYP21-HA vector allows persistent correction of 21-hydroxylase deficiency in a Cyp21(-/-) mouse model. Nature Gene Ther. 2017;24(5):275-281.



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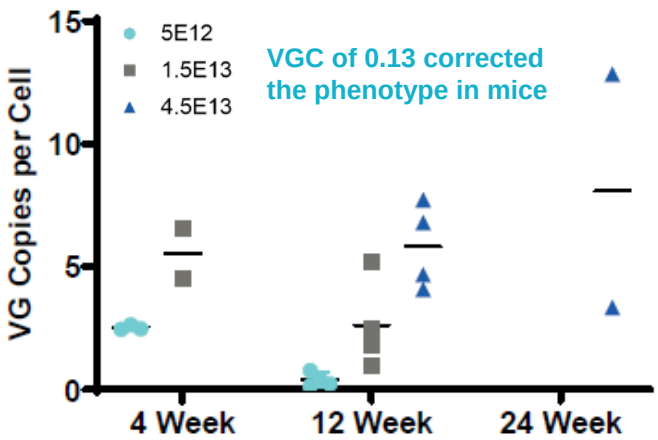
# NHP study showed durable transgene expression with VGC levels above the expected therapeutic threshold

**BBP-631** is our AAV5 gene therapy with a codon optimized 21-OH cDNA, CAG promoter delivered to the adrenal cortex via IV dosing

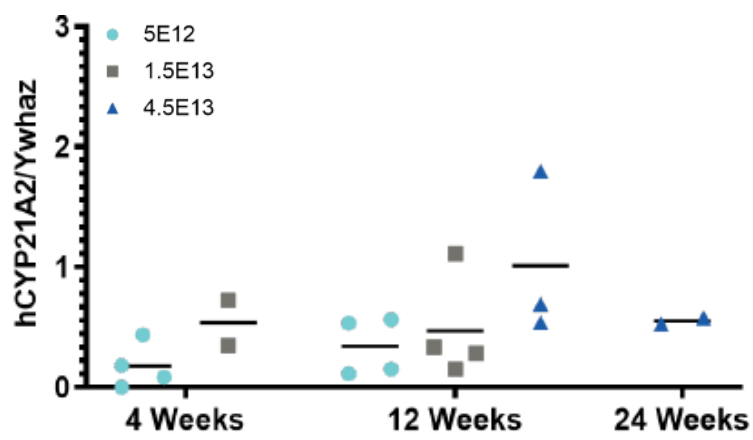
**We can durably transduce the NHP adrenal gland with our construct at >20x the vector required to correct the CAH phenotype in mice**

**BBP-631 vector levels in the adrenal gland**




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

**BBP-631 mRNA levels in the adrenal gland**




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

Source: ESGCT 2019



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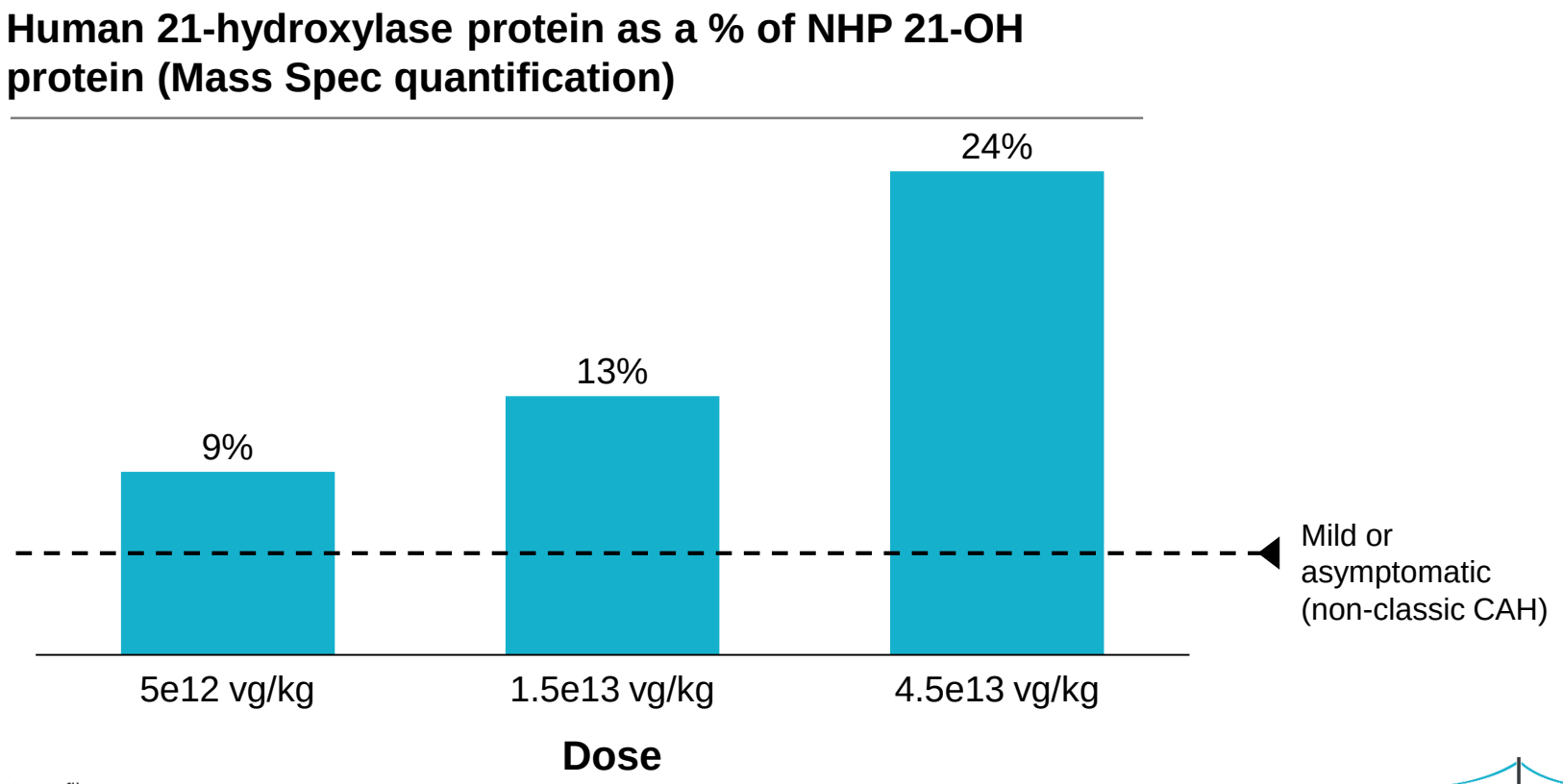
# NHP protein data using mass spec methods suggests potentially therapeutic levels of 21-hydroxylase enzyme

- 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

# BridgeBio gene therapy manufacturing and research capabilities

## Dedicated space at FDA approved commercial facility:

- 5,000 square feet of cGMP space at Catalent's facility at BWI
- 4 cleanrooms which allow us to run multiple 500L suspension bioreactors in parallel
- Flexibility to allow multiple manufacturing platforms including HEK293 triple transfection and baculoviral approaches

## Internal research, process development and analytical capabilities:

- 15,000 square feet of fully equipped lab space in Research Triangle Park, North Carolina
- Equipment mirror our Catalent suite such that upstream and downstream processes can be optimized in-house
- Experienced process development team focused on yield optimization and state-of-the-art analytical methods

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

Alexis and Jackson, ADH1 patients

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

- Opportunity identified in collaboration with global experts at the NIH

## Potential 1st in class CaSR inhibitor 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)

## Prior clinical experience enables accelerated development

- Well tolerated in >1,200 human subjects and increased serum calcium in a dose-dependent manner
- Phase 2 study in ADH1 initiated with proof-of-concept data anticipated in 2021

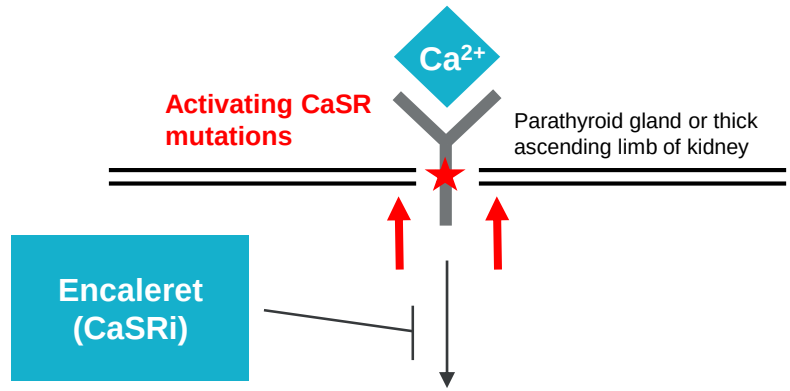
# Encaleret (CaSR inhibitor) is designed to treat ADH1 at its genetic source

## CaSR activating mutations cause:

- Low serum calcium levels and high urinary calcium levels
- Low serum parathyroid hormone (PTH) levels
- Chronic kidney damage, seizures, muscle spasm, cardiac disease

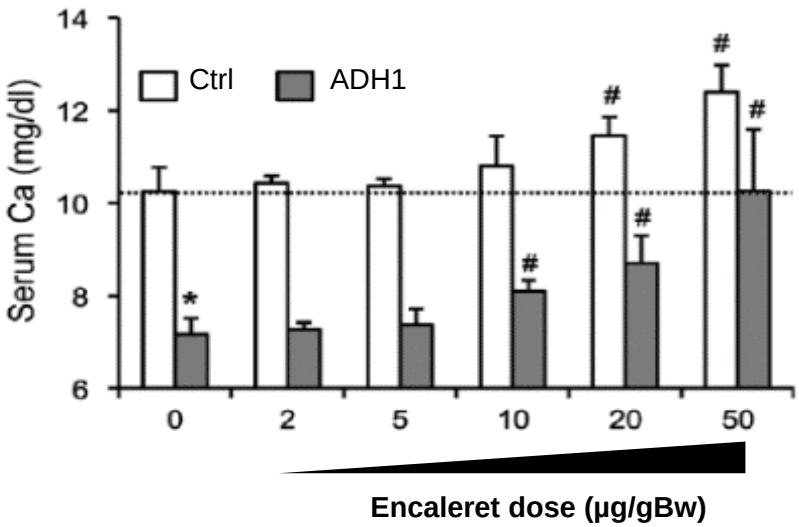
## Our selective CaSR inhibitor has the potential to:

- Increase serum PTH levels
- Normalize serum and urinary calcium levels through PTH-dependent and independent mechanisms
- Reduce risk of chronic kidney damage due to hypercalciuria

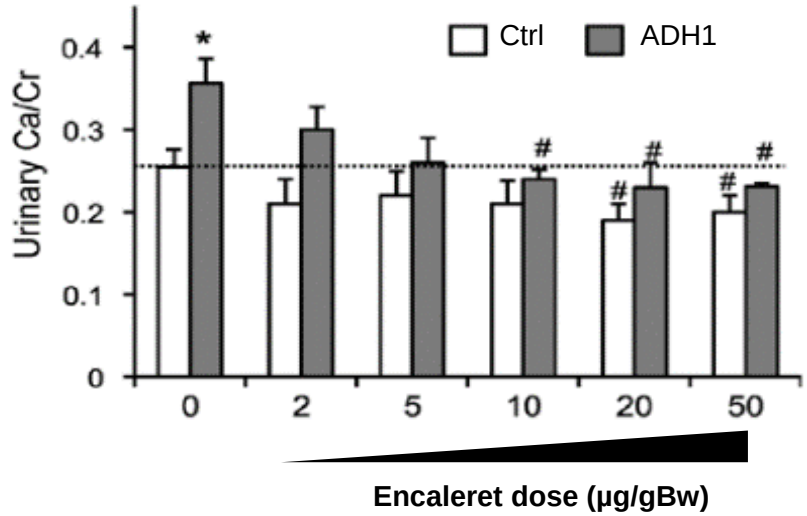


# Encaleret normalized serum and urine calcium in the mouse model of ADH1

**Dose-dependent increases in serum calcium**




**Normalization of urinary calcium**




Source: Dong B., et al. J Bone & Min 2015



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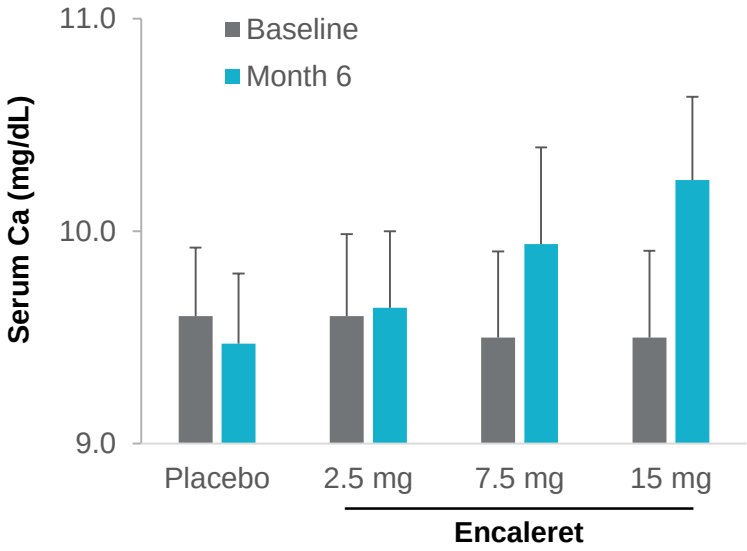
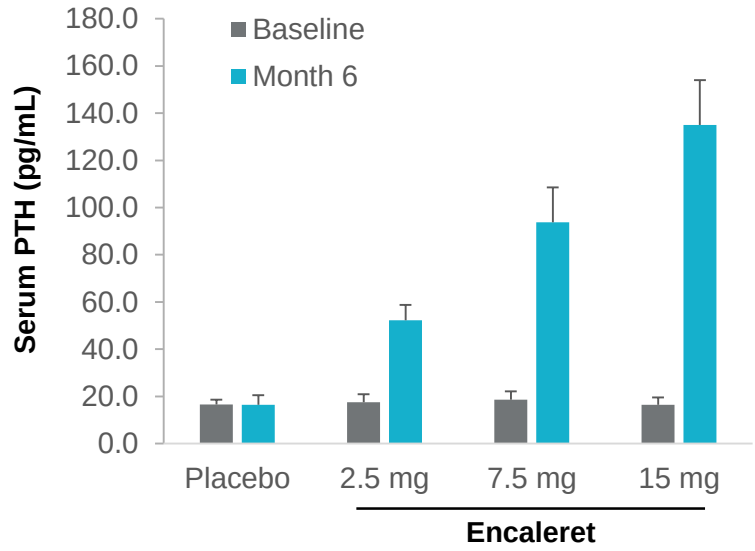
# Human clinical data suggests dose-dependent elevations of serum calcium and parathyroid hormone (PTH) levels

**Encaleret increased serum calcium in clinical trials in patients with osteoporosis…**

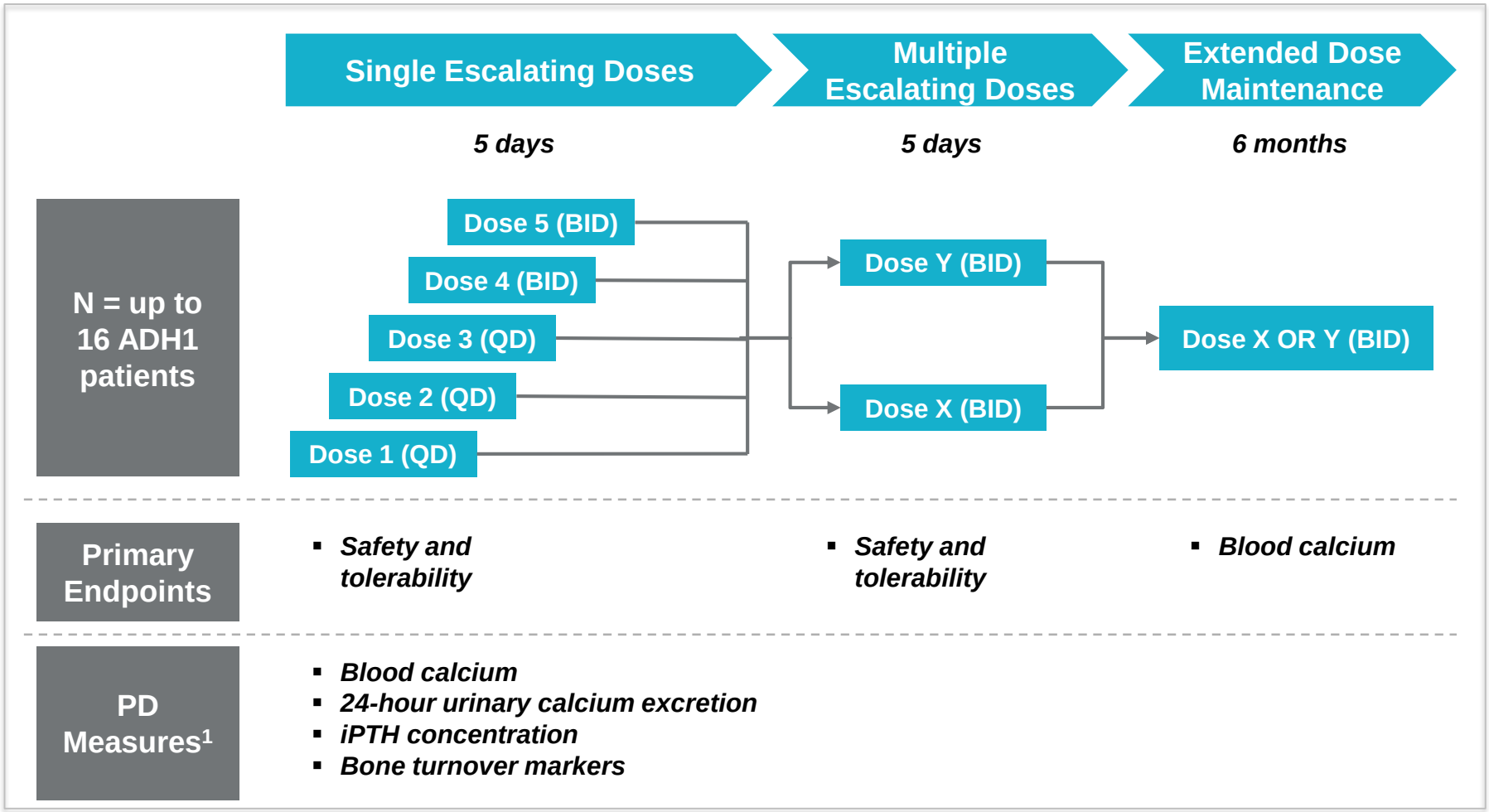



**…while simultaneously increasing serum PTH levels**




Source: 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 expected in 2021**

[1] Pharmacodynamic measurements to be collected through duration of study.

# Early oncology portfolio

Basia, pancreatic cancer patient

## World-class oncology team drives our discovery and development

- **Eli Wallace,** CSO Oncology
- **Frank McCormick**, Chairman of Oncology
- **Richard Scheller**, Chairman of R&D

Peloton Therapeutics · ARRAY BIOPHARMA · Genentech · ONYX PHARMACEUTICALS

## Our KRAS platform has produced 3 pan-mutant programs:

- 1 – H95 approach, designed to block effector signaling
- 2 – KRAS:PI3K blocker approach, designed to block PI3K effector signaling
- 3 – C185 approach, designed to block KRAS prenylation and activation

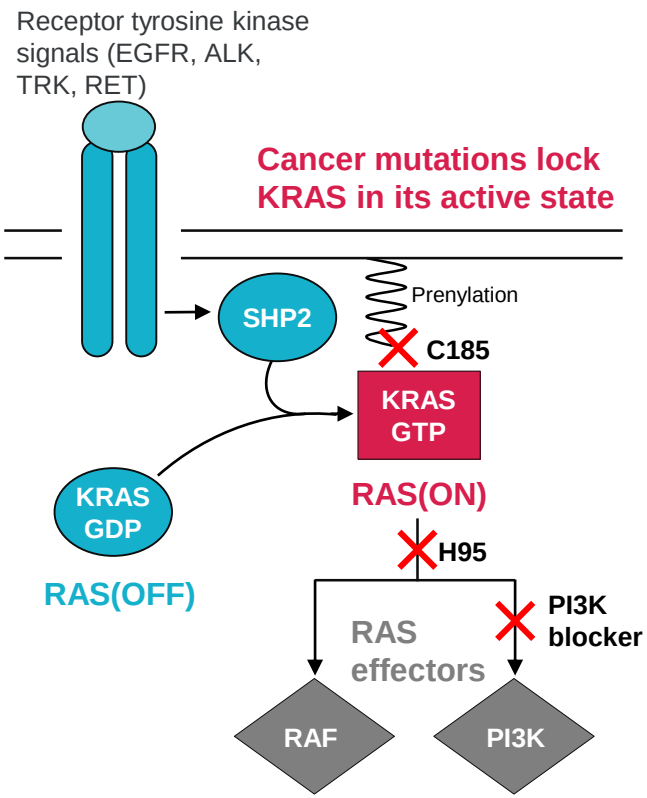
## We are also prosecuting novel targets with extensive academic validation

- **SHP2i** for multiple tumors (10+ recent papers in *Nature, Science, Nature Medicine*)
- **GPX4i** for multiple tumors (10+ recent papers in *Nature, Cell, Science, Cancer Cell*)

| Program | MOA | Disease | Stage | Next anticipated update |
|---|---|---|---|---|
| Pan-mutant KRAS inhibitors | (1) H95 approach<br>(2) PI3K blocker<br>(3) C185 approach | KRAS+ cancer | Discovery | Clinical candidate nomination |
| SHP2 inhibitor | Allosteric inhibitor | Multiple tumors | Pre-IND | IND submission in 2020 |
| GPX4 inhibitor | Covalent inhibitor | Multiple tumors | Discovery | Clinical candidate nomination |

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

## KRAS pathway in cancer

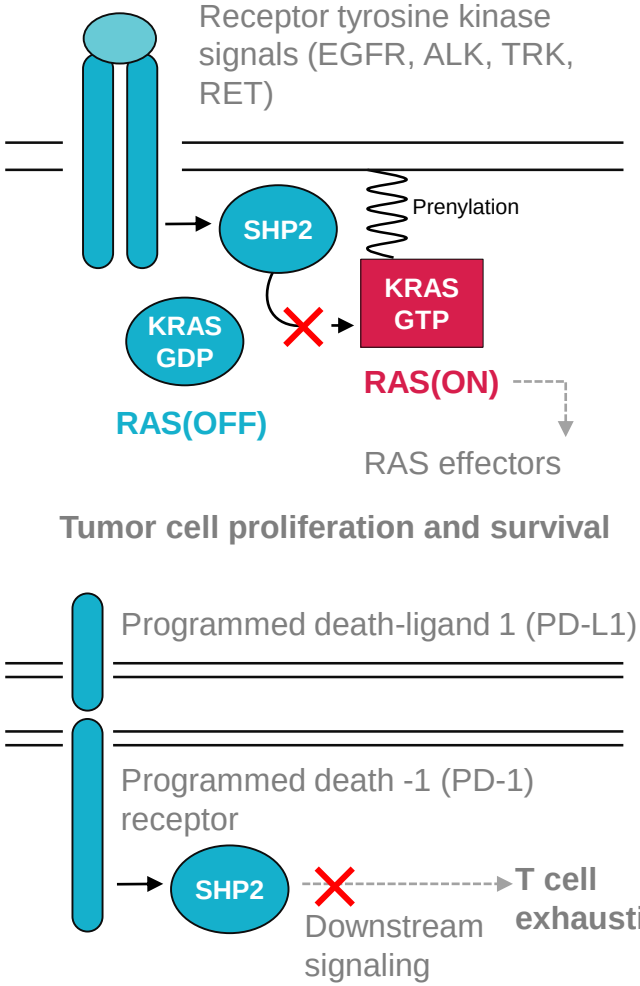



| Program | MOA | Targets KRAS GTP | Pan-mutant | Crystal structure |
|---|---|---|---|---|
| **Program 1: H95 targeting** | ▪ Directly binds activated KRAS through H95<br>▪ Inhibits KRAS from signaling through effectors | ✓ | ✓ | ✓ |
| **Program 2: PI3K effector blocking** | ▪ Blocks specific interaction between KRAS and PI3Ka<br>▪ Blocks PI3K / AKT effector signaling | ✓ | ✓ | ✓ |
| **Program 3: C185 targeting** | ▪ Blocks KRAS from tethering<br>▪ 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 expected to enter 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**

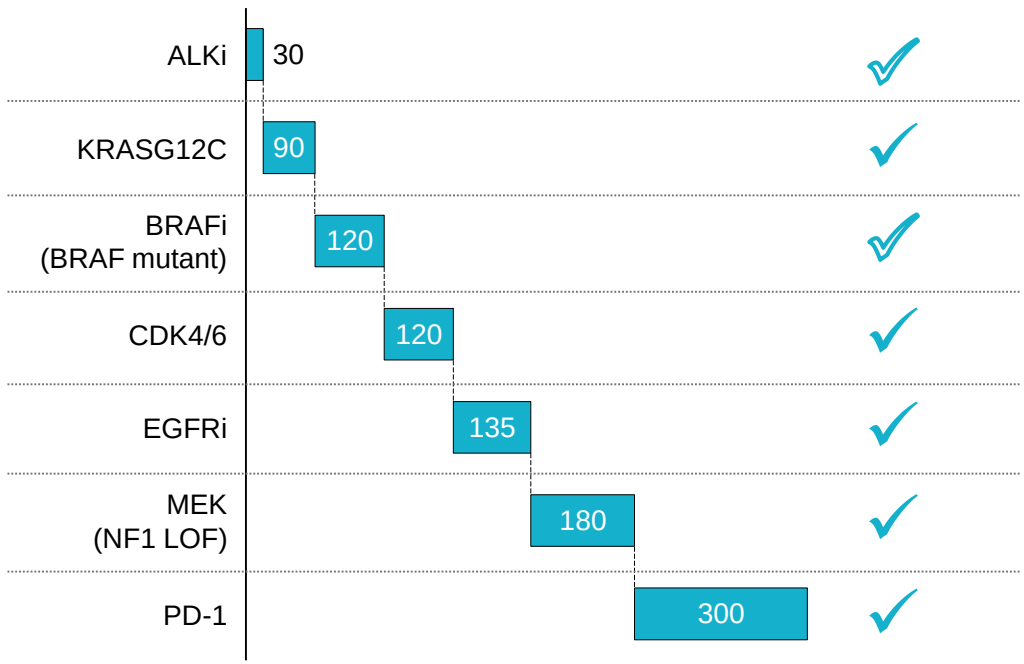
- *hERG IC50 (μM)*: >100: No QT prolongation*

**SHP2i combination potential**

US + EU incidence, '000s

**Supporting evidence[2]**

Peclin data: ✓ BBIO SHP2i ✓ Other SHP2i




**~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

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# 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

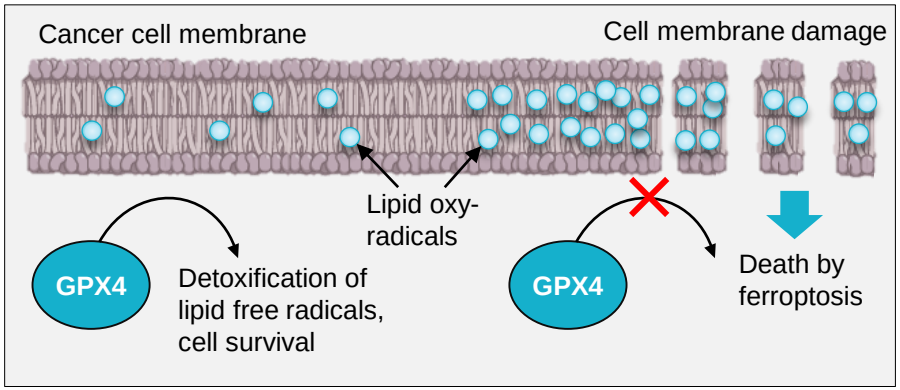
## Initial clinical combinations of focus based on SHP2i preclinical data

| | 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%** |

# GPX4: Potential first-in-class therapy for a novel cancer target

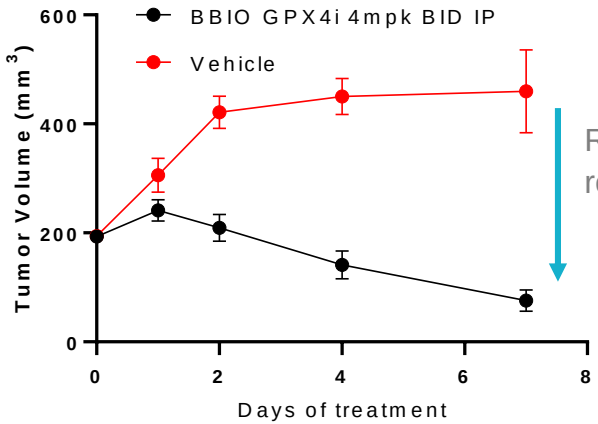
## GPX4 is the key negative regulator of ferroptosis

- GPX4 neutralizes toxic free radicals at the lipid membrane, protecting cells from death (ferroptosis)
- We are developing covalent inhibitors of GPX4 designed to induce ferroptosis in cancer cells
- Recent high profile publications provide preclinical in vivo rationale for monotherapy and combinations with IO, kinase inhibitors and chemotherapy




## In vivo monotherapy activity in RCC xeno model

Model: 786-O RCC xenograft (VHL LOF, p53 LOF)




**Synergy with targeted therapies and immunotherapy using in vitro models**

**Optimization of oral lead compounds ongoing**

Source: Data on file

# Three late-stage programs continue to progress toward the market

| Program | 2019 | 2020 | 2021 |
|---|---|---|---|
| **Fosdenopterin:** cPMP replacement for MoCD type A | ✓ Initiate rolling NDA submission | ✓ Complete rolling NDA submission | ❑ FDA approval / launch<br>❑ Potential PRV sale |
| **Infigratinib:** FGFRi for 2L cholangiocarcinoma with FGFR2 fusion | ✓ Complete enrollment in Ph2 pivotal study | ❑ Complete NDA submission | ❑ FDA approval / launch |
| **Topical patidegib:** SMOi for Gorlin syndrome | ✓ Complete enrollment in Ph3 study | ❑ Last patient last visit | ❑ Topline data<br>❑ Potential payment from Leo |

**We are building a track record of late-stage clinical and regulatory execution**



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# Multiple catalysts anticipated in 2020-2021

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: Ph2 study first patient in
- ❑ FGFRi for cancer: 2L CCA NDA submission

## 2021

### FY

- ❑ TTR stabilizer for ATTR: Complete enrollment of ATTR-CM Ph3
- ❑ 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

**$841mn in cash and equivalents as of 2Q20 expected to provide runway into 2022**



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