WELCOME

R&D DAY 2023

September 12, 2023

Welcome and Opening Remarks

Jean-Jacques Bienaimé

Chairman and
Chief Executive Officer

BIOMARIN

Executing on our strategy

Delivering top and bottom-line growth while fueling a sustainable pipeline of innovative products

Optimizing Revenue

Prioritizing Life Cycle Management

Balancing Profits & Reinvestments

Focusing on Proof of Concepts and the Early-Stage Pipeline

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Optimizing growth through R&D innovation & financial execution

HISTORY OF INNOVATION & SUCCESS

Industry Leading Track Record of Translating Genetic Discoveries Into Transformational Medicines

BREAKTHROUGH POSSIBILITIES

Profitable Enzyme Business **Plus** Launches of Two Potential Blockbusters Underscores Financial Strength and Capabilities

INVESTMENT IN FUTURE GROWTH

Ability to Achieve Goal of **Both** Profit Margin Expansion & Increasing R&D Investment in Innovative Pipeline

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Proven R&D strategy & capability as a foundation for the future

History of R&D Success

100%

Commercialization rate for BioMarin Phase 3 assets

Four for Four on Major De-risking Events Over the Last Two Years

- VOXZOGO EU Approval
- VOXZOGO US Approval
- ROCTAVIAN EU Approval
- ROCTAVIAN US Approval

8 Approved Products

**Market Opportunities > $1 billion annual revenue*

- ROCTAVIAN® (valoctocogene roxaparvovec) Solution for intravenous infusion
- Palynziq® (pegvaliase-pqpz) Injection
- VOXZOGO® (vosoritide) for injection
- VIMIZIM™ (elosulfase alfa)
- KUVAN® (sapropterin dihydrochloride) Tablets or Powder for Oral Solution
- Brineura™ (cerliponase alfa)
- Naglazyme® (GALSULFASE)
- ALDURAZYME® (LARONIDASE)

High Probability of Success for Clinical Programs

Sustained Credibility of Scientific Innovation

Strong Foundation of Commercial Success for Further Expansion and Growth

Hank Fuchs, MD

President, Worldwide Research and Development

R&D Day 2023

sustaining the R&D engine

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Agenda

Welcome and Opening Remarks	**Jean-Jacques Bienaimé** – Chairman and Chief Executive Officer
Sustaining the R&D Engine	**Hank Fuchs, MD** – President, Worldwide Research & Development
ROCTAVIAN	**Tara Robinson, MD, PhD** – Senior Medical Director
ROCTAVIAN Panel	**Drs. Johnny Mahlangu and Guy Young, Professor Amit Nathwani**
VOXZOGO	**Elena Fisheleva, MD** – Executive Medical Director
VOXZOGO Panel	**Drs. Andrew Dauber, Melita Irving, Bradley Miller**
Early-stage Programs	**Dave Jacoby, MD, PhD** – Head Early Clinical Development **Kevin Eggan, PhD** – Chief Scientific Officer
Genomics Revolution: Key to Future Success	**Kevin Eggan, PhD** – Chief Scientific Officer
Sustainable Profitability	**Brian Mueller** - Chief Financial Officer
Q&A	**BioMarin Executive Team**

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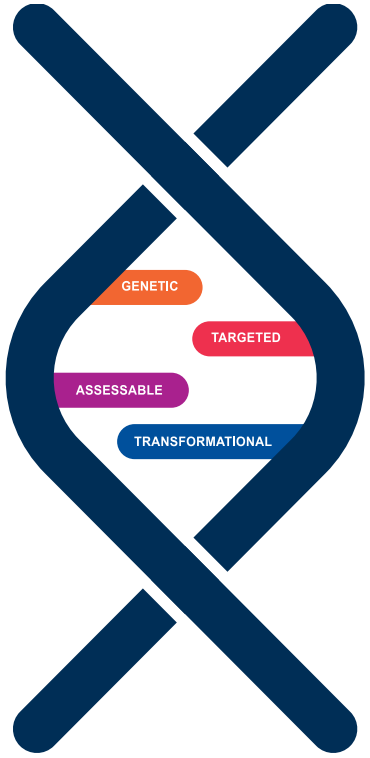
BioMarin's Four Core Attributes

Leveraging genetic discoveries and tools, BioMarin has a clear understanding of the underlying disease mechanism

Study designs use readily assessable biomarkers/ endpoints that yield clear efficacy signals and reliably translate into clinical benefit



BioMarin can develop a targeted therapy that directly or proximally addresses the fundamental defect of the disease

The medicine has a transformational impact on patients' lives by profoundly improving the way they feel, function, and survive

TRANSLATING GENETIC DISCOVERIES INTO TRANSFORMATIVE MEDICINES

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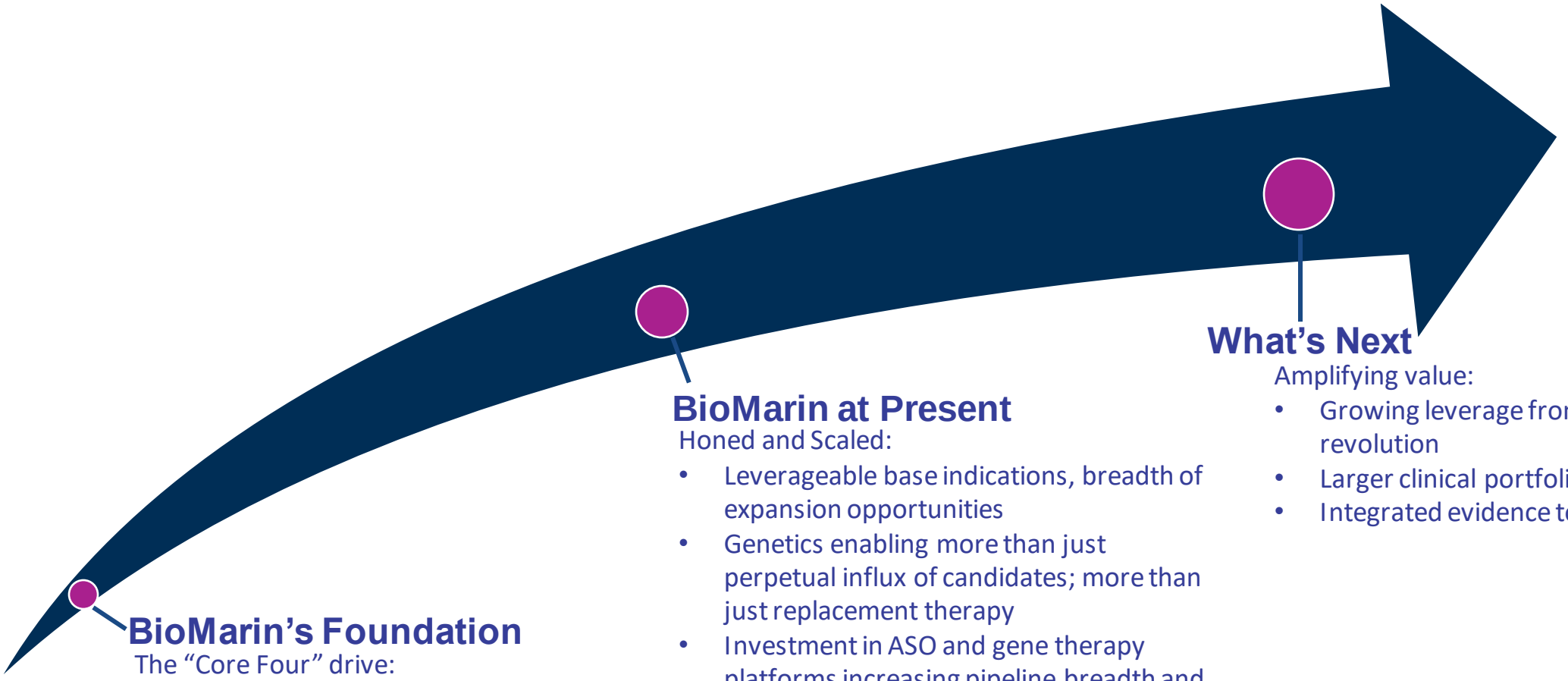
Translating Genetic Discoveries into Transformative Medicines



BioMarin's Foundation

The "Core Four" drive:

- Efficient development platform
- Complex biologic production
- Durable revenues

BioMarin at Present

Honed and Scaled:

- Leverageable base indications, breadth of expansion opportunities
- Genetics enabling more than just perpetual influx of candidates; more than just replacement therapy
- Investment in ASO and gene therapy platforms increasing pipeline breadth and flow

What's Next

Amplifying value:

- Growing leverage from genomics revolution
- Larger clinical portfolio
- Integrated evidence to support value

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Dense Pipeline Supports New Assets and Indications

	2023	2024	2025	2026
New Investigational Products	BMN 351 DMD BMN 349 AATD BMN 293 HCM	BMN 355 LQTS BMN 365 ACM BMN 333 LA CNP BMN 255 RSF	TBA01* TBA02* BMN 331 HAE BMN 351 DMD BMN 349 AATD BMN 293 HCM	BMN 365 ACM BMN 355 LQTS

Near- to Longer-Term Progress

New Indications	**ROCTAVIAN:** Japan, Adolescents, Prior inhibitor, Active inhibitors, HDACi, AAV5+ **VOXZOGO:** Hypochondroplasia, Select Genetic Short Stature Conditions, Idiopathic Short Stature **PALYNZIQ**: Adolescents**

IND

Clinical Proof of Concept

*Asset not yet disclosed; **EU approved indication includes 16 years and older, Japan approved indication includes 15 years and older

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The Five Things You'll Hear Today

01 ROCTAVIAN and VOXZOGO base indications feed near-term revenues and fuel pipeline growth through expansion opportunities and leveraged data

02 Next wave of candidate programs genetically enabled, targeted, readily assessable and potentially transformative

03 Genomic insights and tools sustain the influx of high-probability candidates; further amplify each opportunity by increasing expansion opportunities and their eligible populations

04 Robust data collection for efficient generation of evidentiary bridge between health authority needs, payer needs, access and adoption

05 Large volume of highly-differentiated opportunities tracking toward 2 INDs/year and anticipated sustainable growth

Tara Robinson, MD, PhD

Senior Medical Director,
Late-Stage Clinical Development

ROCTAVIAN

program update

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ROCTAVIAN APPROVED!

First Gene Therapy for Adults with Severe Hemophilia A

- Approved in 2 major markets
  - Approved in EU, US
- Global commercialization underway in key markets
- International expansion underway
  - Taiwan, Brazil, and Mexico marketing authorizations submitted, and Australia submission by EOY
- Japan Clinical Trial Notification submitted August 2023

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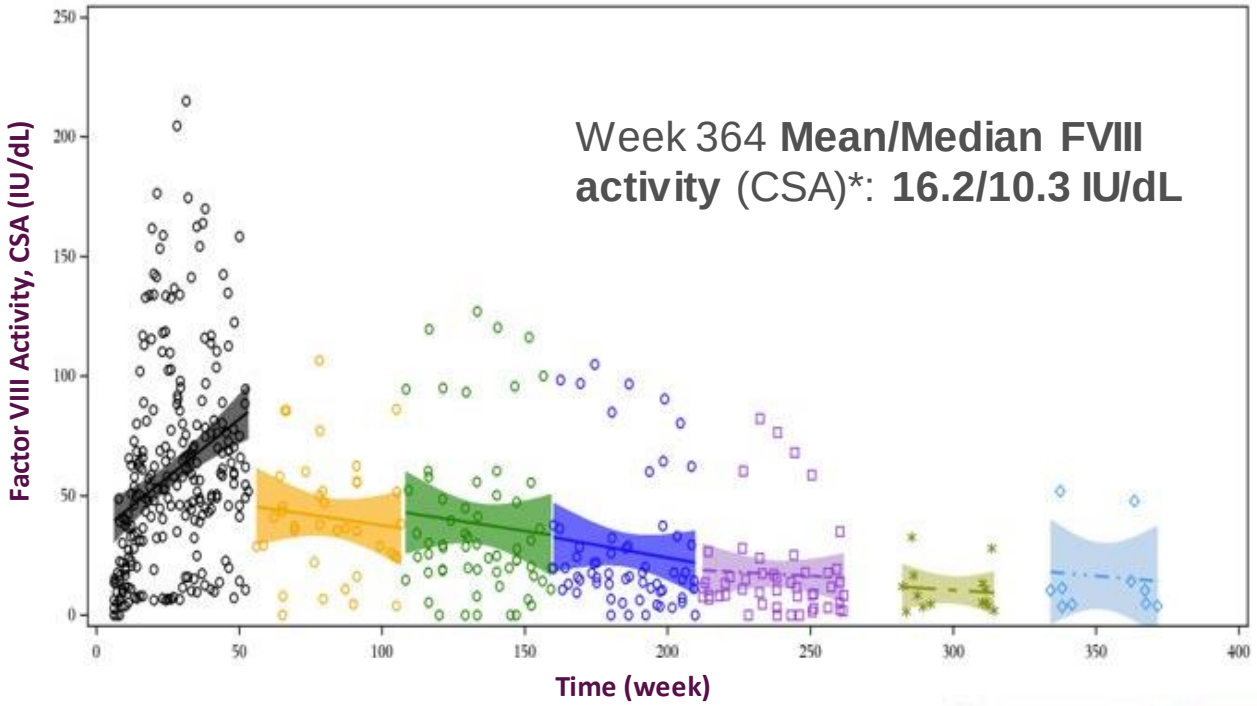
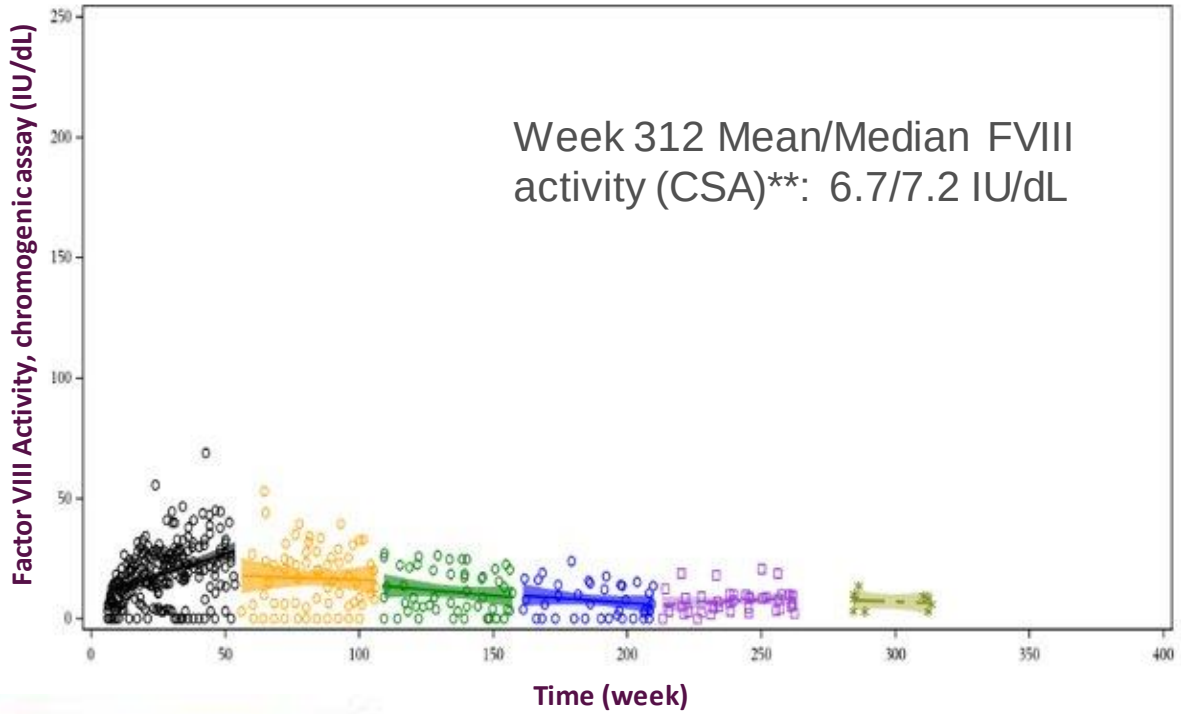
Phase 2 Update: Durable FVIII activity through 7 years

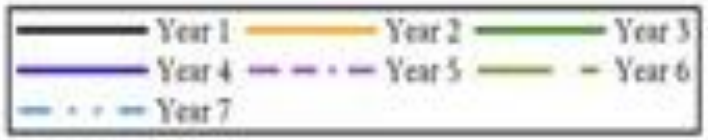
Eleven of 13 participants remain free of prophylactic therapy and with acceptable ABR

6×10^{13} vg/kg Cohort



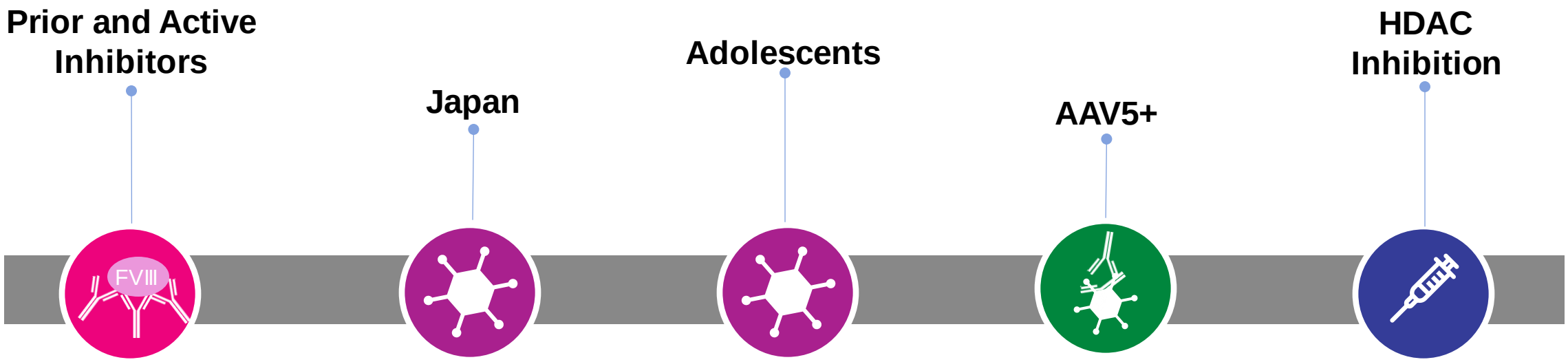
4×10^{13} vg/kg Cohort





CSA: chromogenic substrate assay *Excludes 2 participants who returned to prophylaxis; ** Excludes one participant with transient (1 month) return to prophylaxis during year 5

ROCTAVIAN new indication expansion opportunities abound



GENEr8-INH

Safety, efficacy, and immune tolerance induction in adults

GENEr8-JPN

Safety and efficacy in Japanese population (bridging study)

GENEr8-TEEN

Safety and efficacy in adolescents (15-17 years old)

GENEr8-AAV5

Anti-AAV5-Ab reduction in severe hemophilia A adults

GENEr8-HDACi

Re-activation of expression in ROCTAVIAN treated adults

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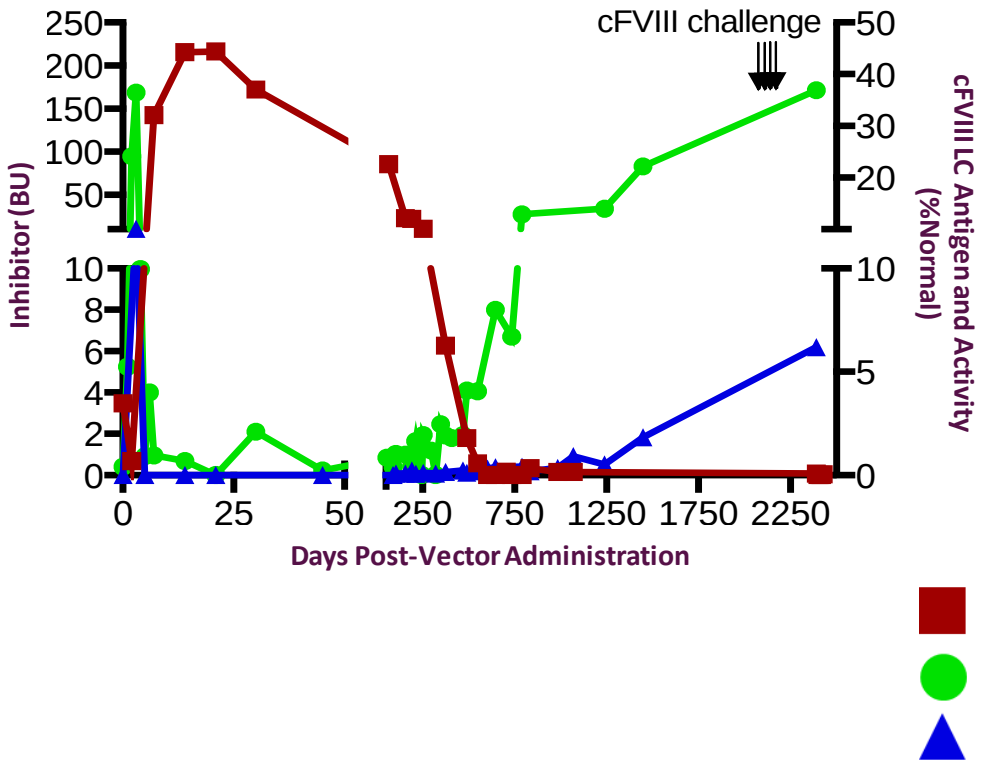
Potential to benefit populations with active or prior inhibitors

Demonstration of Tolerance in Canine Model of FVIII inhibitors



Status and Next Steps

- Active Inhibitors (Part A): 2/3 participants dosed
- Prior Inhibitors (Part B): 2/10 participants dosed
- Early results:
  - No safety signals, including no re-emergence of inhibitors in Part B
  - Encouraging interim efficacy data, consistent with expectations

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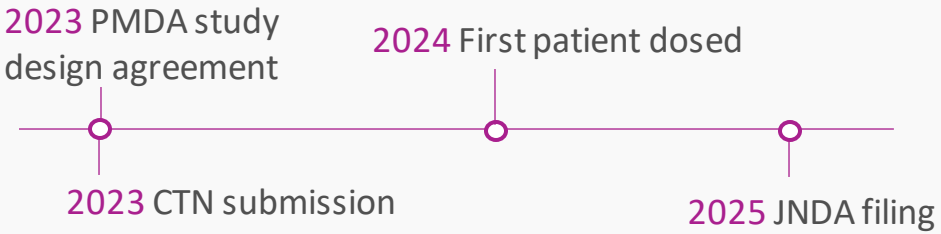
Japan program underway, potential to benefit large population

Rationale and Approach

- 5k+ Japanese patients diagnosed with HA in 2018[1]
  - Approximately 50% with severe HA
- Bridging study required to demonstrate safety and efficacy in Japanese populations
- No expected differences between US/EU and Japanese populations

Status and Next Steps

- Met all requirements for initiating studies in Japan
- Submission to Japanese health authority August 2023
- Pre-submission agreement on study design with PMDA
- Feasibility underway, ample interest from sites



CTN: Clinical Trial Notification; HA: hemophilia A; JNDA: Japanese equivalent of New Drug Application; PMDA: Pharmaceuticals and Medical Devices Agency;
[1]Ministry of Health Labor and Welfare Nationwide Survey on Blood Coagulation Disorders 2018. Published by the Japan Foundation for AIDS Prevention [Japanese]

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Treatment in adolescents: Potential to prevent irreversible joint damage with earlier treatment

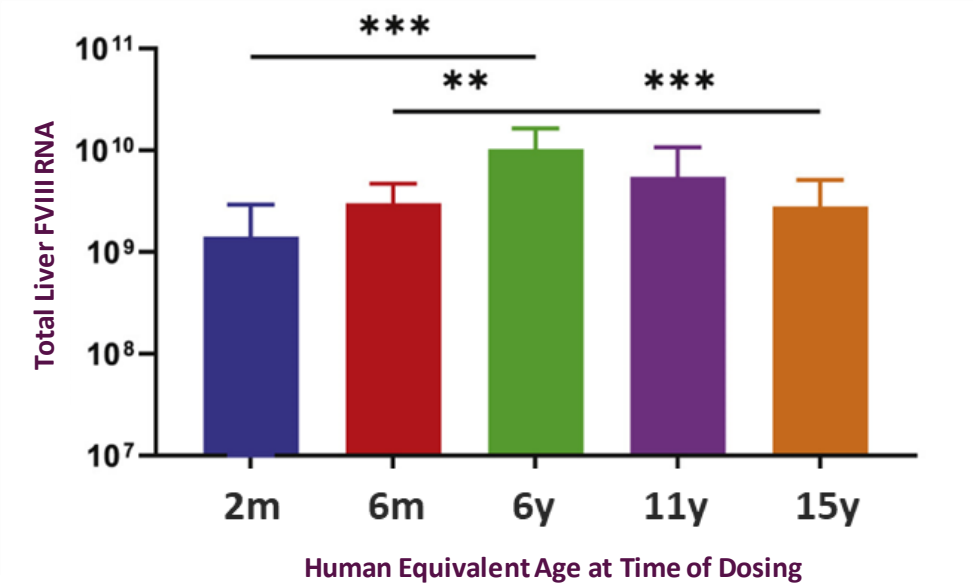
Development Rationale & Approach

- Large potential benefit in large population
  - Potential to prevent irreversible complications and joint damage
  - Large eligible population anticipated due to lower prevalence of chronic viral hepatitis and other risk factors for liver pathology, no special safety concerns in adolescents
- Durability and efficacy anticipated similar to adults
  - Stepwise approach to successively younger ages will be taken, first cohort aged 15-17 years old
  - Liver size mostly mature in 15-17 year olds, mitotic effects not expected to be significant

Status and Next Steps

- Pediatric investigational plan agreed in EU
- Planned interaction with FDA to align on global program
- Anticipate enrollment in 2024

FVIII levels in mice at equivalent human age, by age at time of dosing



∗p < 0.05; ∗∗p < 0.01; ∗∗∗p < 0.001; ∗∗∗∗p < 0.0001

Mouse age equivalents (PND; post-natal day) to human age: PND7=2m; PND14=6m; PND28=6y; PND42=11y; PND56=15y; *Zhang et al. Mol Ther Methods & Clin Dev., 2022*

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Pre-existing AAV antibodies remain a barrier to treatment

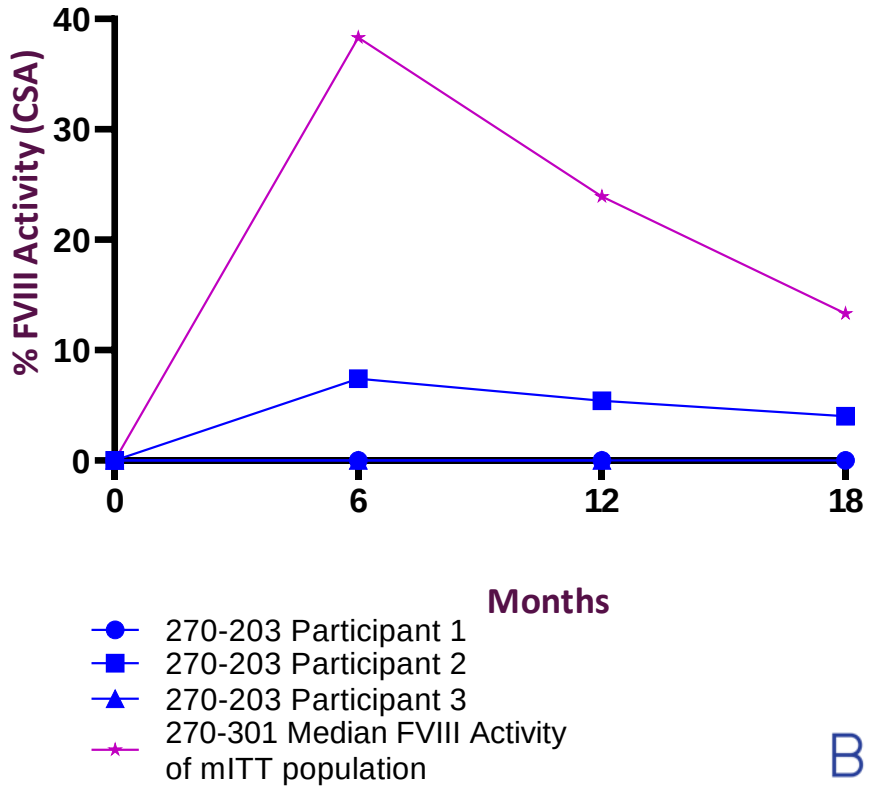
Rationale and Approach

- Patients with preexisting anti-AAV5 antibodies ("AAV5(+) patients") excluded from ROCTAVIAN registrational studies
- AAV5(+) patients ineligible for approved therapy
- Screening for anti-AAV antibodies increasingly common
- Reduction of anti-AAV antibodies has potential to further unlock value of ROCTAVIAN for large additional subset of patients
  - 30% global seroprevalence for AAV5

Data and Next Steps

- Three AAV(+) participants did not show meaningful FVIII activity levels (blue lines with circles)
- Confirms anti-AAV5 antibodies barrier to treatment
- Data analysis to further inform next steps for BioMarin's AAV platform, including antibody clearance methods

AAV5(+) Participants (●) Show Lower- to No Expression Compared with AAV5(-) (★) Participants



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Preclinical data support two strategies for dosing AAV(+) populations

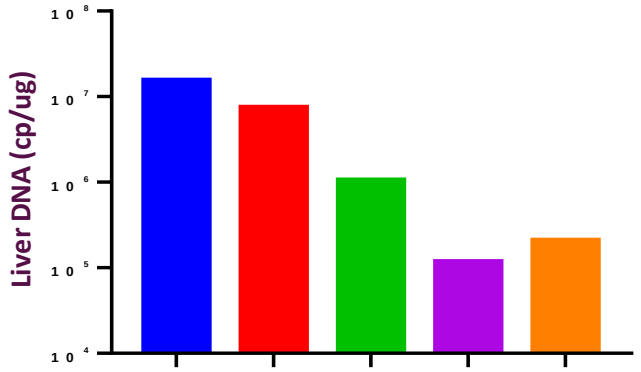
Rationale

- Potential to enable AAV-mediated treatment in populations with anti-AAV antibodies
  - Initial and repeat dosing
  - ROCTAVIAN and future AAV-gene therapies

Early Data

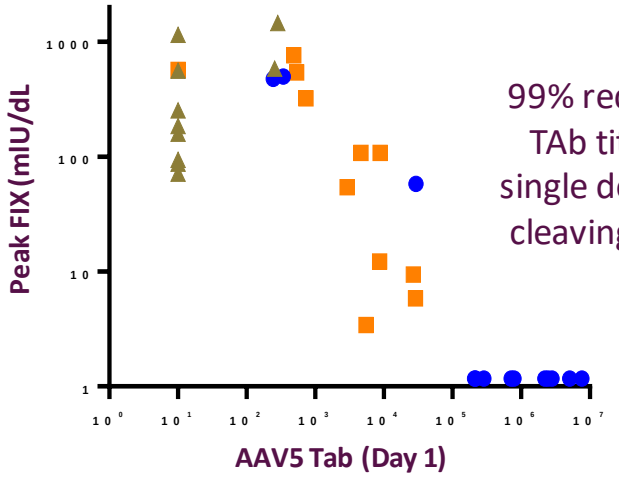
- Non-clinical experiments validate two clearance strategies:
  1. Antibody removal: plasmapheresis
  2. *In vivo* antibody cleaving enzyme

Plasmapheresis: FIX DNA increases following plasmapheresis in 4 AAV5(+) NHPs Rechallenged with 6E13 AAV5-FIX



Subject	TAb(-) Control	NHP1	NHP2	NHP3	NHP4
Daily Cycles IA-P	NA	3-4	4	4	4
Days IA-PP	NA	3	2	1	1
TAb Titer at Start	Neg	3714	43,406	52,945	42,181
TAb Titer at Rechallenge	Neg	59	158	599	2416

Pretreatment with Antibody Cleaving Enzyme: FIX protein expression correlates with TAb Titer on day of rechallenge in rabbits



- Sensitized, challenged with AAV5-FIX
- Sensitized, cleaving enzyme, challenged with AAV5-FIX
- Unsensitized, challenged with AAV5-FIX

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GENEr8-3 results: No advantage to Day 1 prophylactic steroid initiation

- Single arm prophylactic corticosteroid (CS) study: CS administered Day 1 through Week 19 and reactive as needed
- First data cut (> 52 weeks for all participants; n=22) demonstrated levels ~1/3 those observed in pivotal study
- Prophylactic corticosteroids did not prevent/mitigate ALT elevations and protect against potential loss of FVIII expression
- Complete results to be presented early next year at upcoming scientific congress; manuscript preparation underway
- Study results do not support a modification of the reactive CS approach in approved labels
- ROCTAVIAN learnings are being applied to gene therapy programs in early clinical development

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HDACi addresses durability mechanisms in preclinical models

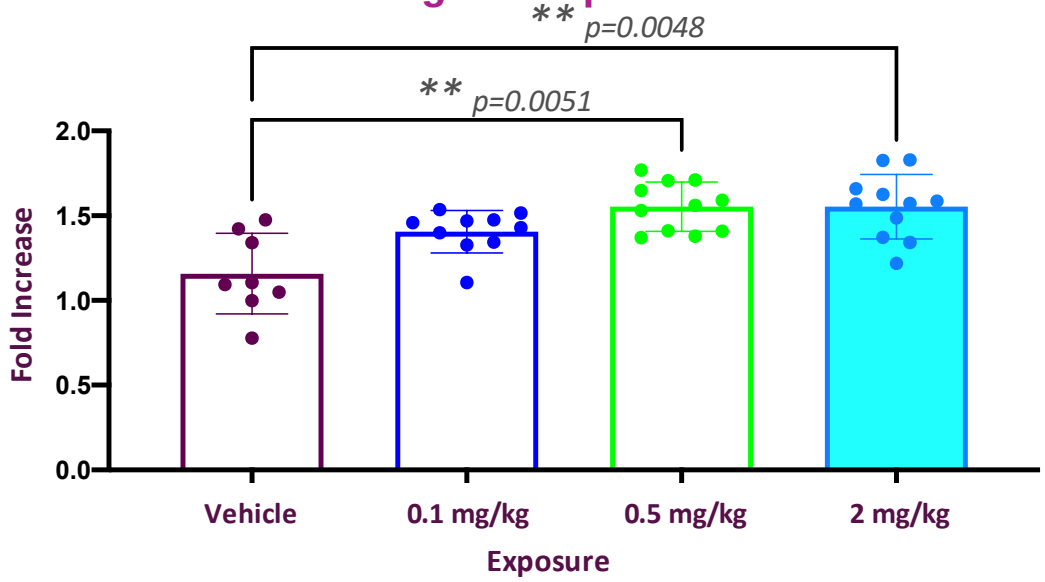
Rationale and Approach

- While most patients have durable FVIII expression following ROCTAVIAN, a small percentage lose expression over years and return to standard of care therapies
- Histone deacetylase inhibitors (HDACi) may increase expression of durable transgenes by converting DNA from inactive to active forms

Status and Next Steps

- Pre-clinical studies ongoing to better understand magnitude, variability, and duration of FVIII increase
- Health authority interactions planned around pre-clinical data and clinical proof of concept study

HDACi Increases Transgene Expression in Murine Model



Statistical analysis: One-Way-ANOVA/Kruskal Wallis

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Unlocking the full potential of ROCTAVIAN

ROCTAVIAN program update summary

- Phase 2 study data demonstrate that the trend in FVIII activity remains stable and provides durable hemostatic efficacy out to 7+ years
- Patient and physician communities are demonstrating high interest in ROCTAVIAN
- Value can be unlocked in Japan, adolescents, and patients with prior inhibitors
- Additional value can be unlocked in patients with AAV5 antibodies and active inhibitors, as well as with ground-breaking work on modulating transgene expression with HDACi

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ROCTAVIAN™
(valoctocogene roxaparvovec-rvox)

Moderated by:
Hank Fuchs, MD
President, Worldwide Research and Development

Professor Johnny Mahlangu, MBBCh, MMed, FCPath

Director Haemophilia Comprehensive Care, Charlotte Maxeke Johannesburg Academic Hospital

Professor of Haematology, University of the Witwatersrand and National Health Laboratory Service, Johannesburg

Doctor Guy Young, MD

Director, Hemostasis and Thrombosis Center and Clinical Coagulation Laboratory, Children's Hospital

Professor of Pediatrics, University of Southern California's Keck School of Medicine, Los Angeles

Professor Amit Nathwani, MBChB, FRCP, RCPath, PhD

Director of the Katharine Dormandy Hemophilia Centre, Royal Free Hospital, London

Elena Fisheleva MD
Executive Medical Director
Late-Stage Clinical Development

VOXZOGO

program update

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First Approved Treatment for Children with Achondroplasia

- FDA PDUFA (under 5 years) 2023
- CHMP opinion (under 2 years) 2023
- Approved in Japan for treatment from birth; in Brazil and Australia from age 2
- Pursuing regulatory approvals globally
  - Marketing applications under review in Argentina, Taiwan, Israel, Mexico, Chile, Colombia
  - Plans to submit several additional new marketing applications in coming months
- Pivotal development program in hypochondroplasia imminent
- Expansion into other short stature conditions underway
  - Idiopathic Short Stature
  - Select short stature genetic conditions (Turner's Syndrome, SHOX, Noonan's Syndrome)

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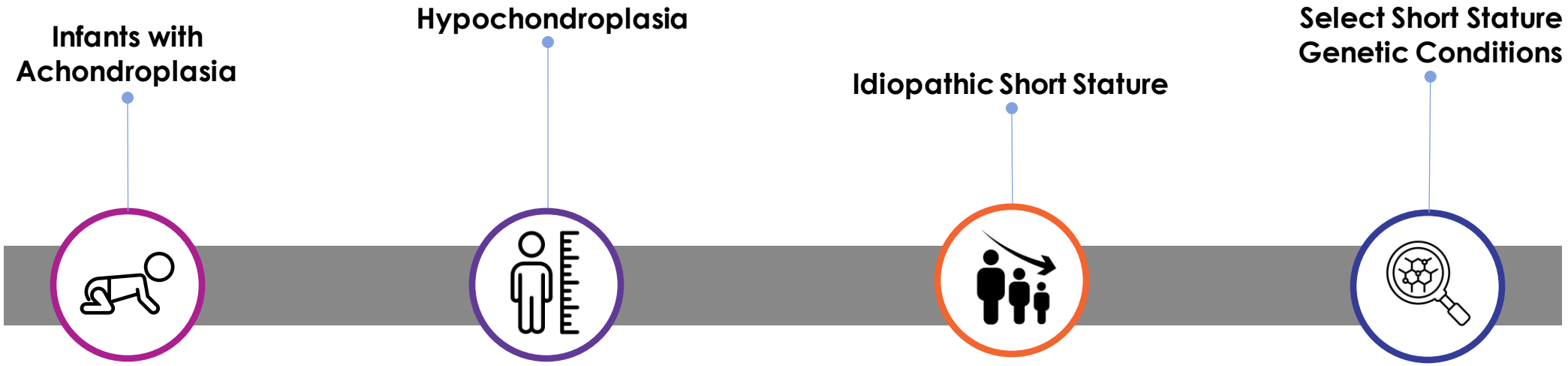
VOXZOGO new indication expansion opportunities abound



2023
Label expansion in infants and younger children with achondroplasia

2023 (NH) 2024 (Pivotal)
Initiate pivotal development program in hypochondroplasia

2024 (NH, Interventional)
Initiate evaluation of efficacy and safety in idiopathic short stature

2024
Initiate evaluation of efficacy and safety in conditions in which CNP is implicated in disrupted pathways

NH: Natural history;

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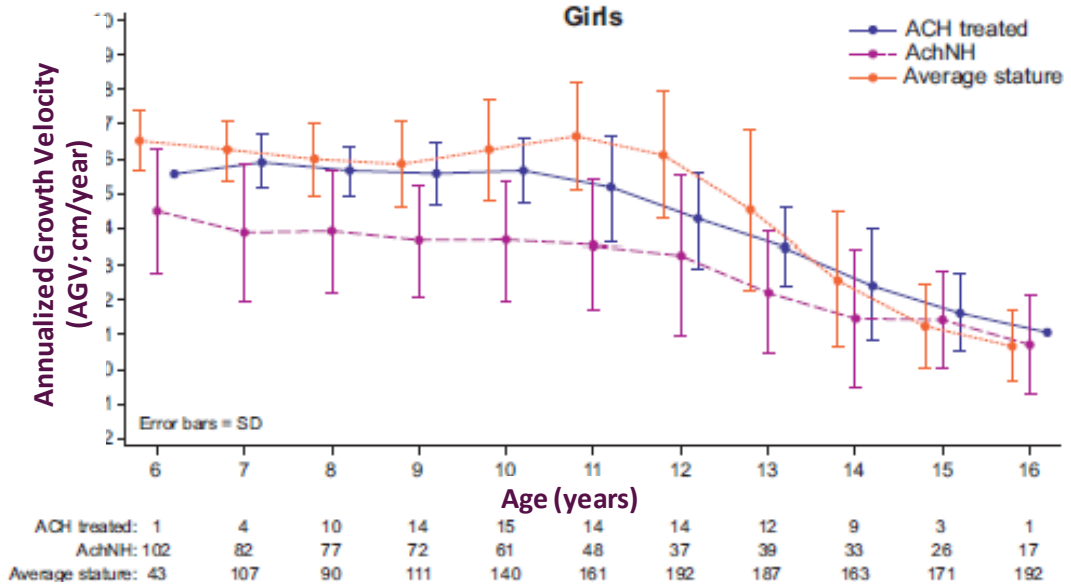
Durable efficacy and benefit of early treatment in achondroplasia

Mean 12-month Interval AGV in Vosoritide-Treated Children is Higher Compared to Age-Matched Untreated Children



- Durability of effect confirmed after 7 years of treatment
- Incremental height gain of 13cm for boys and 9 cm for girls

Restoration of substantial proportion of deficit in growth velocity in youngest children treated with VOXZOGO

	Height Gain after 1 year of treatment (cm)					
	Placebo			Vosoritide		
Cohort #	1 24-60m (n=16)	2 6-24m (n=8)	3 0-6m (n=8)	1 24-60m (n=19)	2 6-24m (n=12)	3 0-6m (n=12)
Average Stature	7.06	10.69	15.05	6.98	10.33	15.65
ACH	5.51	8.01	10.32	6.38	9.04	11.29
% Height gain ACH vs Average Stature	78.04%	74.96%	68.55%	91.45%	87.50%	72.16%

COMING SOON @ ESPE (Sept 2023) - Data on consistent and durable treatment effect of vosoritide on growth in young children who started treatment before age 5 years, demonstrating benefit of early treatment initiation

Bacino et al (2023) GIM Open; Hoover-Fong et al (2023) GIM Open

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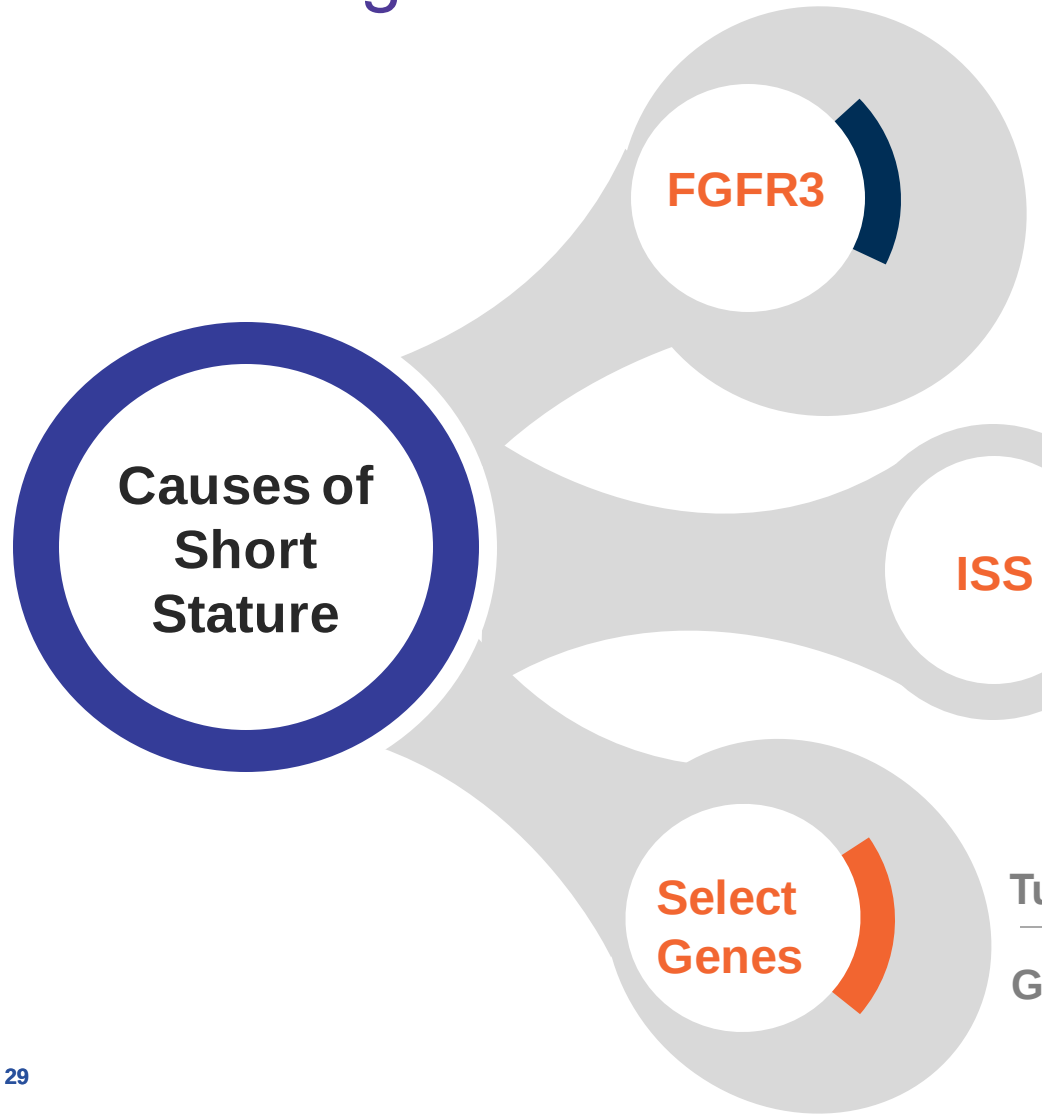
Unlocking the Full Potential of VOXZOGO



Achondroplasia (ACH)

Hypochondroplasia (HCH)

Indication expansion 2023

Pivotal study 2024

Idiopathic Short Stature (ISS)

GH Indication in US

Clinical program 2024

Turner's Syndrome | SHOX | Noonan's Syndrome

GH Indications Globally

Clinical program 2024

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Expansion opportunity in hypochondroplasia underway

Rationale and Approach

- Pathogenesis similar to achondroplasia caused by mutation in *FGFR3*[1]
- Incidence estimates similar to achondroplasia
  - 1/15,000 to 1/40,000 births
  - Stature overlaps with achondroplasia (3rd to 50th percentile)
  - Disproportionality, other manifestations
- Target population with severe disease at height deficit beyond -3 standard deviations (SD)
- Consistent with population studied in Investigator Sponsored Study (IST)

Status and Next Steps

- Capitalizing on established safety and durability data in achondroplasia, and preliminary data in hypochondroplasia from IST[2]:
  - Agreement with FDA to progress straight into phase 3
- Registration-enabling 52 week randomized, double-blind placebo- controlled study; Primary outcome change in AGV

AGV: Annualized growth velocity; CDP: clinical development plan; [1]Arenas 2019; [2]NCT04219007 (PI A. Dauber)

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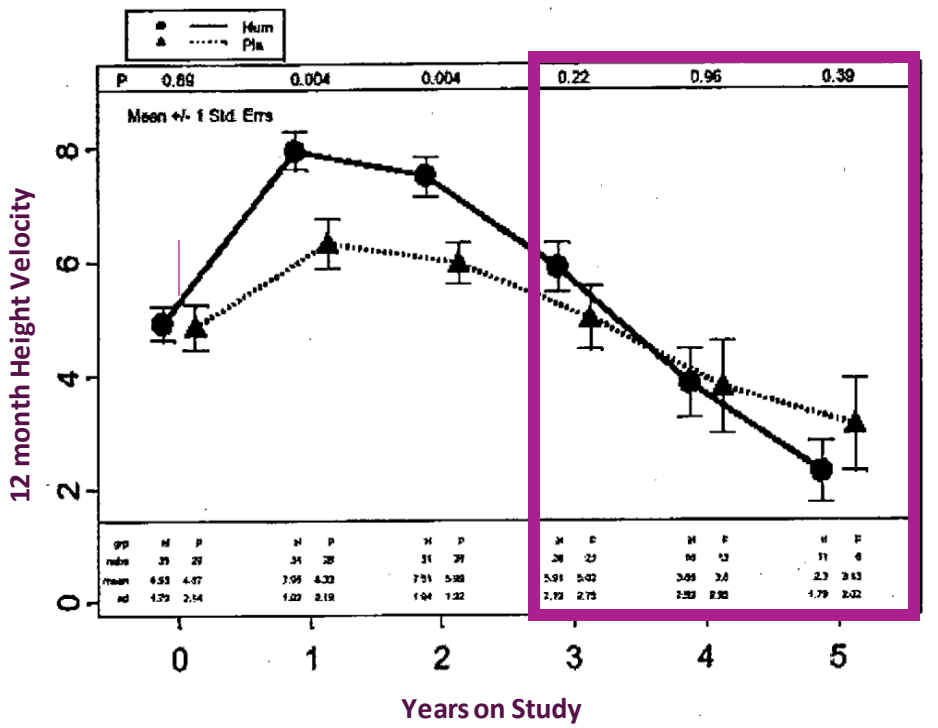
Precision medicine: CNP is a master regulator of growth

- In short stature conditions without growth hormone (GH) deficiency, treatment with GH produces variable responses and a waning effect over time
- CNP is a pivotal physiologic stimulator of endochondral bone growth
  - Bi-directional effect of CNP in human growth: altered CNP signaling results in either severe short stature (inhibition) or marked tall stature (overexpression)
- In non-GH, endocrine, and metabolic disorders:
  - Short stature likely caused by pathological genetic variations in growth plates
  - CNP targeted precision intervention of choice

Waning Effect of Growth Hormone over Time



CNP: C-type natriuretic peptide; GH: growth hormone [1]Blum et al (2022) *J Endocr Soc*; [2]Baron et al (2015) *Nat Rev Endocrinol* [3]Humatrope FDA filing (Eli Lilly and Company).

Expansion opportunity in Idiopathic Short Stature (ISS)

Rationale and Approach

- ~0.6% of population have a height < -2.5 SD
  - ~2/3 without specific diagnosis → "ISS"
  - Genomic insights to further inform patient population
- Growth Hormone approved in US, select other markets
  - Waning efficacy, modest effect on final adult height
- VOXZOGO could transform management, drive long-term and durable growth
- Expedited development combining dose confirmation and pivotal outcome
  - Growth hormone or placebo comparisons

Status and Next Steps

- Confirmation of design in health authority engagements; supportive of progress into registration-enabling studies
- Natural history study to initiate in 2024
- Anticipate dosing in 2024

SD = Standard Deviation ISS=Idiopathic Short Stature

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Expansion opportunity in select short stature conditions with defined genetic cause

Rationale and Approach

- Noonan's Syndrome, Turner's Syndrome and SHOX deficiency
  - CNP pathways implicated
- Growth hormone approved, but efficacy inconsistent and not durable
- Preliminary positive data with VOXZOGO from investigator sponsored trial
- Expedited development combining dose confirmation and pivotal outcome

Status and Next Steps

- Confirmation of design in health authority engagements to support progress into registration-enabling study

SHOX: Short stature homeobox gene

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Unlocking the full potential of VOXZOGO

VOXZOGO program update summary

- Label expansion in ACH into infants and younger children
  - Durability data and data in young children confirm benefit of early treatment initiation
- Agreed registrational program in hypochondroplasia
  - Natural History study to be initiated in 2023 with first patient dosed anticipated in 2024
- Expansion into ISS and select short stature conditions with defined genetic cause
  - Confirmation of expedited development plans with FDA
  - Natural History study in ISS to be initiated in 2024 and anticipate first patient dosed soon after
- Initiation of study in Select Genetic Short Stature conditions planned in 2024

ACH = Achondroplasia ISS=Idiopathic Short Stature

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VOXZOGO®
(vosoritide) for injection

Moderated by:
Jonathan Day, MBBS, PhD
Group Vice President,
Late-Stage Clinical Development

Andrew Dauber, MD

Chief of Endocrinology, Children's National Hospital

Melita Irving, MBBS

Consultant in Clinical Genetics, Guy's and St. Thomas' NHS Foundation Trust, Evelina Children's Hospital, London, UK

Bradley S. Miller, MD, PhD

Director, Division of Endocrinology, M Health Fairview Masonic Children's Hospital

Professor, Department of Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota

BMN 255 for Hyperoxaluria in NAFLD

Dave Jacoby, MD, PhD

Group Vice President
Head of Experimental Medicine and
Early Clinical Development

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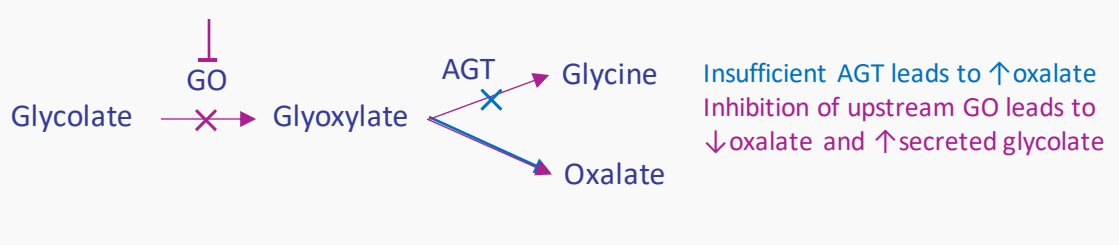
BMN 255	BMN 331	BMN 351	BMN 349	BMN 293	BMN 365	BMN 355
small molecule	AAV gene therapy	oligonucleotide	small molecule	AAV gene therapy	AAV gene therapy	monoclonal antibody
for NAFLD with AGT deficiency	for hereditary angioedema with C1-INH deficiency	for exon51 Duchenne's muscular dystrophy	for alpha-1 antitrypsin deficiency	for MYBPC3 hypertrophic cardiomyopathy	for PKP2 arrhythmogenic cardiomyopathy	for long-QT syndrome

BMN 255 Development Thesis: An identifiable subset of NAFLD cases have serious comorbidities caused by hyperoxaluria amenable to correction with glycolate oxidase (GO) inhibition

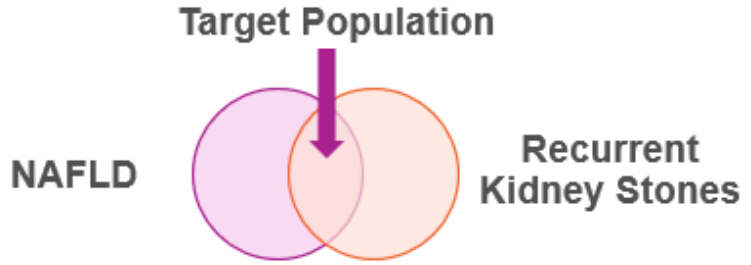
Development Rationale & Approach

- Genetic hyperoxaluria reveals pathway underlying severe comorbidities in genetic and non-genetic forms
  - *AGXT* mutations cause severe nephrolithiasis in PH1
  - Human biology connect nephrolithiasis in NAFLD to same pathway
  - Known, readily assessable markers enable rapid evaluation of concept (POC)
  - Response to therapy reliably predicted by oxalate and glycolate levels in plasma and urine



Transformative Potential

- BOI: Debilitating pain, hospitalizations, risk of infection, high proportion of recurrence, chronic kidney disease
- SOC: Pain control, medical expulsion, antibiotics, intervention
- Modality: Small molecule; potent, highly specific, rapid onset
- Potential Addressable Patient Population*: 800,000



BOI: burden of illness; AGT: alanine:glyoxylate-aminotransferase; GOi: glycolate oxidase inhibitor; NAFLD: Non-alcoholic fatty liver disease; PH1: primary hyperoxaluria; SOC: standard of care; *diagnosed prevalent patients appropriate for therapy in BioMarin territories

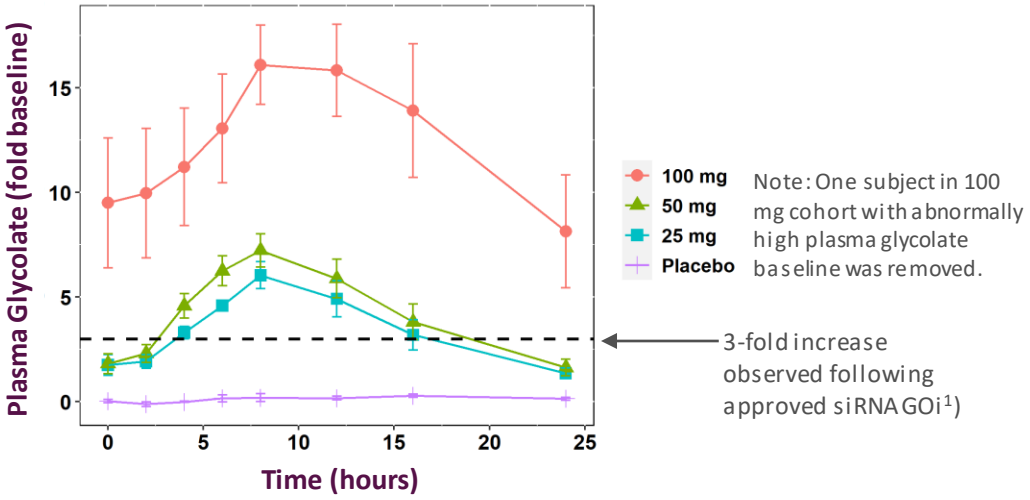
BIOMARIN

BMN 255 Development Thesis: An identifiable subset of NAFLD cases have serious comorbidities caused by hyperoxaluria amenable to correction with glycolate oxidase (GO) inhibition

Evidence to Date

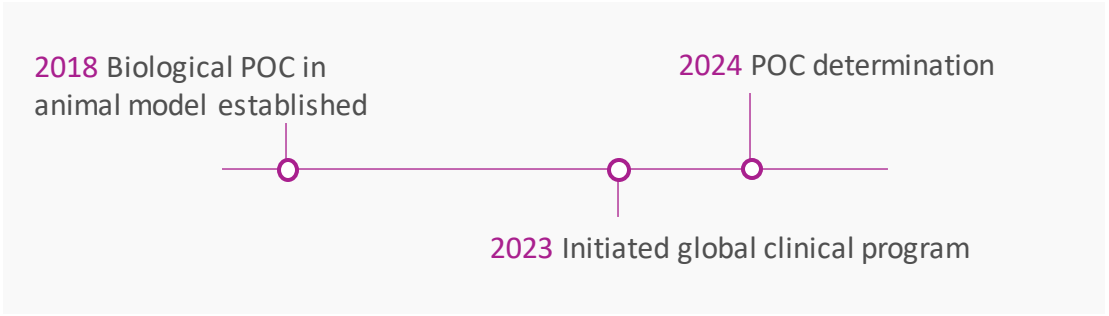
- Phase 1 SAD/MAD completed in healthy people
  - Potent enzyme inhibition with rapid onset
  - No signal in kidney safety panel
  - Pharmacokinetic profile supports once daily oral dosing

Plasma Glycolate Levels following BMN 255 administration



Status and Next Steps

- Pharmacodynamic study to Identify treatment responsive patients by clinical or biochemical enrichment
- Natural history data to characterize GOi-responsive patients
- Gating for pivotal Ph2/3 study



GOi; glycolate oxidase inhibitor; MAD: Multiple ascending dose; POC: proof of concept; SAD: single ascending dose; siRNA: short interfering RNA[1]*Frishberg et al. Clin J Am* Soc Nephrol. 2021;16(7):1025-1036

Dave Jacoby, MD, PhD

Group Vice President
Head of Experimental Medicine and Early Clinical Development

BMN 331 for Hereditary Angioedema

BIOMARIN

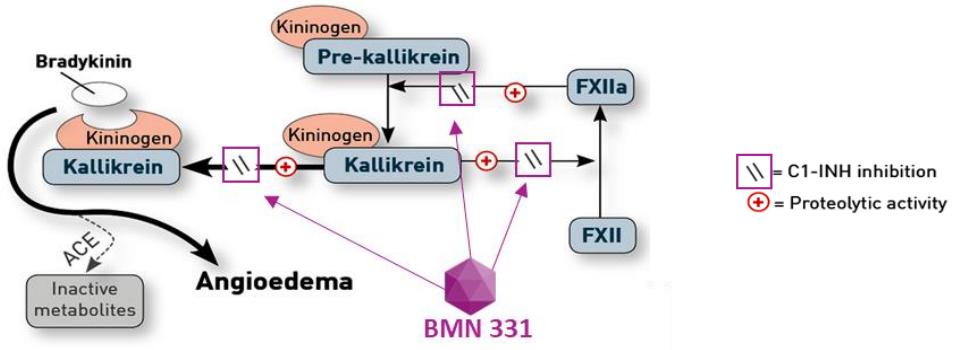
BMN 331 Development Thesis: Single administration therapy to sustain normal expression of C1-INH protein and reduce attacks

Development Rationale & Approach

- Known genetics and pathway for targeted intervention:
  - Mutations in *SERPING1* lead to a deficiency in functional C1 esterase inhibitor (C1-INH) and recurrent attacks
  - BMN 331 delivers a functional copy of *SERPING1*
- Clear markers for clinical evaluation
  - Characterized relationship between C1-INH levels and risk of attack

Transformative Potential

- BOI: Debilitating pain, life-threatening swelling, quality of life impacted by fear and anxiety
- SOC: Chronic prophylactic subcutaneous treatment
- Modality: AAV-mediated gene transfer for improved attack control due to constitutive C1-INH protein expression
- Potential addressable patient population*: 13,000

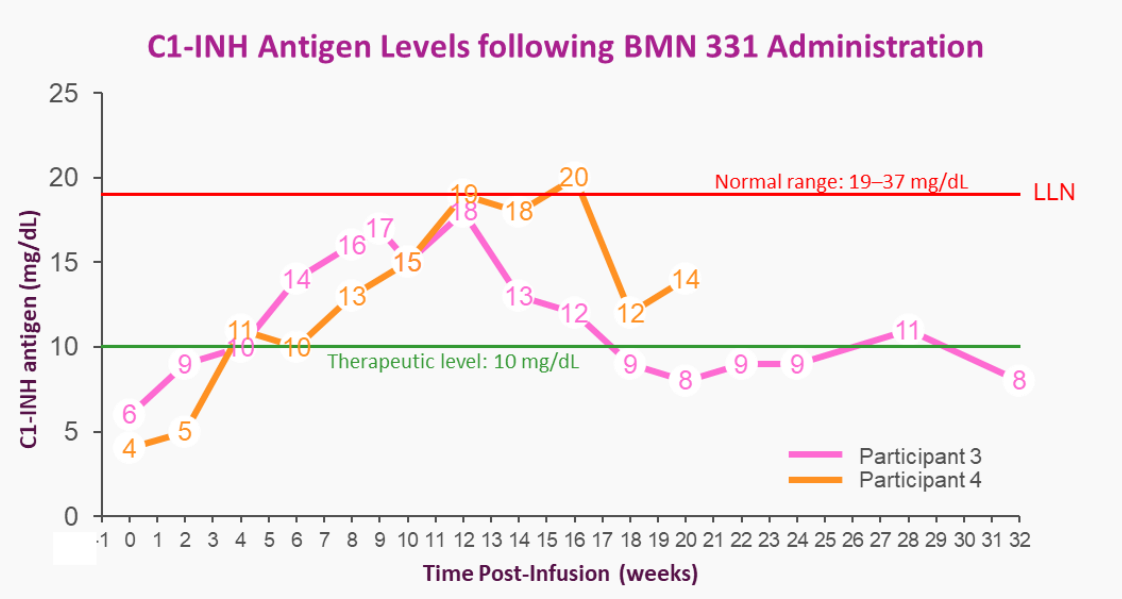


BOI: burden of illness; C1-INH: C1 esterase inhibitor; SOC: standard of care; *diagnosed prevalent patients appropriate for therapy in BioMarin territories

BMN 331 Development Thesis: Single administration therapy to sustain normal expression of C1-INH protein and reduce attacks

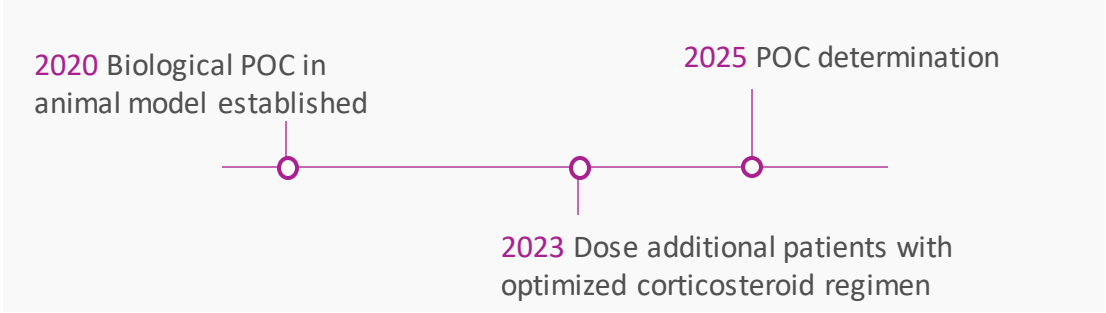
Evidence to Date

- C1-INH expression in therapeutically relevant range observed in participants receiving 6×10^{13}vg/kg BMN 331
- Safe and well-tolerated



Status and Next Steps

- Dosing with optimized corticosteroid regimen
- Expansion to n=10 at dose level predicted to eliminate attacks



C1-INH: C1 esterase inhibitor; POC: proof of concept

BMN 351 for Duchenne's Muscular Dystrophy

Dave Jacoby, MD, PhD

Group Vice President
Head of Experimental Medicine and
Early Clinical Development

BIOMARIN

BMN 351 Development Thesis: Antisense oligonucleotide targeted to novel splice site can restore levels of near-full length functional dystrophin sufficient to preserve ambulation

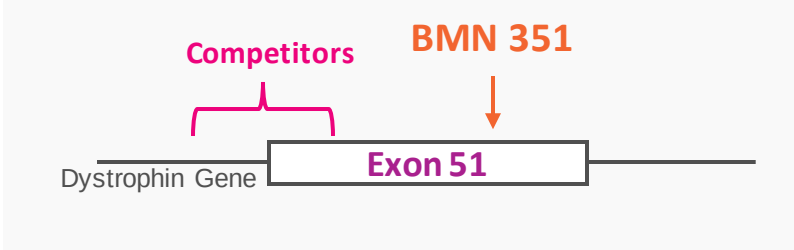
Development Rationale & Approach

- Near-full length dystrophin genetically shown to support muscle function
- Better Biology: Next generation antisense oligonucleotide (ASO) for improved exon 51 skipping*
  - Encouraging data in cultured patient muscle cells, humanized mice & non-human primates
  - Restores near-full length dystrophin
  - Novel target enhances potency by more than 10x

Transformative Potential

- BOI: Rapidly progressive loss of ambulation; wheelchair-dependent in early adolescence, full-time care required, mortality in third decade
- SOC: Supportive care, limited therapeutic options
- Modality: Oligonucleotide to express near-full length protein at therapeutically relevant levels
- Potential addressable patient population**: 7,600

Key Differentiation: Novel Skipping Target



BOI: burden of illness; SOC: standard of care; *relative to drisapersen; **diagnosed prevalent patients appropriate for therapy in BioMarin territories

BIOMARIN

BMN 351 Development Thesis: Antisense oligonucleotide targeted to novel splice site can restore levels of near-full length functional dystrophin sufficient to preserve ambulation

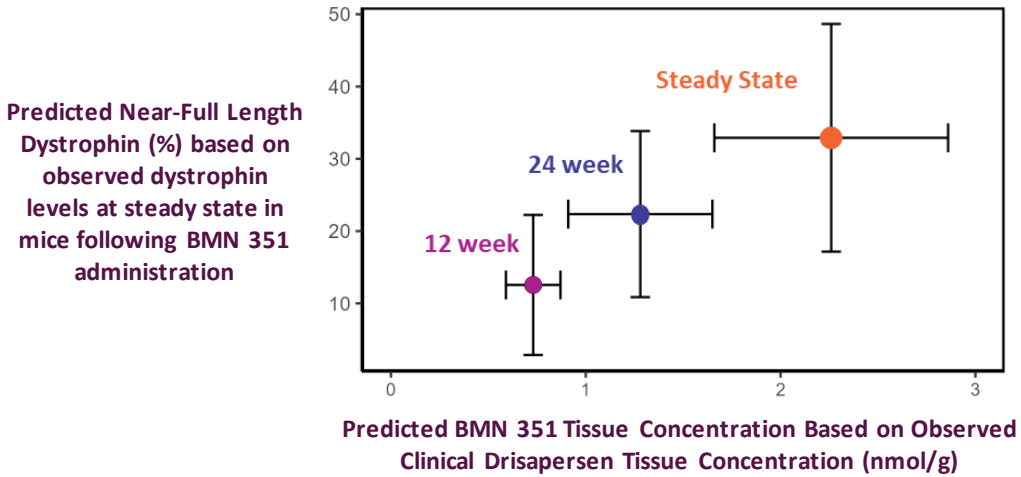
Evidence to Date

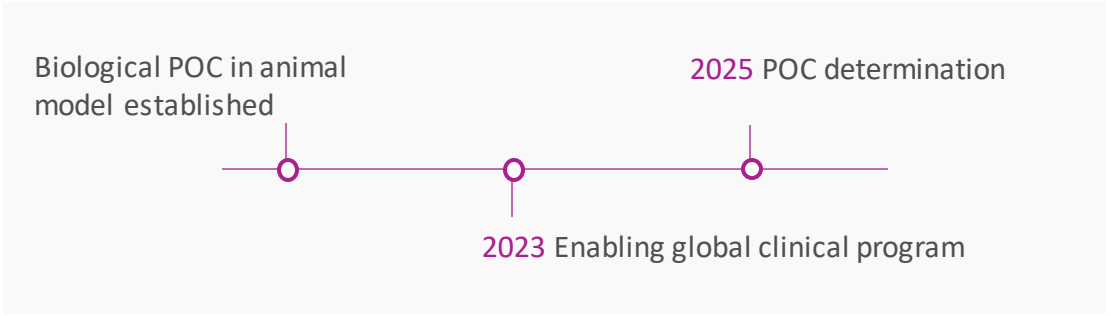
- Hypothesis: Human muscle concentrations approximating those observed in drisapersen Phase 3 will result in levels of near-full length dystrophin sufficient for functional benefit

Status and Next Steps

- Enabling global clinical program
- Muscle biopsy dystrophin levels drive development pathway
- Active pursuit of early approval options in the US and Japan upon successful clinical proof of concept

BMN 351 Uptake Similar to Drisapersen Predicted to Drive Functionally Meaningful Expression of Near-Full Length Dystrophin





POC: proof of concept

BMN 349 for Alpha-1 Antitrypsin Deficiency

Dave Jacoby, MD, PhD

Group Vice President
Head of Experimental Medicine and Early Clinical Development

BIOMARIN

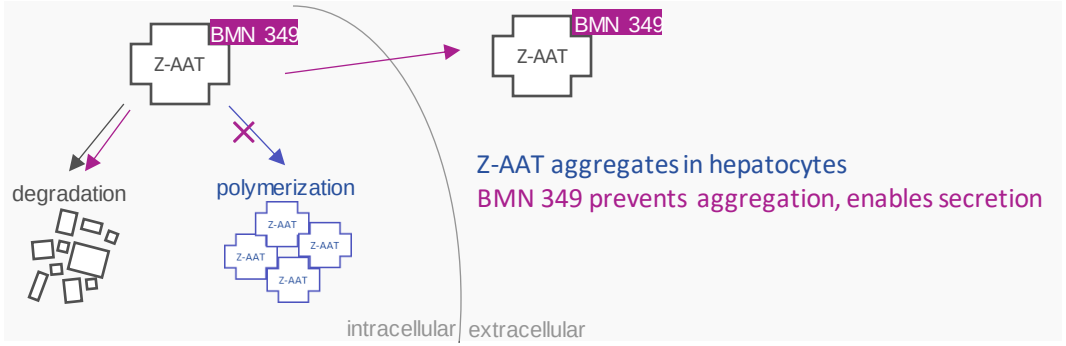
BMN 349 Development Thesis: Rapidly mobilize mutant protein liver polymers; normalize liver function and improve outcomes

Development Rationale & Approach

- Understood genetics and pathway for targeted intervention:
  - Single mutation (Z) causes aggregation; Z-polymers drive fibrosis and progressive liver disease
  - BMN 349 binds Z-protein, prevents aggregation, enables secretion and polymer debulking, improved liver health and fibrosis
- Clear markers for clinical evaluation
  - Liver polymers and serum protein levels
  - Proteomics nominate candidate markers of improving liver function

Transformative Potential

- BOI: Progressive liver disease with risk of end-stage liver disease and hepatocellular carcinoma
- SOC: No current medical treatment; supportive until transplant
- Modality: Oral small molecule; Rapid onset
- Potential addressable patient population*: 52,000 ZZ adults



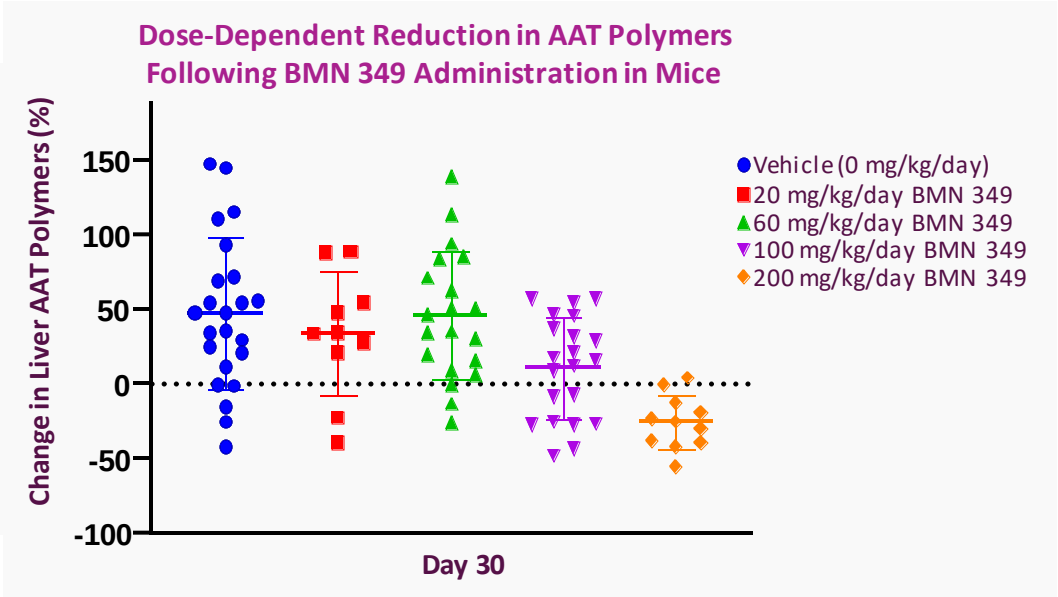
BOI: burden of illness; SOC: standard of care; *diagnosed prevalent patients appropriate for therapy in BioMarin territories

BIOMARIN

BMN 349 Development Thesis: Rapidly mobilize mutant protein liver polymers; normalize liver function and improve outcomes

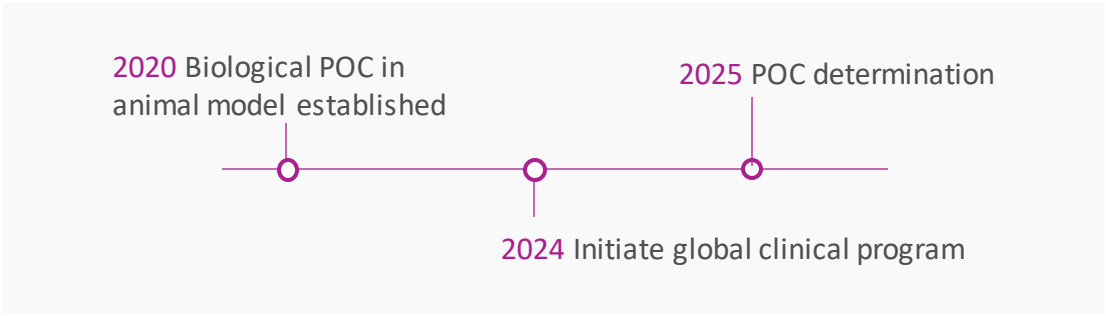
Evidence to Date

- PiZZ mice relevant animal model of liver disease
- Short-term treatment associated with reduction in polymer accumulation and debulking



Status and Next Steps

- IND-enabling milestones achieved
- Phase 1 clinical study in healthy humans
- POC study in symptomatic adult ZZ patients
- Analyses underway to identify predictive markers for vulnerable pediatric and heterozygote populations



IND: investigational new drug; POC: proof of concept

Kevin Eggan, PhD

Chief Scientific Officer

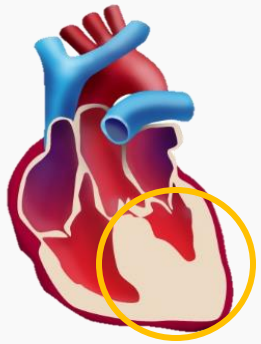
BMN 293 for MYBPC3 Hypertrophic Cardiomyopathy

BIOMARIN

BMN 293 Development Thesis: Single dose therapy to restore cardiac *MYBPC3* expression and improve symptomatic heart disease

Development Rationale & Approach

- Known genetics and pathway for targeted intervention:
  - Mutations in *MYBPC3* and haploinsufficiency of cMyBPC protein is leading cause of hypertrophic cardiomyopathy (HCM)
  - Disrupted muscle contraction and architecture leads to hypertrophy
- Readily assessable markers for clinical evaluation
  - Reduction in left ventricular mass
  - NT-proBNP to be confirmed as early marker of clinical efficacy



thickened heart muscle

Transformative Potential

- BOI: Arrhythmia, chest pain, fatigue, dizziness, heart failure; sudden cardiac death
- SOC: Beta blockers, cardiac myosin inhibitors (emerging)
- Modality: AAV-mediated gene transfer for normalization of cardiac muscle contractions by constitutive protein expression
- Potential addressable patient population*: 161,000

BOI: burden of illness; MYBPC3: gene encoding cMYBPc3; SOC: standard of care; NT-proBNP: N-terminal prohormone B-type natriuretic peptide; *diagnosed prevalent patients appropriate for therapy in BioMarin territories

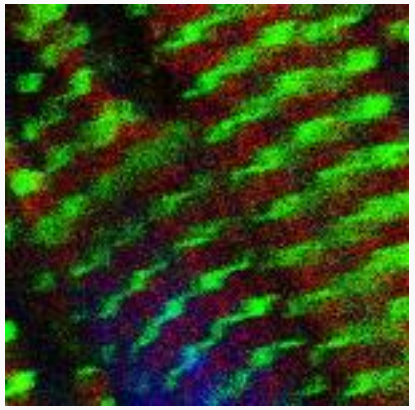
BMN 255	BMN 331	BMN 351	BMN 349	**BMN 293**	BMN 365	BMN 355
small molecule	AAV gene therapy	oligonucleotide	small molecule	AAV gene therapy	AAV gene therapy	monoclonal antibody
for NAFLD with AGT deficiency	for hereditary angioedema with C1-INH deficiency	for exon51 Duchenne's muscular dystrophy	for alpha-1 antitrypsin deficiency	**for MYBPC3 hypertrophic cardiomyopathy**	for PKP2 arrhythmogenic cardiomyopathy	for long-QT syndrome

BMN 293 Development Thesis: Single dose therapy to restore cardiac *MYBPC3* expression and improve symptomatic heart disease

Evidence to Date

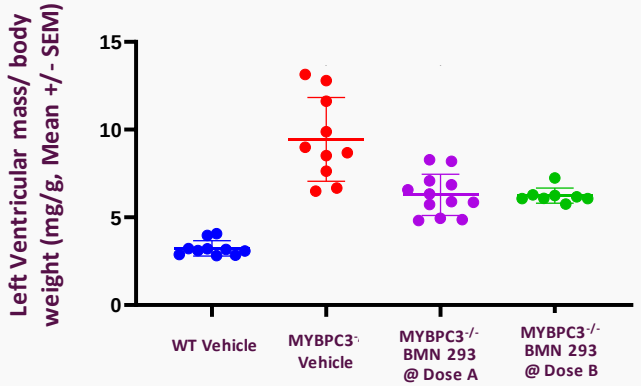
- Functional improvement observed in MYBPC3$^{-/-}$ mice
- Widespread cardiac transduction and protein expression demonstrated tolerability
- HEK293 production platform selected and scaled to support clinical development

cMyBP-C Restored following BMN 293 Administration



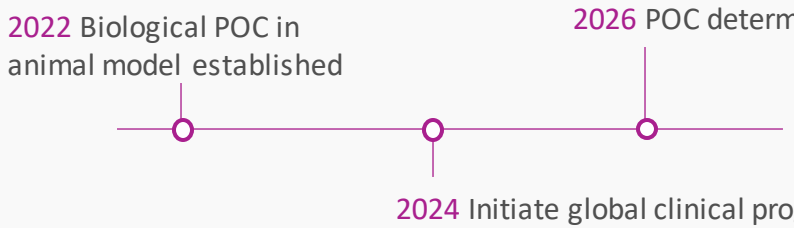
αActinin cMyBP-C DAPI

Significant Reduction in Left Ventricular Mass following BMN 293 Administration in Mice



Status and Next Steps

- IND filing status and progress
  - IND-enabling non-clinical activities on track
  - Dose range for human trials being established
  - Clinical protocol for POC developed



cMyBP-C: cardiac myosin binding protein C; MYBPC3: gene encoding cMYBPc3; NHP: non-human primate; NT-proBNP: N-terminal prohormone B-type natriuretic peptide; POC: proof of concept; WT = wild-type

NEW

Kevin Eggan, PhD

Chief Scientific Officer

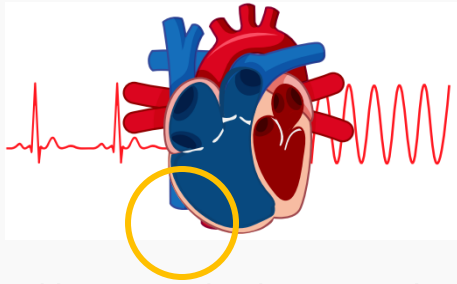
BMN 365 for PKP2 Arrhythmogenic Cardiomyopathy

BIOMARIN

BMN 365 Development Thesis: Broad cardiac distribution of PKP2 to restore cardiac function and prevent life-threatening arrhythmias

Development Rationale & Approach

- Known genetics and clear mechanistic rationale:
  - *PKP2* mutations and reduced plakophilin-2 protein are the most common cause of arrhythmogenic cardiomyopathy (ACM)
  - Without normal plakophilin-2, cardiomyocytes uncouple causing life-threatening arrhythmias and reduced contractile function
- Readily assessable markers for clinical evaluation
  - Reduction in arrhythmias
  - Imaging: Normalization of ventricular size and function



thinner, weaker heart muscle

Transformative Potential

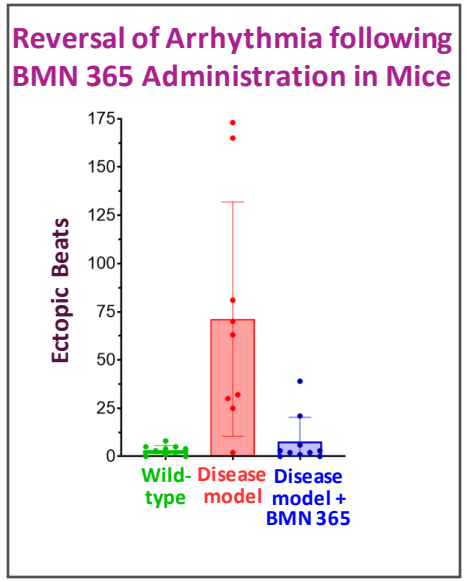
- BOI: Life-threatening arrhythmias
- SOC: antiarrhythmic medications, catheter ablation procedures, and ICD implantation
- Modality: AAV-mediated cardiac-directed protein expression to normalize cardiac conduction and improve cardiac muscle structure and function
- Diagnosed prevalent population with genetic mutation*: 140,000

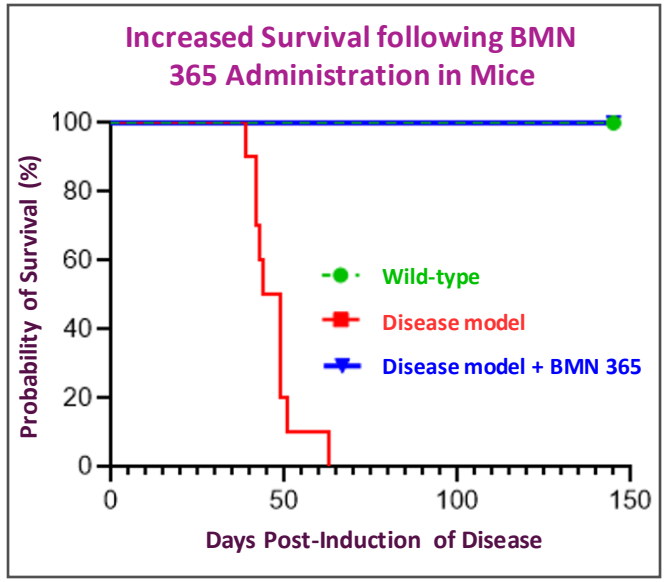
AAV: adeno-associated virus; BOI: burden of illness; PKP2: gene encoding plakophilin-2; SOC: standard of care; *in BioMarin territories ICD: implantable cardioverter-defibrillator

BMN 365 Development Thesis: Broad cardiac distribution of PKP2 to restore cardiac function and prevent life-threatening arrhythmias

Evidence to Date

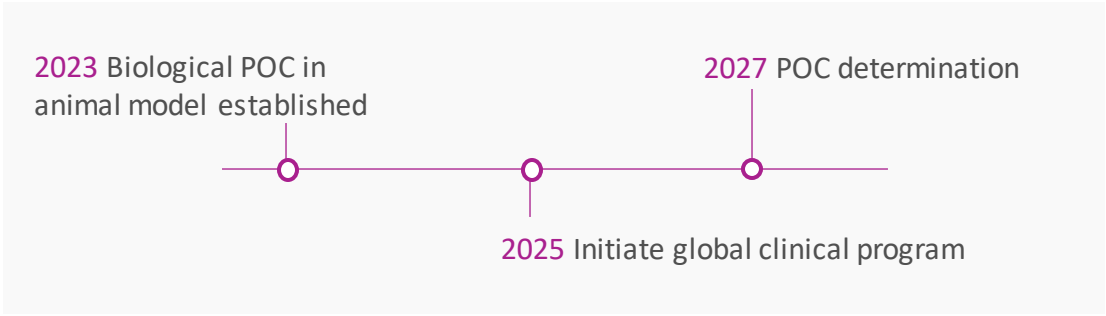
- Dose-dependent restoration of contractility in patient cells
- Efficient transduction and tolerability in mice and NHPs
- Restoration of desmosome binding partners, reversal of arrhythmia, and increased survival in *PKP2*-ACM mice





Status and Next Steps

- Toxicology studies and GMP manufacturing
- Completion of IND-enabling studies and pre-IND health authority interactions
- Clinical trial design underway



ACM: arrhythmogenic cardiomyopathy; GMP: good manufacturing practices; IND: investigational new drug; NHP: non-human primate; PKP2: gene encoding plakophilin-2; POC = proof of concept

NEW

Kevin Eggan, PhD

Chief Scientific Officer

BMN 355 for Long-QT Syndrome

BIOMARIN

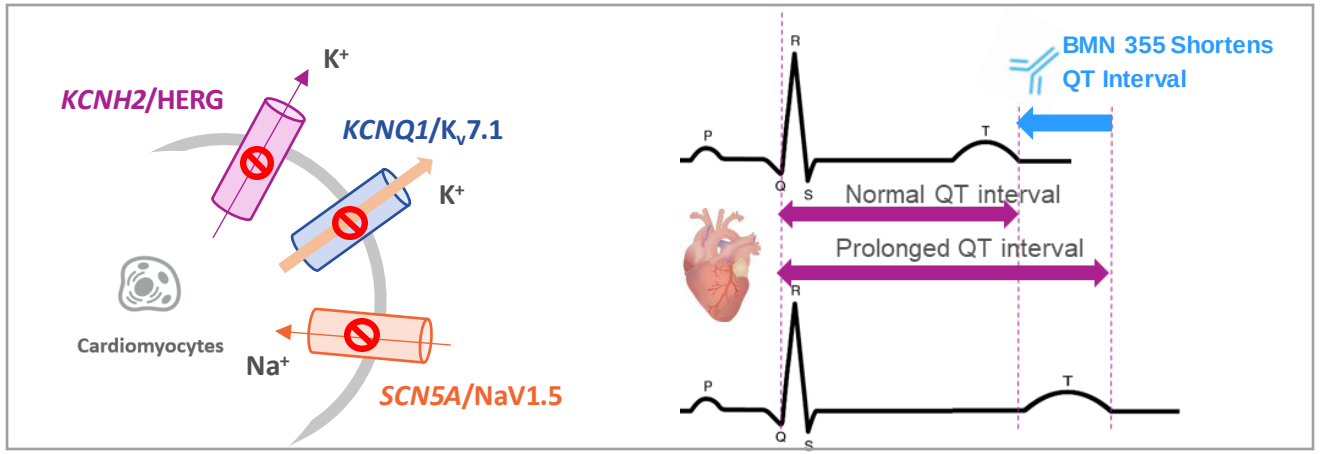
BMN 355 Development Thesis: A monoclonal antibody that selectively increases $K_v7.1$ ion channel activity can shorten the QT interval and prevent fatal arrhythmias

Development Rationale & Approach

- Familial long QT syndrome (LQTS) is caused by mutations in genes regulating cardiac electrophysiology (*KCNH2*, *SCN5A*, *KCNQ1*)
- Antibodies targeting the $K_v7.1$ channel encoded by *KCNQ1* can be more selective than small molecule K^+ channel modulators
- Readily assessable measures exist for clinical evaluation and proof of concept

Transformative Potential

- BOI: Fatal arrhythmias
- SOC: No disease modifying treatments available
- Modality: Monoclonal antibody targeting $K_v7.1$ to increase channel function
- Diagnosed prevalent population with genetic mutations*: 120,000



BOI: burden of illness; SOC: standard of care; K^+ = potassium ion; *in BioMarin territories

BIOMARIN

BMN 355 Development Thesis: A monoclonal antibody that selectively increases $K_v7.1$ ion channel activity can shorten the QT interval and prevent fatal arrhythmias

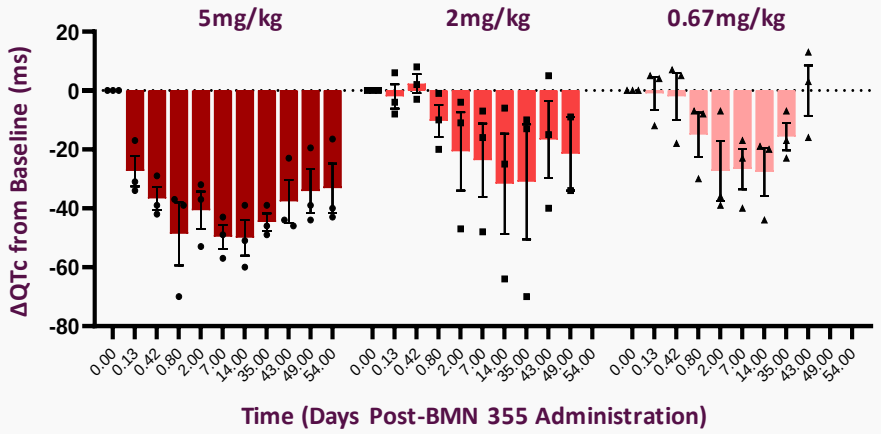
Evidence to Date

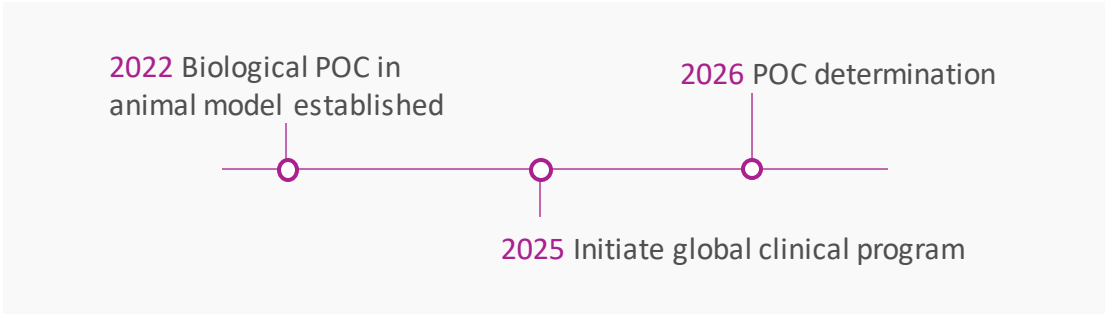
- Anti-$K_v7.1$ ion channel antibodies correct electrophysiological phenotypes in human cardiomyocyte model of LQTS
- A single subcutaneous dose of BMN 355 shortens rabbit baseline QT interval for >30 days

Status and Next Steps

- Initiated activities enabling GMP manufacturing
- Pre-IND health authority interactions and IND-enabling studies complete

Dose-dependent shortening of QT interval following Subcutaneous Administration of BMN 355





GMP: good manufacturing practices; IND: investigational new drug; LQTS: long QT syndrome; POC = proof of concept

Kevin Eggan, PhD

Chief Scientific Officer

R&D Day 2023

sustainable pipeline

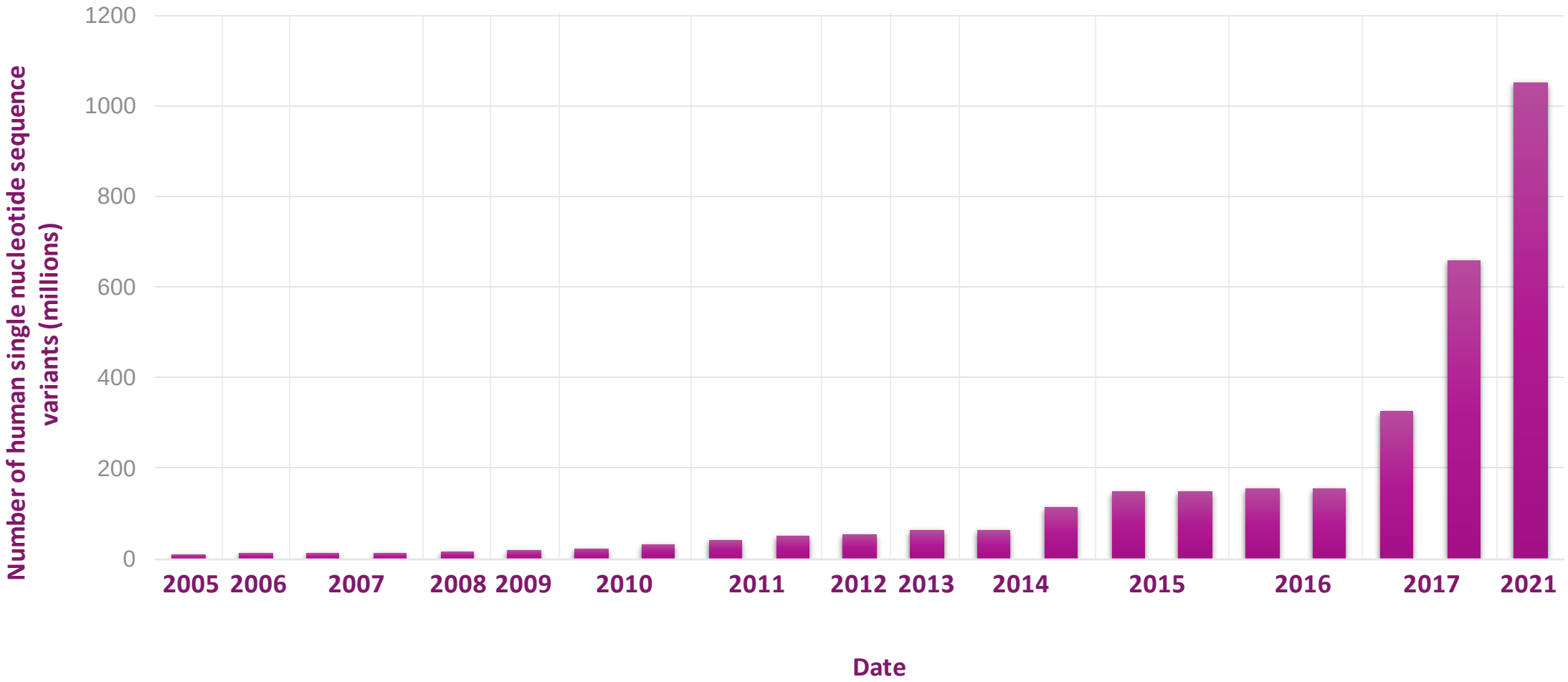
BIOMARIN

Cleverly leveraged progress in genetics and genomics can fuel sustainable growth for products and research pipeline

- The catalog of human genetic information is growing faster than it is being understood, creating opportunities for therapeutic application and discovery
- Determining the impact of genetic variation on patients is allowing BioMarin to better identify more patients to treat with our pipeline and portfolio assets
- Growing genetic knowledge is fueling the growth of BioMarin's pipeline through an increased understanding of the biology underlying disease, providing many, better targets
- We have begun harnessing our ability to understand human genetic variation, which can fuel our pipeline for many years

BIOMARIN

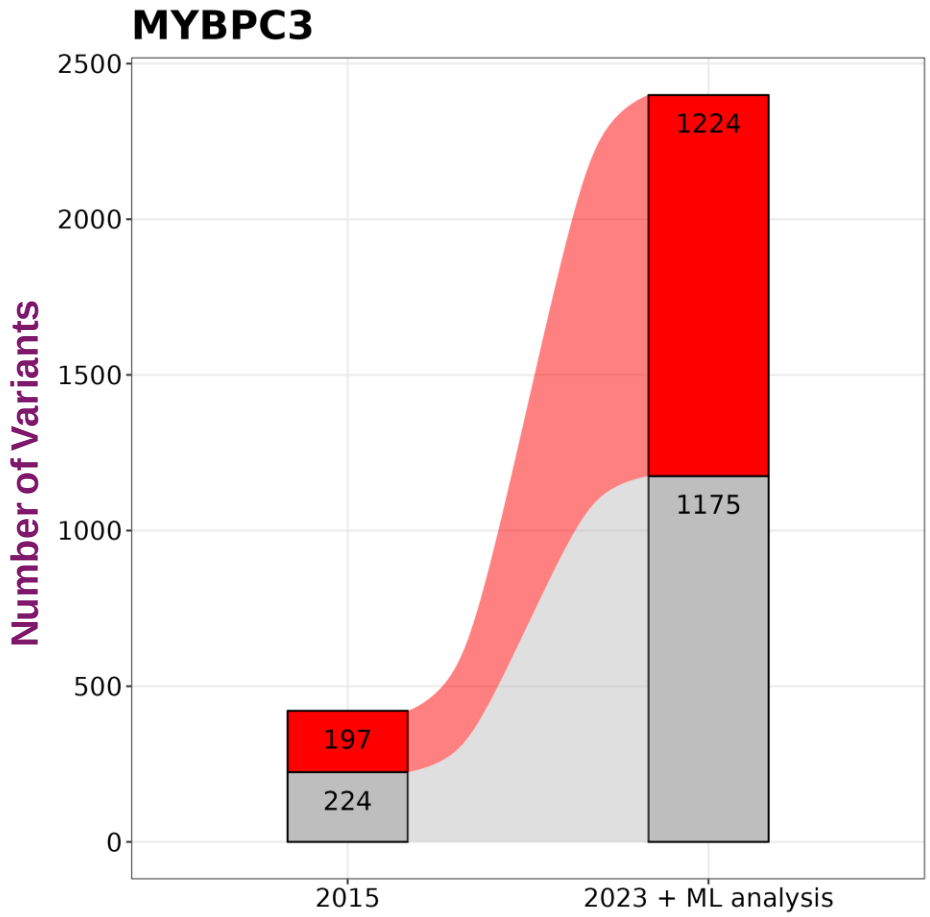
Number of identified DNA sequence variants growing exponentially



BioMarin analysis of DNA variants reported in NCBI dbSNP database

BIOMARIN

Increasing DNA sequencing has and will continue to identify many more patients to address with BioMarin therapies



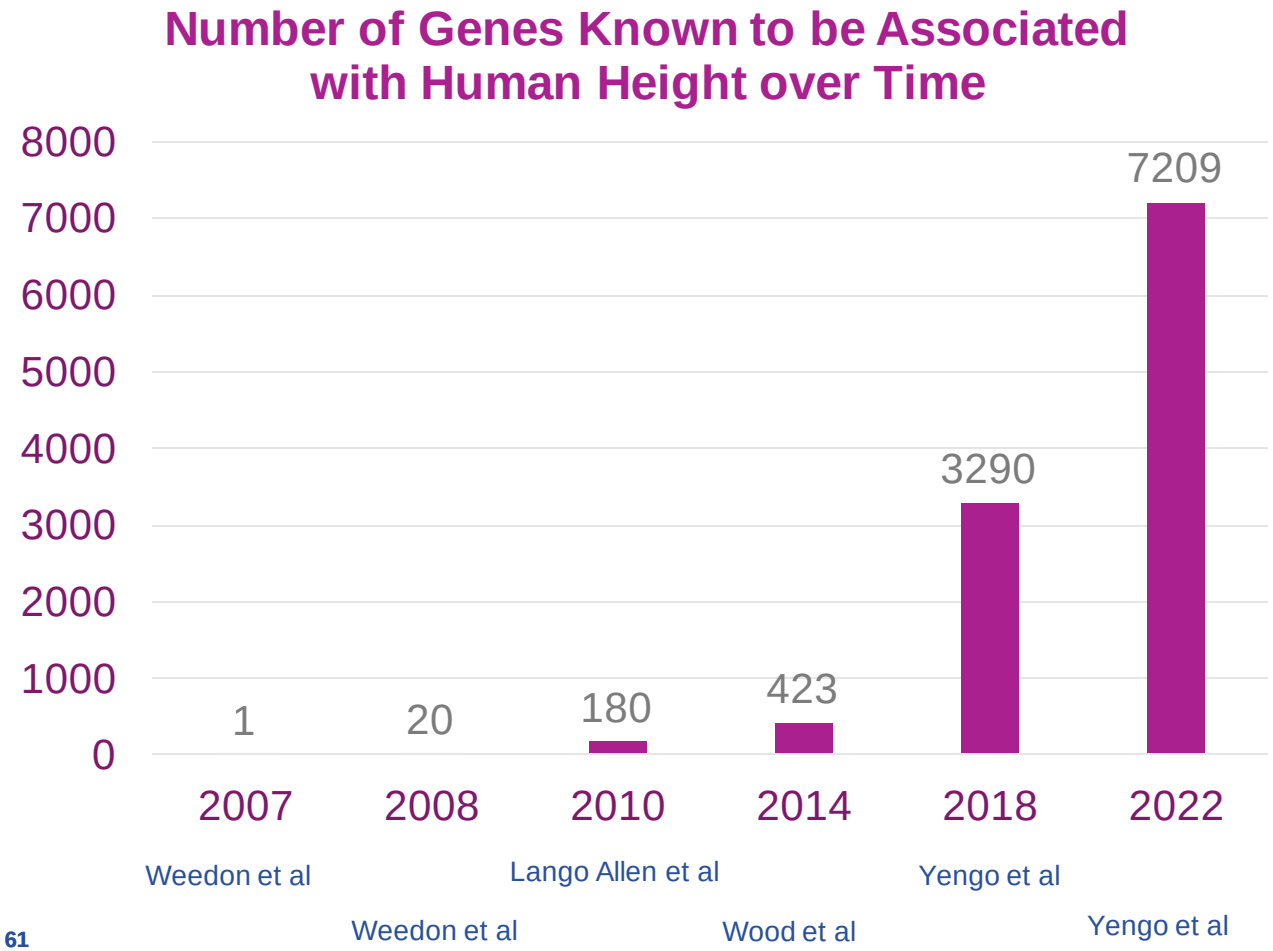
- Wider use of diagnostic exome sequencing and machine learning (ML) approaches has increased:
  - Number of known mutations in *MYBPC3*
  - Number of likely addressable patients

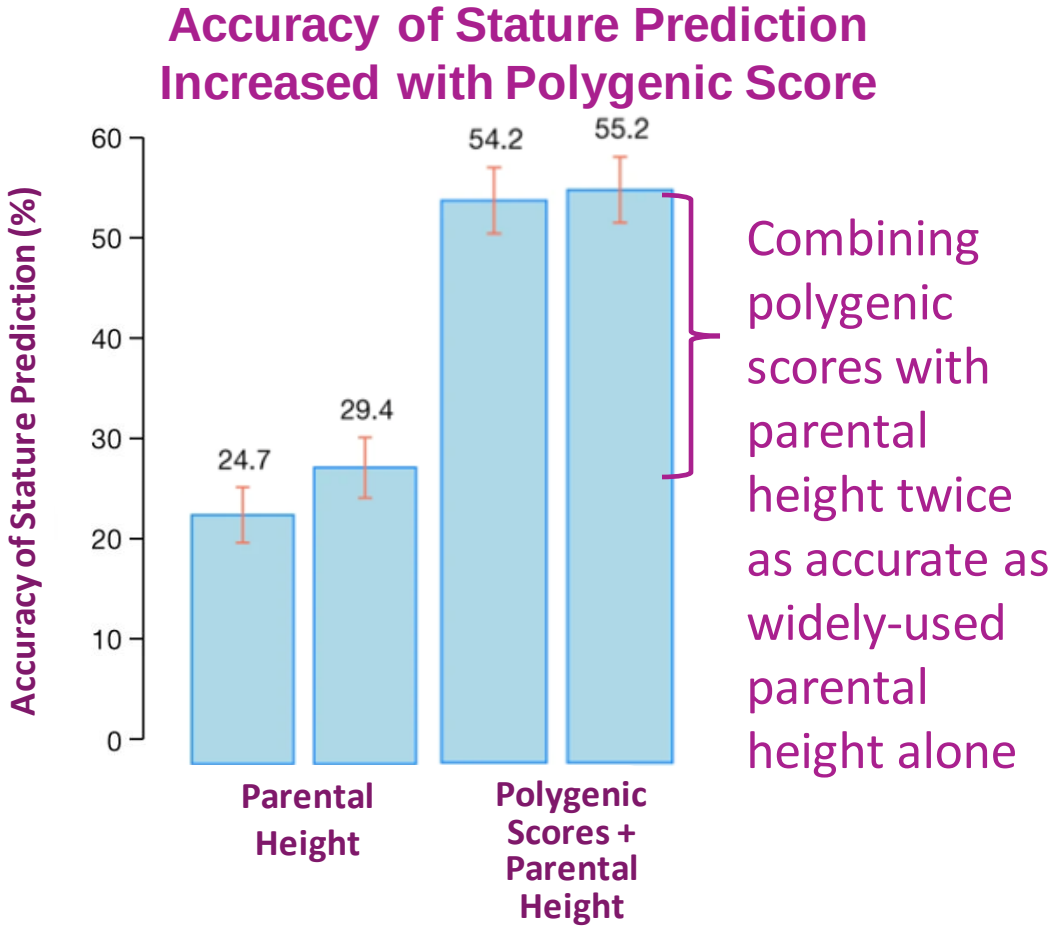
Mutation that clearly damages protein and may be used for diagnosis in future

Mutation with unclear impact on protein

Data source: Invitae Explorer

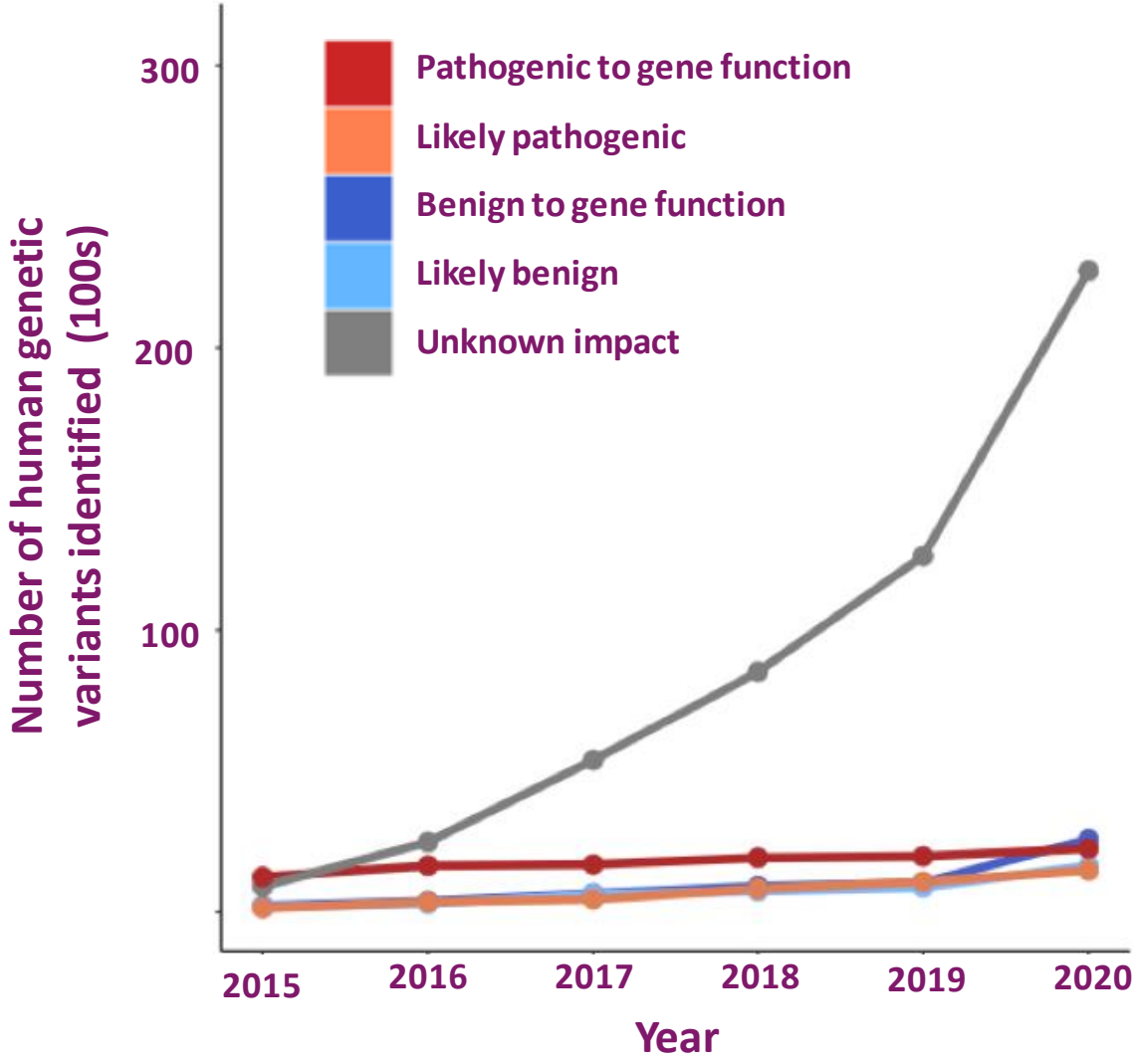
New genetic approaches like polygenic risk scores may allow patients to be identified for treatment earlier





2022 Yengo et al

Unknown function of most genetic variants create many opportunities for companies like BioMarin with strong genomics capabilities

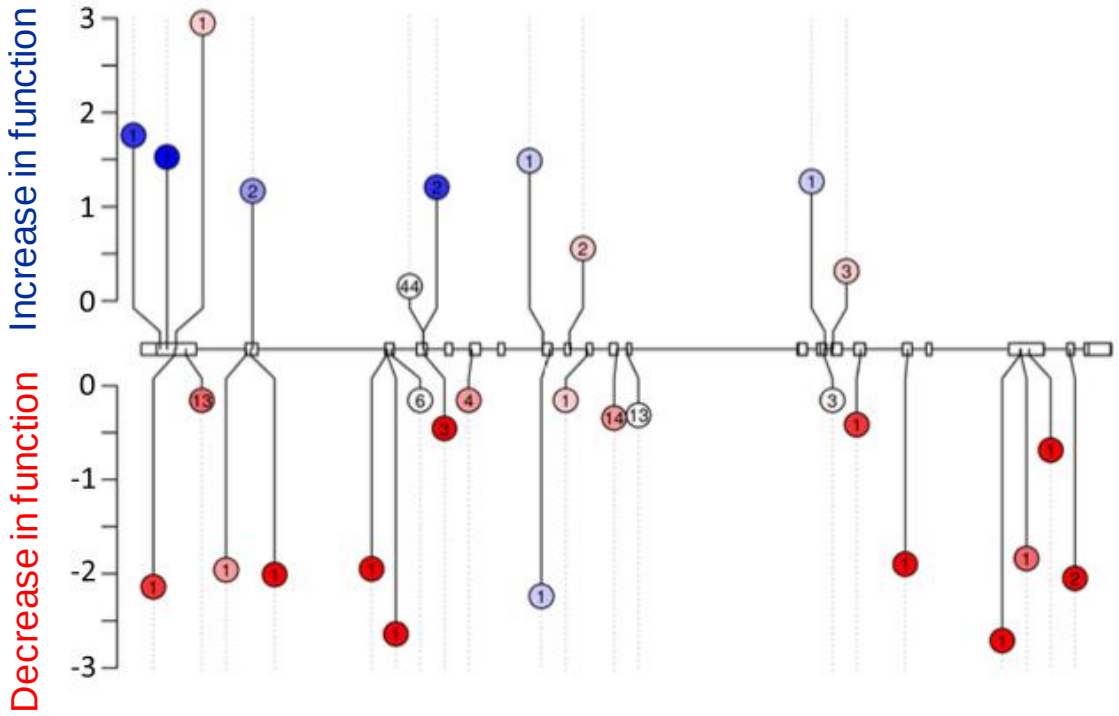


Identification of DNA sequence variation happening much faster than its function can be reported

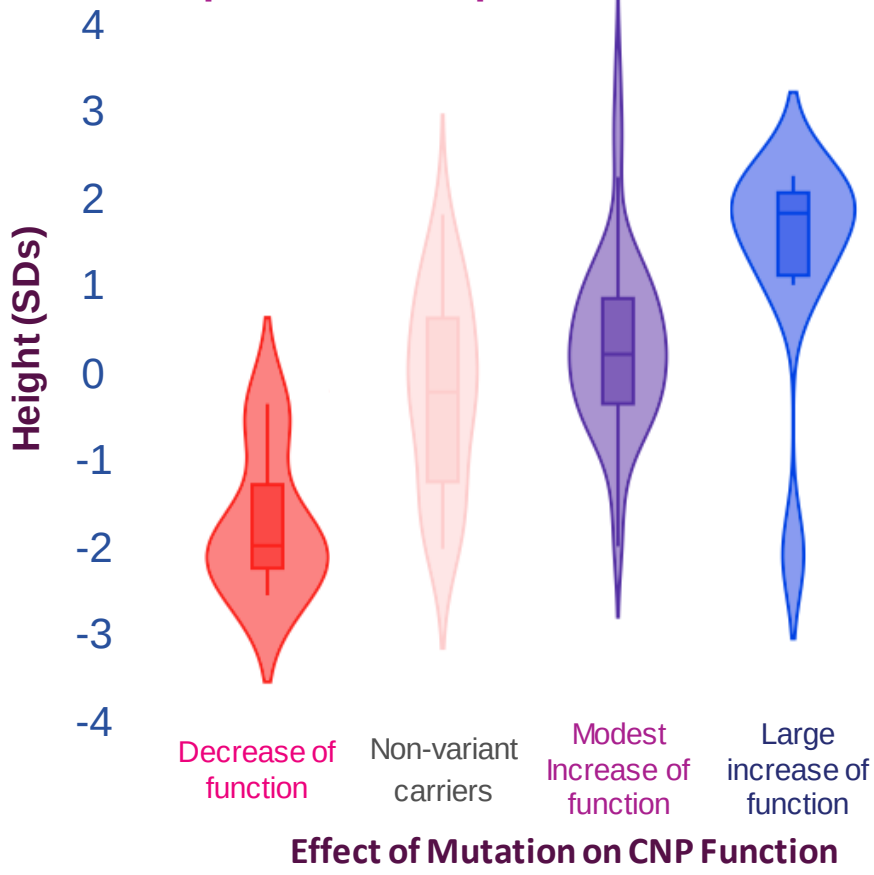
Fayer et al, 2021

BioMarin analysis of variants in CNP receptor has fueled confidence that activating this pathway will drive growth in most individuals

Lab quantification of DNA variant impact on pathway activity by location on CNP receptor gene sequence[1]

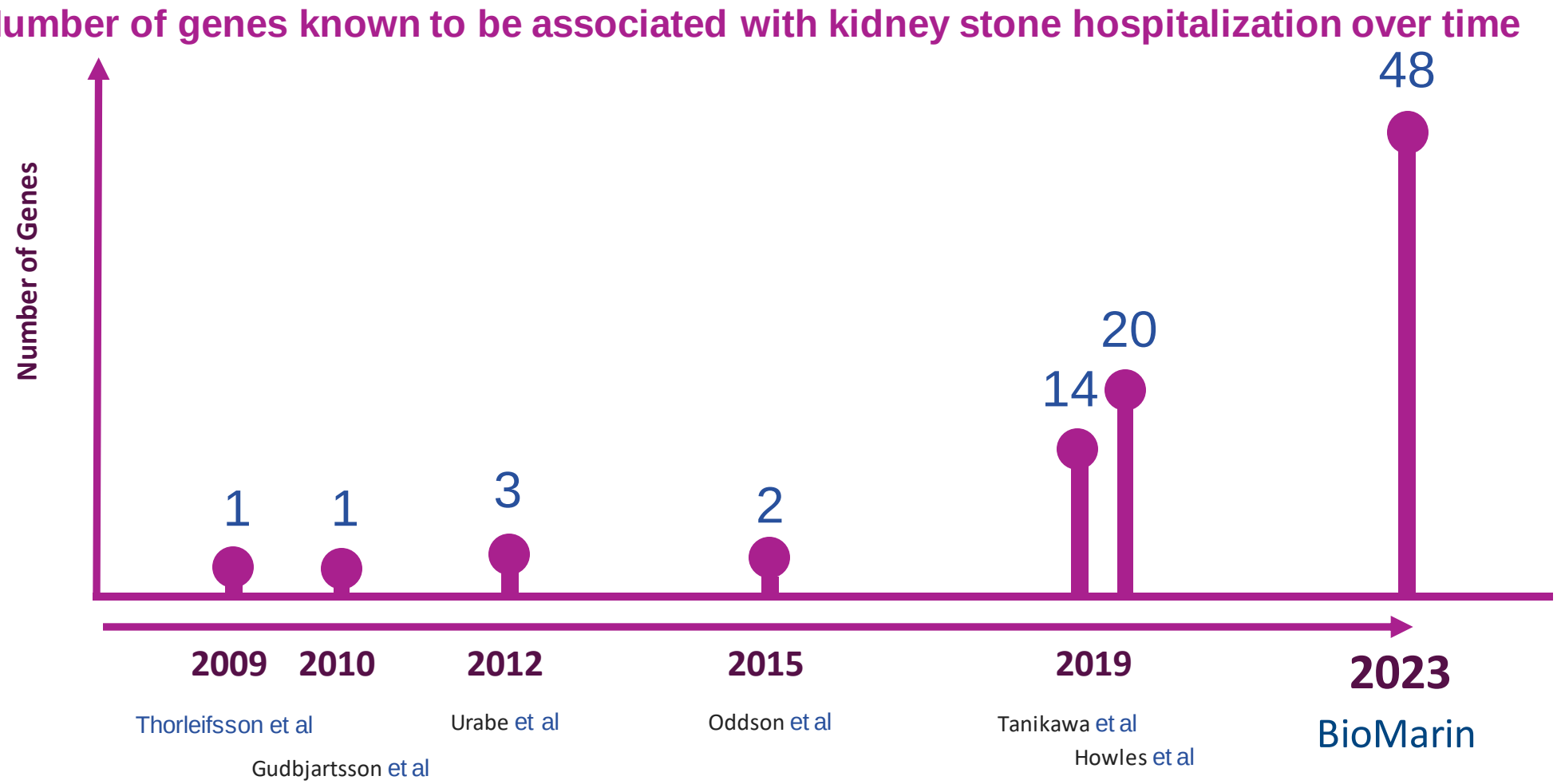


CNP receptor variants predictive of adult height[2]



[1]Per UK Biobank; [2]Modified from Estrada et al, 2021

BioMarin analysis of public sequence data has fueled internal insights into genetic mechanisms contributing to kidney stones

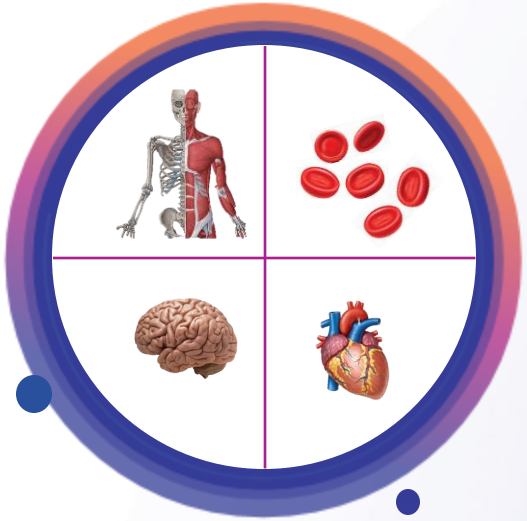


BioMarin

Translating Genetic Discoveries into Transformative Medicines

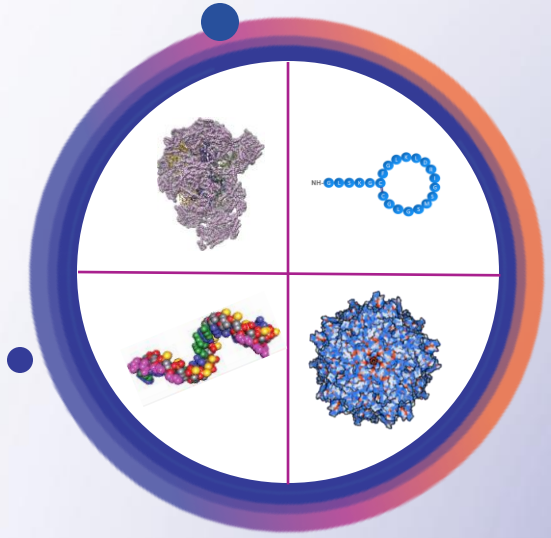
Pipeline Sustainability via Genetically-Enabled Discovery

Virtually limitless influx of potential therapeutic targets, populations, and pipeline candidates through expansion, discovery, and business development



High PTS Candidates via Expertly-Informed Screening and Development

Targeted investment in select therapeutic areas builds leverage through concentrated internal expertise

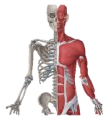
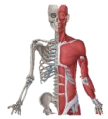
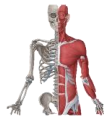


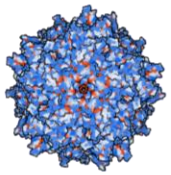
Transformative Medicines using the Optimal Modality

Proven excellence in the development of multiple treatment modalities to enable agility in treatment optimization

Building Momentum:
Indication expansion, therapeutic area expertise, platform investment

VOXZOGO (vosoritide) for injection

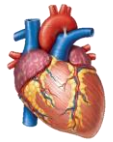
Achondroplasia →  Hypochondroplasia →  Select genetic short stature conditions →  Idiopathic short stature



Gene Therapy

ROCTAVIAN (valoctocogene roxaparvovec) Solution for intravenous infusion →

BMN 331 →



BMN 293
BMN 365

Central Nervous System

Brineura™ (cerliponase alfa) →

CLN 2

Genetic epilepsies
Developmental Disorders

BIOMARIN

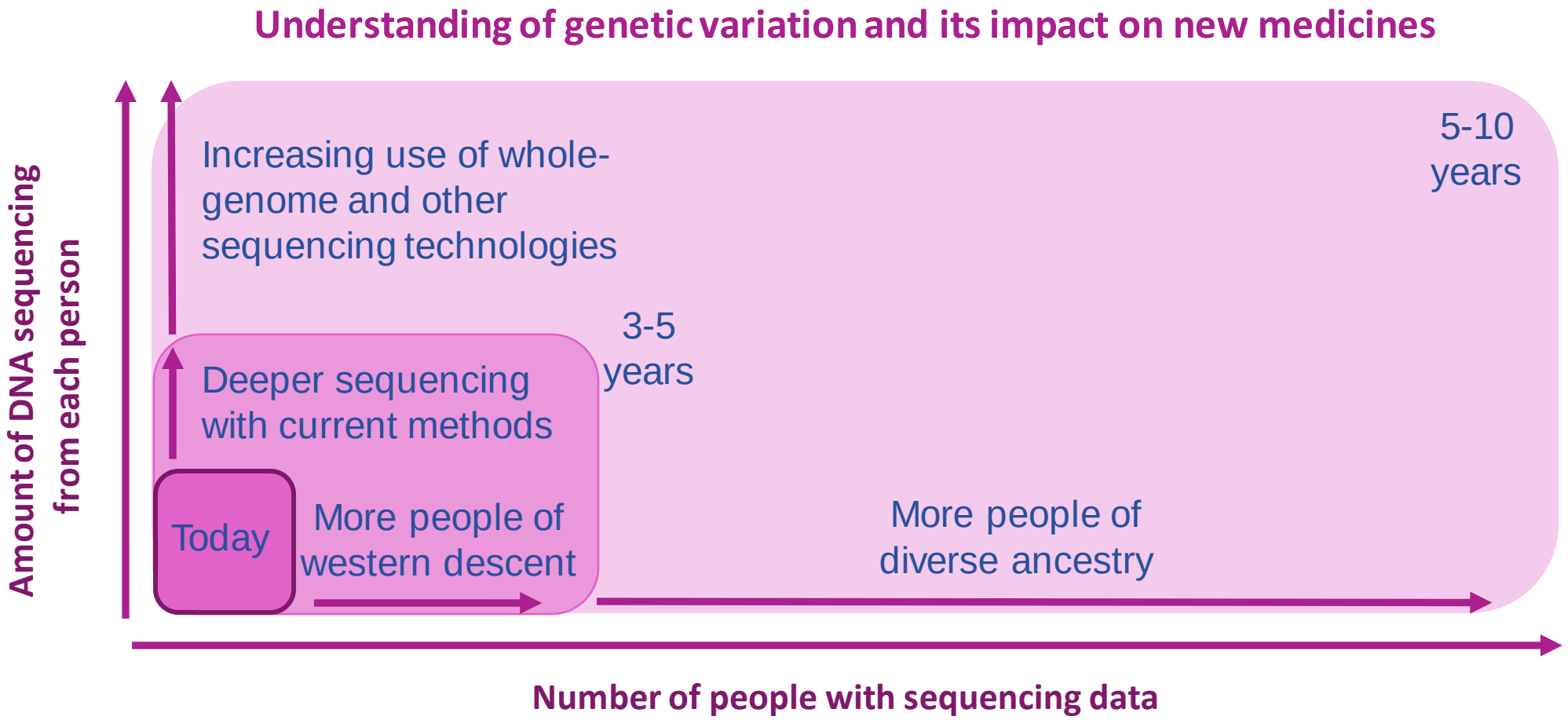
Genetic Insights Drive Unprecedented Diversity and Potential Value

Research and Early Development

Product Candidate	Research	IND-Enabling	Phase 1	Phase 2
BMN 255 Hyperoxaluria (Small Molecule)				
BMN 351 DMD (Exon 51 Oligonucleotide)				
BMN 349 A1ATD (Small Molecule)				
BMN 333 Long Acting CNP (Peptide)				
MSK (Oligonucleotide)	4 Candidates			
MSK (Gene Therapy)				
Metabolic (Biologic)	2 Candidates			
HEM (Biologic)				
HEM (Oligonucleotide)	2 Candidates			
BMN 331 HAE (AAV Gene Therapy)				
BMN 293 MYBPC3 HCM (AAV Gene Therapy)				
BMN 365 PKP2 ACM (AAV Gene Therapy)				
BMN 355 for LQT (Monoclonal Antibody)				
CV (AAV Gene Therapy)	2 Candidates			
CV (Oligonucleotide)	2 Candidates			
CV (Monoclonal Antibody)				
CNS (AAV Gene Therapy)	4 Candidates			
CNS (Oligonucleotide)	3 Candidates			
CNS (Biologic)				

- Musculoskeletal (MSK)/Metabolic
- Non-Oncology Hematology
- Cardiovascular (CV)
- Central Nervous System (CNS)
- Opportunistic

The field has only just begun to discover how genetic variation shapes health and translating it into transformative medicines



BIOMARIN

Brian Mueller

Executive Vice President
Chief Financial Officer

Sustainable Growth & Profitability

BIOMARIN

Optimizing growth through R&D innovation & financial execution

Increasing R&D Investments

Ability to fund investments in indication expansion opportunities and largest R&D pipeline in BioMarin history

Strategic Prioritization

Prioritizing R&D spend to focus on opportunities with highest potential of scientific and commercial success

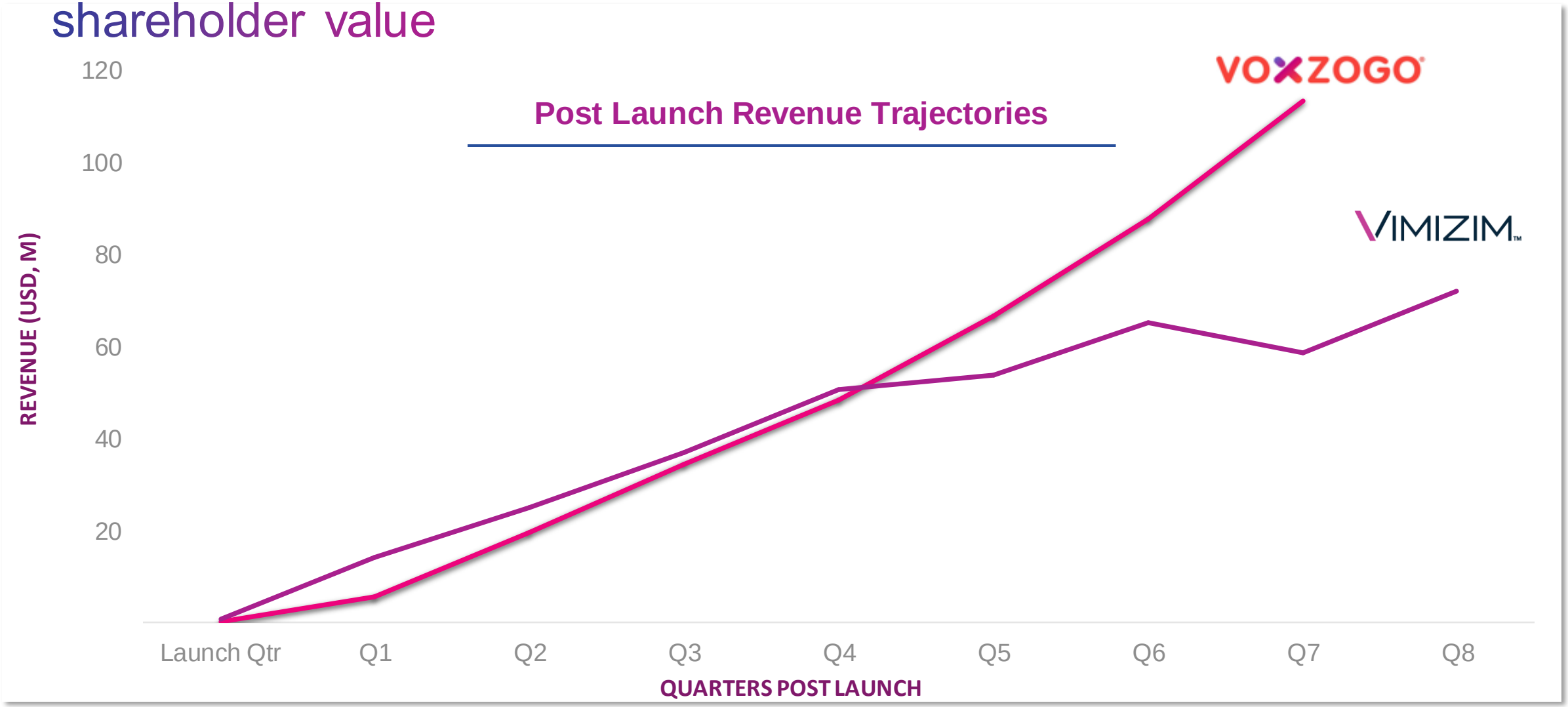
Leveraged Growth

Leveraging a resilient, diversified business model and mature global infrastructure to drive margin expansion and cash generation

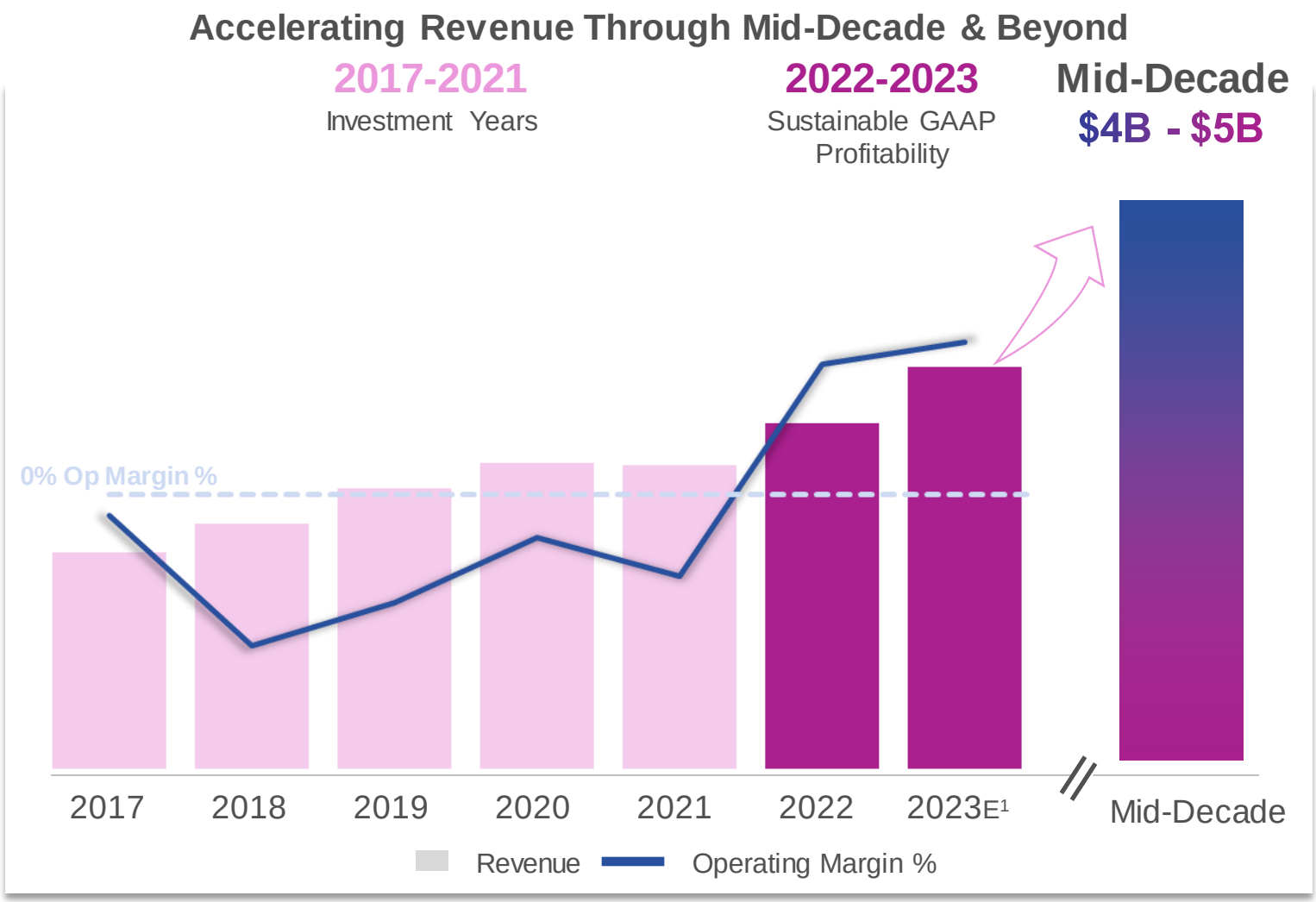
Sustainable Growth through Strong Cash Generation and Cash Management

BIOMARIN

Global commercial excellence: Converting scientific innovation to shareholder value



Financial Strength Demonstrated By Revenue Growth and Margin Expansion



Near Term Financial Execution Priorities

1. Strong Double-Digit Revenue Growth
2. Committing to Large BioPharma Peer Profit Margins
3. Significant Investments in R&D fund sustainable innovation
4. Cash Generation Poised to Create Capital Allocation Optionality

[1] 2023 represents Q2 2023 earning Mid-Point Guidance
Note: Financials are not shown to scale

Thank you

Q&A