JP Morgan
2023 Healthcare Conference

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President and CEO

Forward looking statements

Cautionary note regarding forward-looking statements: This presentation contains forward-looking statements, including, but not limited to, statements regarding our expectations and projections regarding our future operating results and financial performance, anticipated cost or expense reductions, plans with respect to commercializing our product and product candidates, our translational research program, expectations regarding our manufacturing capabilities, the expected timing of release of additional data for our product candidates, plans to initiate additional studies for product candidates and timing and design of these studies, plans regarding ongoing studies for existing programs, our liquidity position as of the most recent fiscal quarter end, expectations regarding the adequacy of clinical data to support marketing applications and approvals of product candidates, our intent to file, and potential timing and success of, marketing applications and other regulatory approvals, expectations regarding timing of receiving potential approval of product candidates, expectations regarding prevalence of patients, future regulatory interactions, and the value to be generated by our pipeline. Such forward-looking statements involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, our reliance on our third party partner, Kyowa Kirin Co., Ltd., for the supply of Crysvita, the effects from the COVID-19 pandemic on our clinical trial activities, business and operating results, fluctuations in buying or distribution patterns from distributors and specialty pharmacies, the transition back to Kyowa Kirin of our exclusive rights to promote Crysvita in the United States and Canada and unexpected costs, delays, difficulties or adverse impact to revenue related to such transition, smaller than anticipated market opportunities for our products and product candidates, manufacturing risks, competition from other therapies or products, uncertainties related to insurance coverage and reimbursement status of our newly approved products, our evolving integrated commercial organization, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of our regulatory filings the uncertainties inherent in the clinical drug development process, including the potential for substantial delays and risk that earlier study results may not be predictive of future study results, and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the availability or commercial potential of our product and product candidates, and our ability to integrate acquired businesses, which are more fully described in our most recent Form 10-Q or Form 10-K under the caption “Risk Factors” and elsewhere in such reports. Any forward-looking statements made by us reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Accordingly, our actual results may materially differ from our current expectations, estimates, and projections. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

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Our mission since 2010

Going beyond every day...

to transform the lives of people living with rare disease.

4 approved therapies

5 indications

>3,200 patients globally treated including commercial & expanded use

~70% success rate
from clinic to approval

7 clinical programs
(5 in pivotal studies)

Well capitalized	Significant revenue growth YOY	Financial discipline

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Our specialized approach to drug development

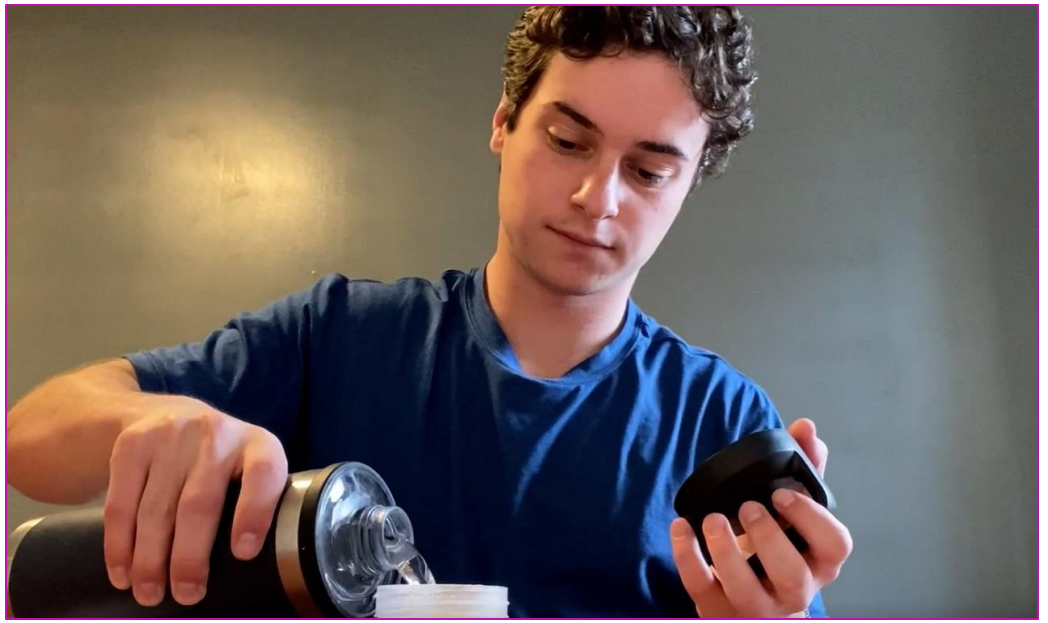
Match deep understanding of disease biology → with the right drug modality and tools → informed by patient experience

CRYSVITA® burosumab-twza Injection 10, 20, 30 mg/mL

For X-linked hypophosphatemia (XLH)

(left to right) *Alison, her son Caden, her niece Macy and sister Renee; all living with XLH*

AAV gene therapy for glycogen storage disease 1a



Jonah, who is living with GSDIa

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Driving revenue growth and key clinical data generation while increasing operational leverage

Operational efficiency

- Focus on large / pivotal programs
- Leverage current pipeline and infrastructure
- Financial discipline & alignment of resources

Revenue growth

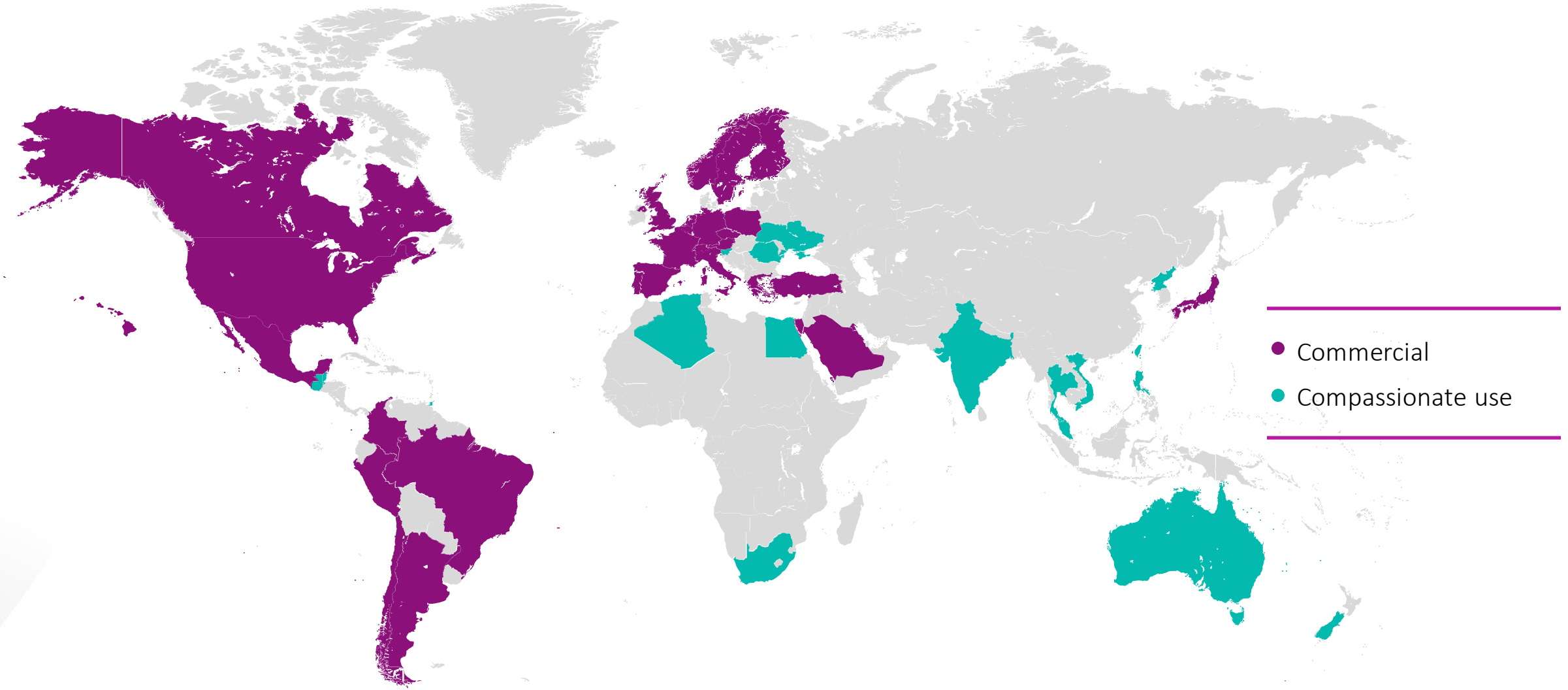
Expanding current markets, increasing commercial revenue

Data generation

Key portfolio programs

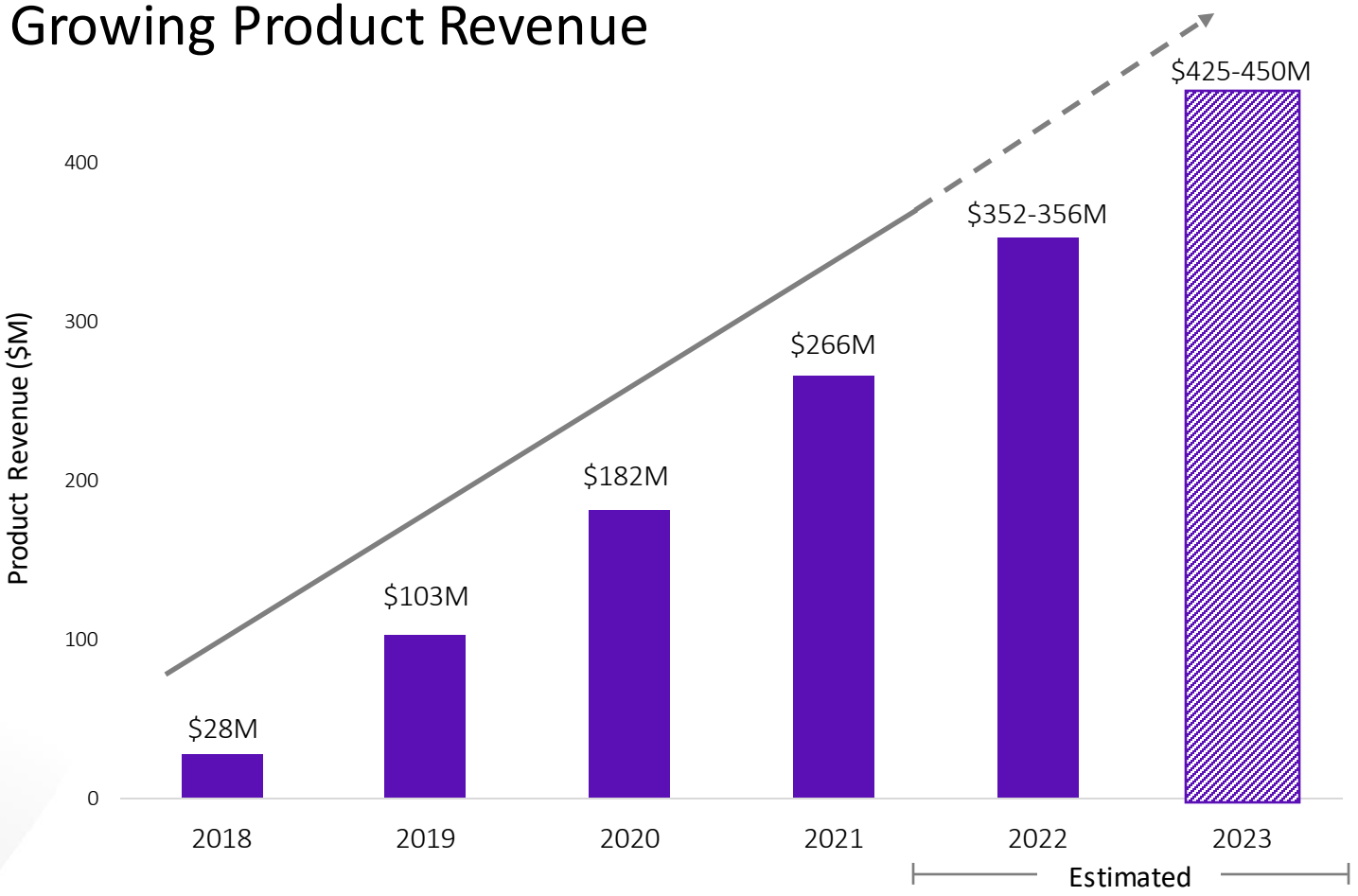
- Angelman syndrome
- Osteogenesis Imperfecta
- Gene therapy studies

Reaching patients around the world



Growing base of revenue driven by established and expanding commercial portfolio

Growing Product Revenue

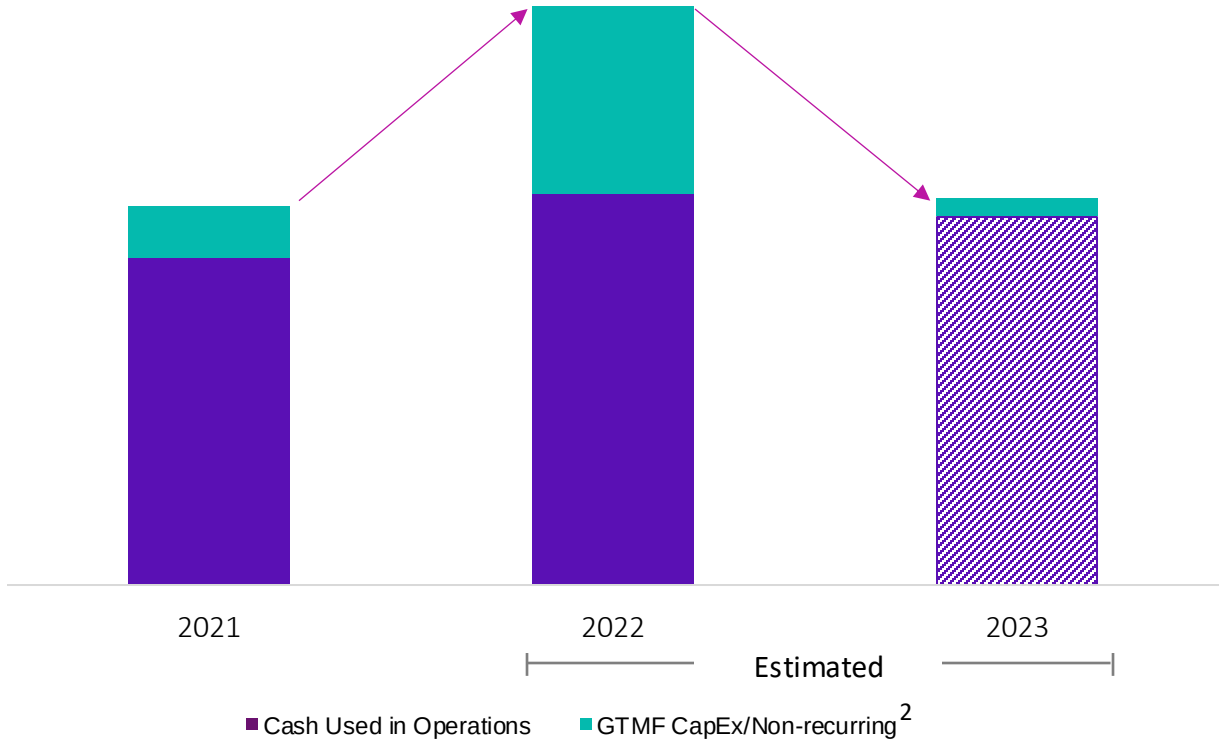


Product	2022 Estimate[1]	2023 Guidance
Crysvita[2]	$277-279M	$325-340M
Dojolvi	$55-56M	$65-75M
Total Product Revenue[3]	$352-356M	$425-450M

1 Preliminary and unaudited
2 Total Crysvita revenue, including North America, Latin America, and Europe
3 Total Product Revenue includes Crysvita, Dojolvi, Mepsevii, and Evkeeza

Strong balance sheet and operational efficiency provide runway to execute on value creating programs

Uses of Cash[1]



Cash and equivalents[3] of
~$900M as of Dec 31, 2022

2023 Cash Used in Operations
less than $400M

1 Cash used in operations, Gene Therapy Manufacturing Facility (GTMF) Capital Expenses and select non-recurring uses of cash
2 2021: ~$55M GTMF; 2022: ~$90M GTMF, $75M GeneTx Acquisition, $30M Evkeeza License; 2023: ~$20M GTMF
3 Estimated cash, cash equivalents, and available-for-sale investments as of December 31, 2022 (unaudited)

Leverage and focused investments to grow value, manage cash use

Mature, integrated rare disease company

Growing revenue base and reducing cash use

Driving value through advancement of large and late-stage clinical programs

Increasing leverage from operational and program investments:

- Established global commercial operations leveraging people and regional structures
- GeneTx acquisition provides full control of Angelman program
- New gene therapy manufacturing facility provides cost and speed efficiencies
- Leveling and rebalancing of headcount to focus on priority programs

Key upcoming clinical catalysts

PROGRAM	OBJECTIVE	EXPECTED TIMING
UX143 Osteogenesis Imperfecta	Ph 2 LPI Ph 2 data readout and Ph 3 transition Initiate young pediatric study	Early 2023 Mid-2023 1H23
GTX-102 Angelman syndrome	FPI for Expansion Cohorts Ph 1/2 data readout	1H23 2023
DTX401 GSDIa	Ph 3 LPI Ph 3 data readout	✓ 1H24
UX701 Wilson disease	Stage 1 enrollment completion Stage 1 safety and initial efficacy	Mid-2023 Early 2024
DTX301 OTC deficiency	Ph 3 FPI	1Q23

UX143 (setrusumab)
for Osteogenesis Imperfecta (OI)

Abnormal bone metabolism leads to increased bone resorption, inadequate bone production

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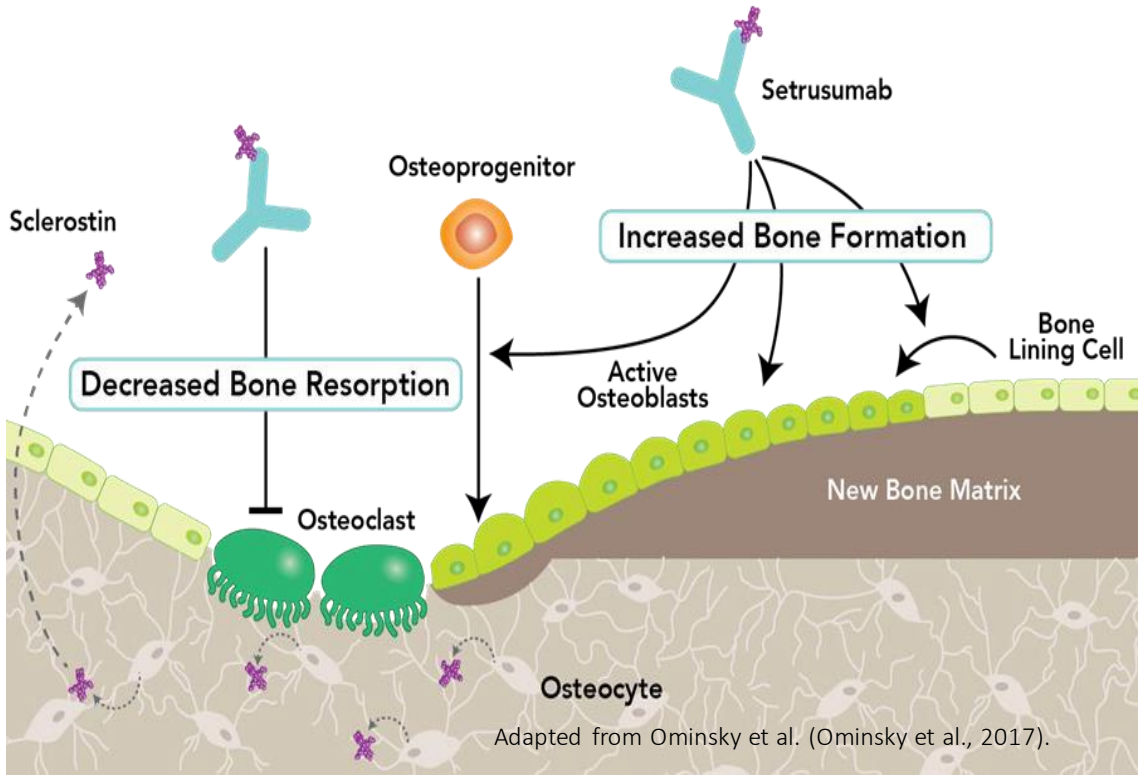
UX143 for osteogenesis imperfecta (OI)
Reverses abnormal bone biology, repressing excess resorption

- **WW prevalence:** ~60,000 (targeting types I/III/IV)
- **No approved treatments:** bisphosphonates anti-resorptive treatments are off-label
- **UX143 (setrusumab):** Fully human anti-sclerostin antibody increases bone formation, density
- **Positive data in adults** from prior Phase 2b study
- **Status:** Continuing enrollment and dosing in pivotal Phase 2/3 study

Mechanism of Anti-Sclerostin Antibody



Adapted from Ominsky et al. (Ominsky et al., 2017).

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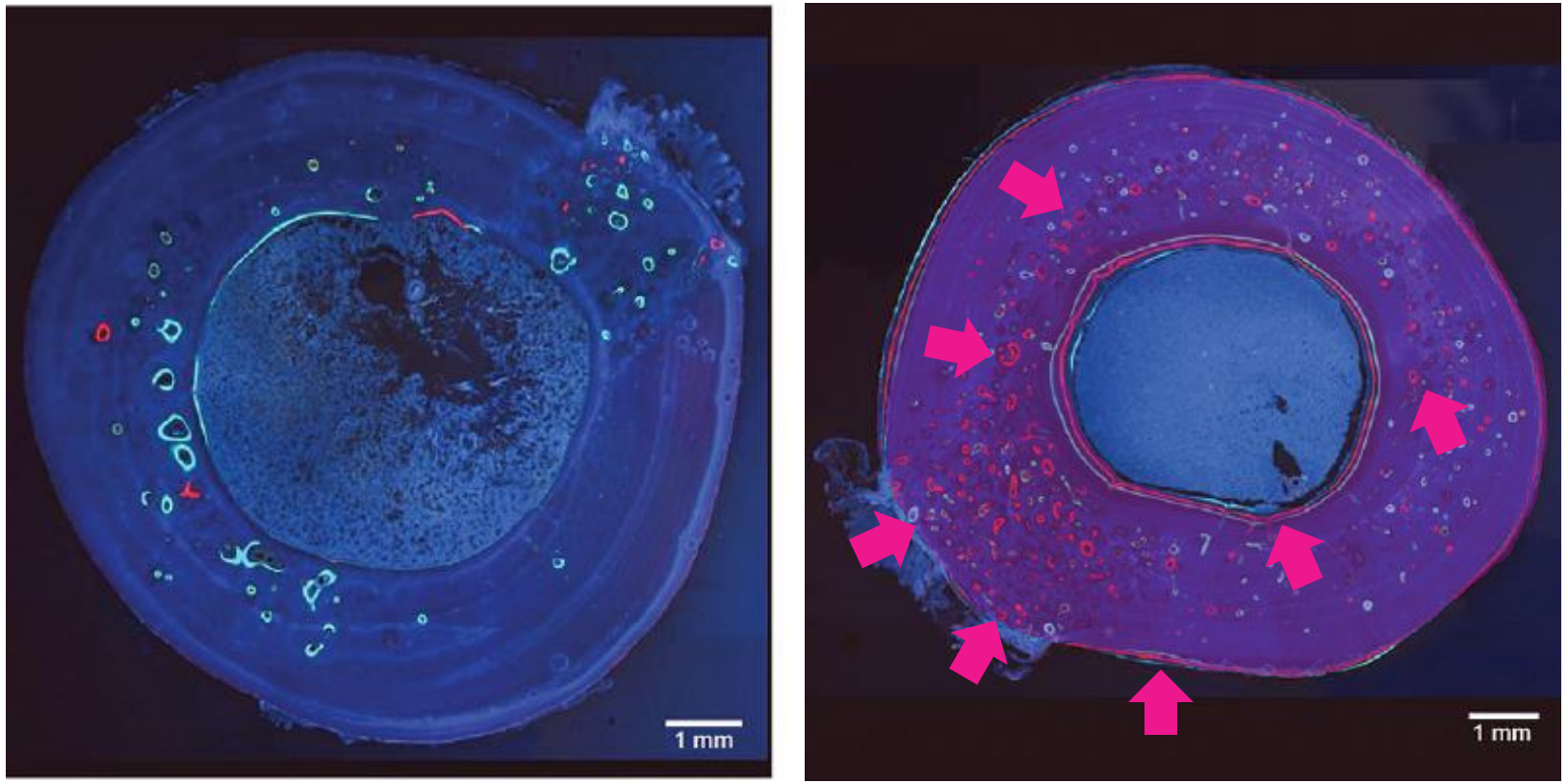
Anti-sclerostin antibody increases bone formation on all bone surfaces

Osteoporotic Monkey Model (12mo Tx)

Vehicle

Sclerostin-Ab

Femur Diaphysis



Red bone formed on the important sites: the bone surface and middle of the bone

Ominsky et al 2017

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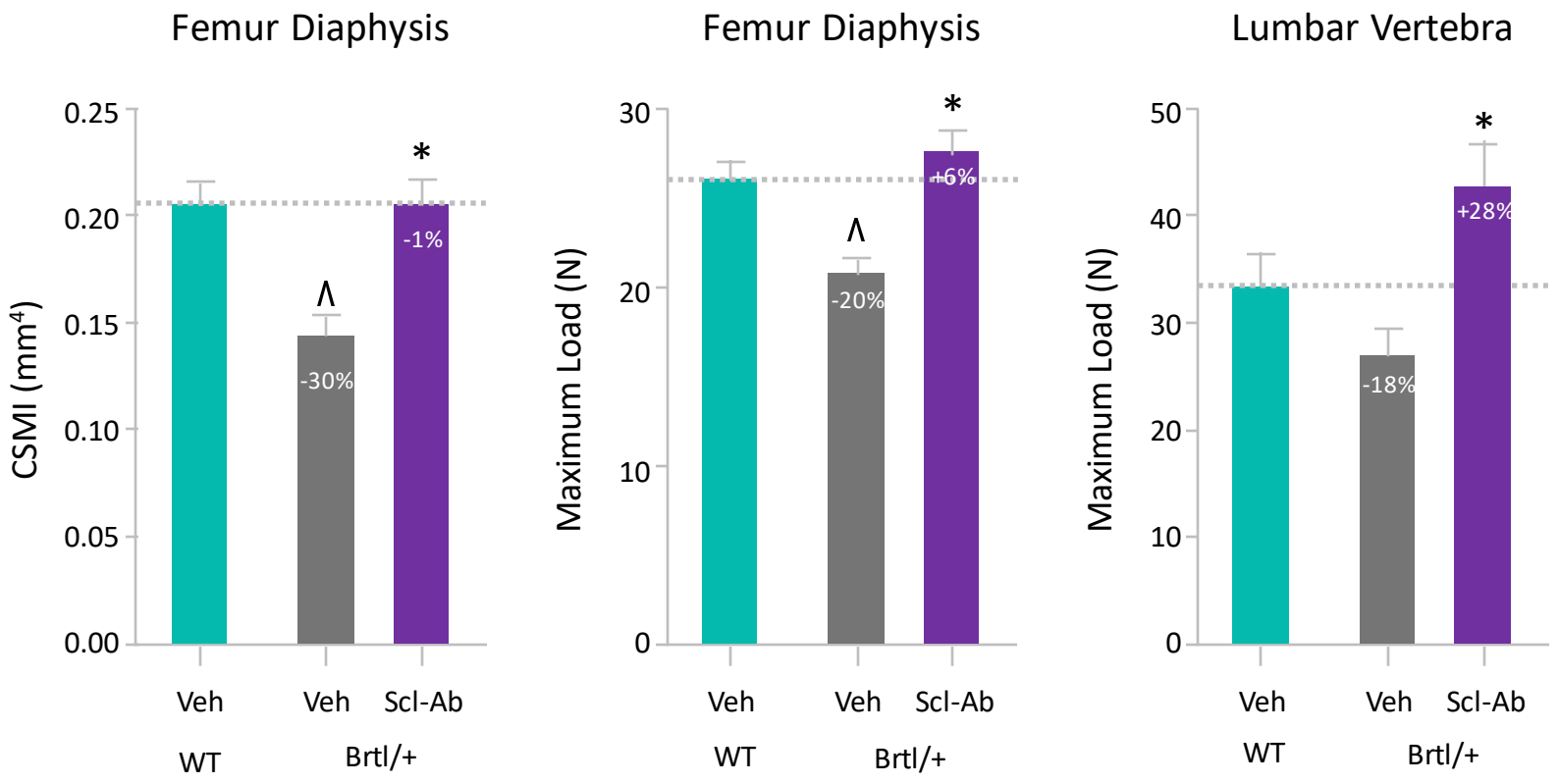
UX143 can normalize bone mass and strength in brittle OI mice *even if collagen still mutated*

- UX143 (5wks) restored cortical bone geometry & strength in Brtl/+ mice to WT levels
- These changes were well correlated, demonstrating that increased bone quantity was sufficient to restore bone strength
- Anti-sclerostin is restoring normal bone physiology of production and resorption



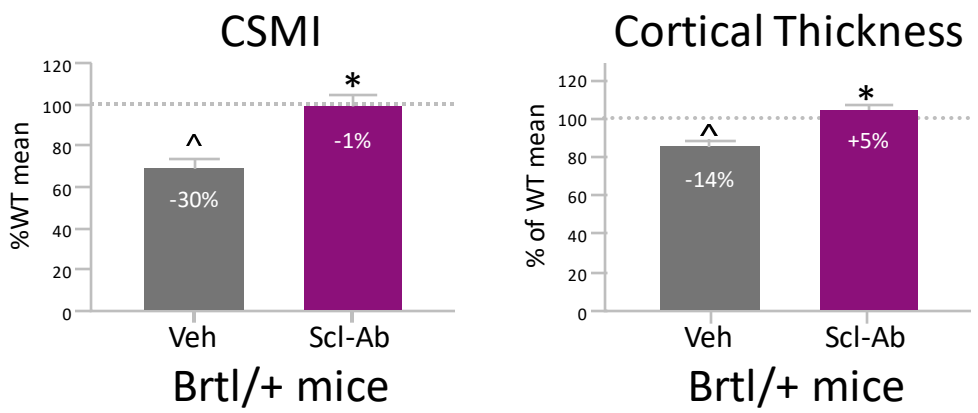
Stephan ASBMR 2021; Mean ± SE, n=19-22/gp
^p<0.05 vs WT+Veh; *p<0.05 vs Brtl + Veh

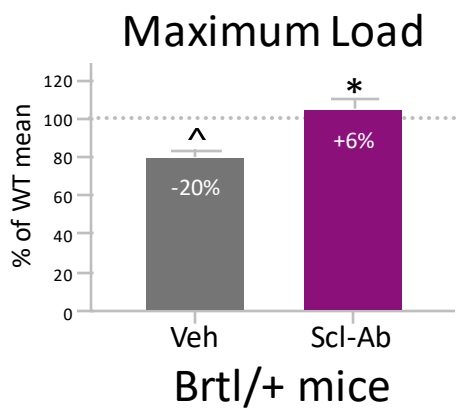
UX143 makes stronger bone than bisphosphonates
5wk UX143 vs 12wk Alendronate in Brittle Mouse OI Model

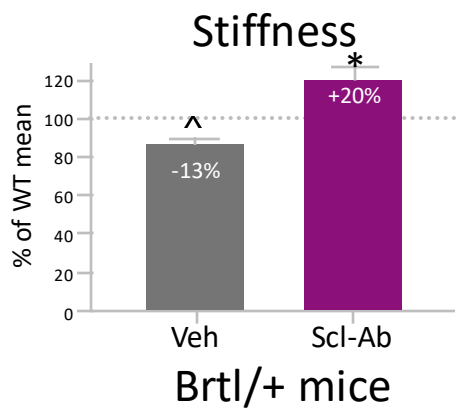
BONE MASS INDICES

BONE STRENGTH INDICES

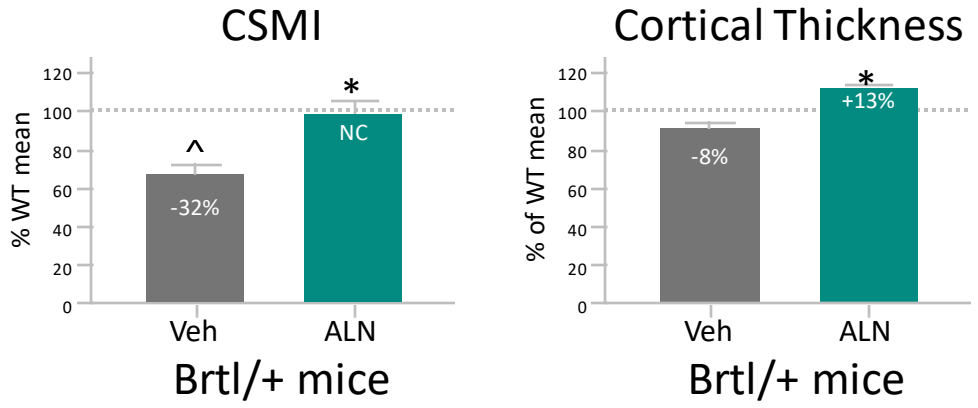
UX143

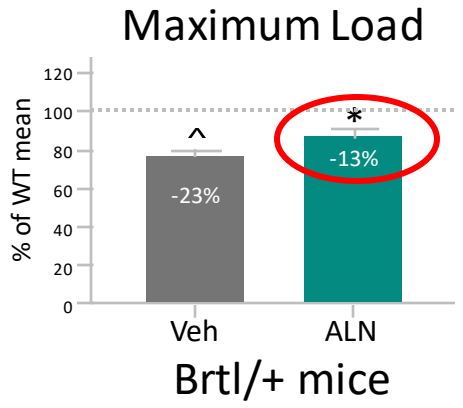


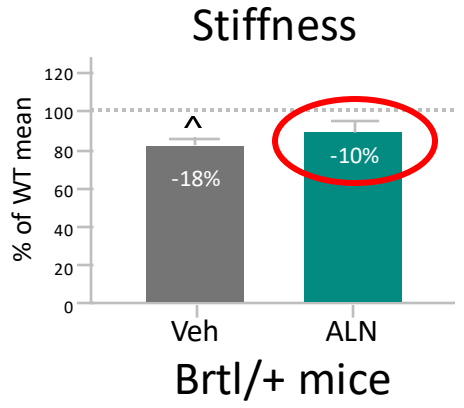




ALENDRONATE







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Phase 2b adult ASTEROID study: UX143 well tolerated
BMD and bone strength dose-dependently improved

Mean % Δ from BL at 12 mos	UX143 20 mg/kg	UX143 8 mg/kg	UX143 2 mg/kg
Lumbar spine aBMD	8.97 (p<0.001)	6.65 (p<0.001)	2.35 (p<0.05)
Total hip aBMD	2.48 (p<0.01)	2.69 (p<0.01)	1.99 (p<0.05)
Radius Total vBMD	1.88 (p<0.01)	0.86	0.04
Radius FE Failure Load	3.17 (p<0.01)	2.33	0.57

BMD increases consistent across site and OI type

Peripheral bone strength indices improved

Data will be available in children with OI as clinical trials progress

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UX143 program next steps

Phase 2/3 *Orbit* study in patients ages 5-25 initiated April 2022

- Phase 2: identify dose strategy based on increases in collagen production using serum P1NP levels
- Phase 3 transition: expected to initiate in mid-2023; evaluate fractures over 15-24 months

Additional randomized bisphosphonate-controlled study in patients <5 years old expected to initiate H1 2023:

- Much higher fracture rate enhances potential for benefit

Osteogenesis imperfecta treatment leverages our successful experiences in XLH and other bone diseases

GTX-102 Program
for Angelman Syndrome (AS)

Neurogenetic disorder caused by loss of expression of *UBE3A* gene

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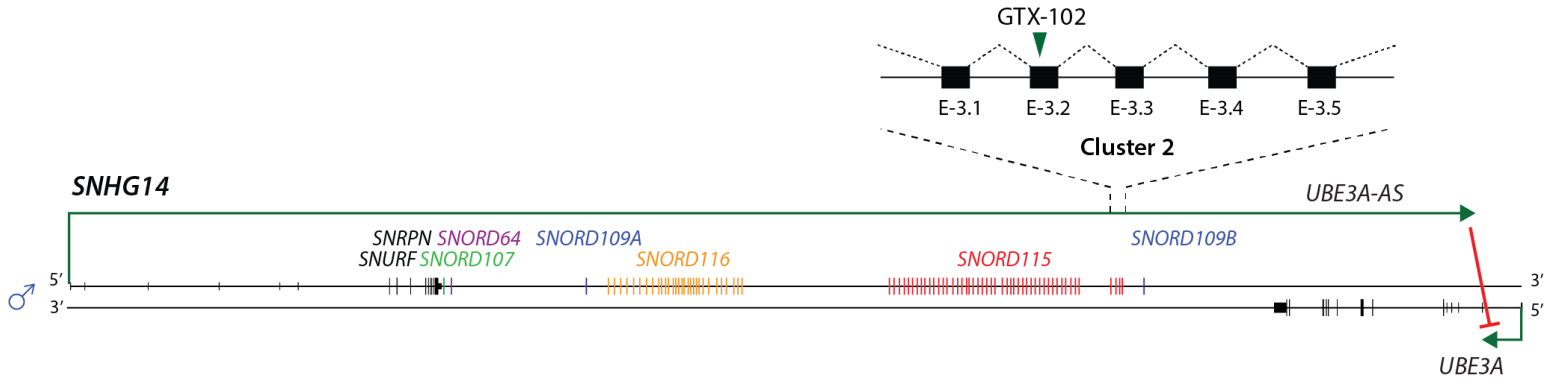
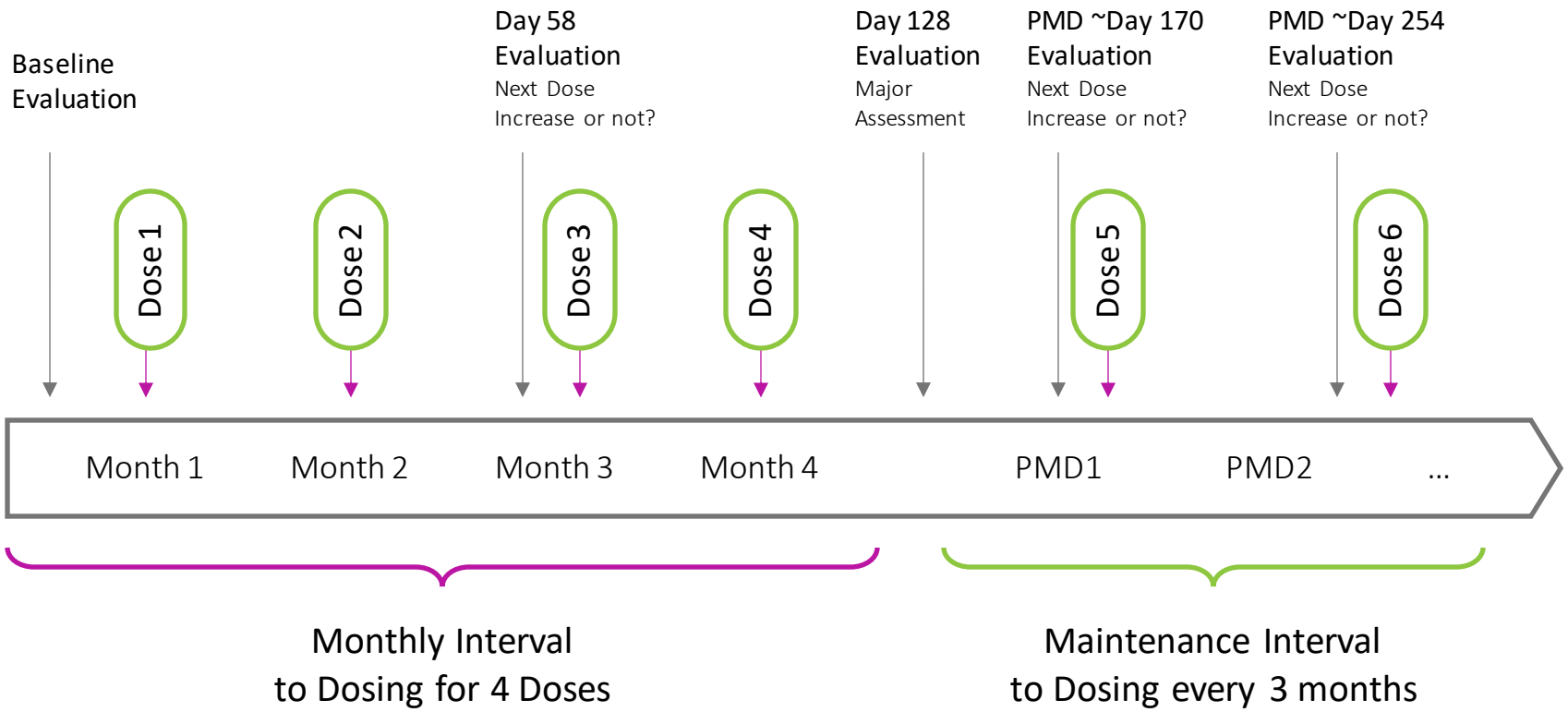
GTX-102 for Angelman syndrome (AS)
Antisense oligonucleotide (ASO) activates UBE3A

- **Devastating neurodevelopmental disorder**
- **WW prevalence:** ~60,000
- **No approved treatments**
- **Currently in Phase 1/2:** dose titration and expansion
- **Provided promising interim data** in July 2022 with acquisition of GeneTx
- **Targeting highly conserved region** across multiple species



Study dosing schematic for GTX-102 in U.K. and Canada



- July 2022 interim update included data from nine patients
  - Six in Cohort 4 (< 8 years old); Three in Cohort 5 (≥ 8 years old)
  - Some improvements over multiple domains across multiple measures
- Additional patients enrolled into Cohorts 6 and 7 at higher starting dose

Increases in receptive and expressive communication
Exceeds threshold to be significant

	Bayley-4 GSV[1] Latest Assessment Change from Baseline[2]	
	Receptive Communication	Expressive Communication
Cohort 4	**6***	3
	7*	4
	3	4
	4	0
	12*	2
	2	**8***
Cohort 5	**8***	5
	21*	**12***
	25*	**-7***

* Statistically significant values: Improvement in green ■ Impairment in red ■

Bayley-4 is an established measure

- Administered by psychologist
- A score of +/-6 or greater is statistically larger than variation observed
- Current Canada/UK patients have a higher frequency of significant changes

In Natural History studies[3] scores on these measures do not meaningfully change

1 Bayley-4 Growth Scale Values. Threshold for statistically significant difference ($p < .05$): RC and EC = 6
2 Interim data previously presented by the company on July 18, 2022 [link]
3 Keute, M et al, *Mol Psych*, 2020 https://doi.org/10.1038/s41380-020-0858-6

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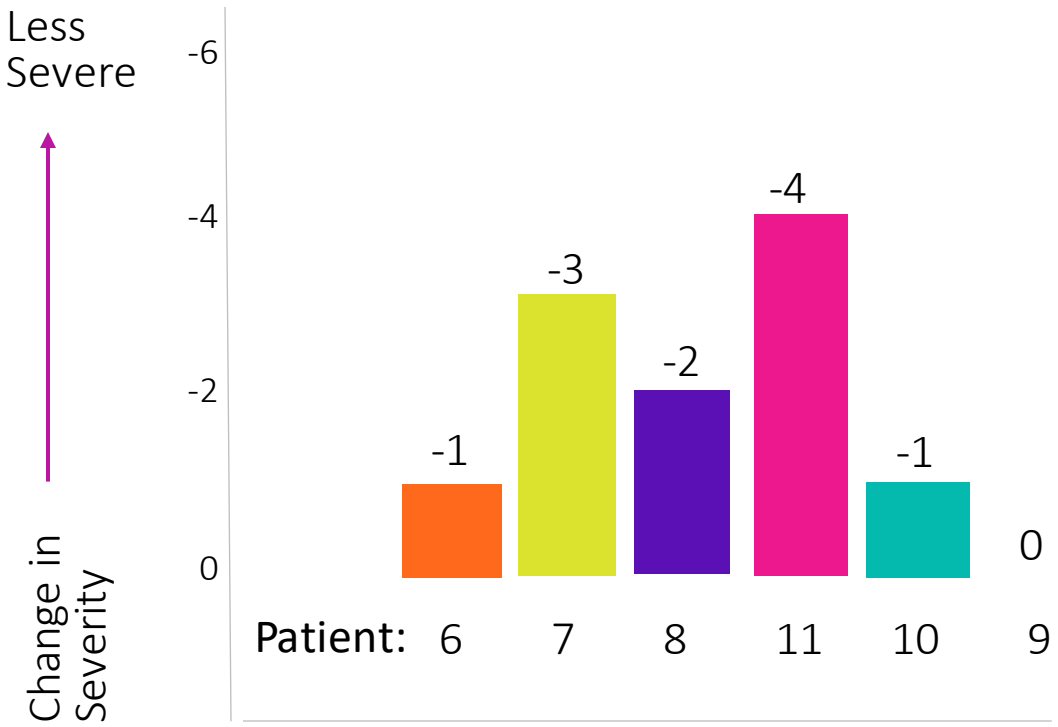
Substantial, clinically meaningful changes in sleep domain[1]

Cohort 4 : AS Sleep Change in Severity



Comments from Caregivers on Sleep

Patient 7 (cohort 4):
Her sleep has improved which is humongous, and very helpful for me and our whole family.

Patient 11 (cohort 4):
Before [the trial], she would wake up like three, four times in the night. Now, she doesn't wake up at all, and she'll sleep for a good 12 hours.

Patient 13 (cohort 5)
(-2 improvement in AS Sleep score): I can say that since mid-trial, I think she's sleeping much more soundly.

1 Interim data previously presented by the company on July 18, 2022 [link]

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GTX-102 safety profile under amended protocol

23 patients dosed: loading doses range from 2 mg to 10 mg, maintenance up to 14 mg
- Ten patients with 6 to 12 months exposure and five with >12 months

Common AEs: COVID-19 infection, vomiting, upper respiratory infection

One AE of special interest (AESI) in 17 year-old with severe scoliosis - decreased ambulation after 4th loading dose (12 mg)
- At baseline: limited walking and dependent on wheelchair
- Moderately elevated CSF protein at level much lower than seen in original 5 pts
- Improved, almost back to baseline within a couple of weeks

No additional cases of lower extremity weakness

Continuing to enroll and dose patients in U.K. and Canada

Encouraging signs of clinical activity
Successfully redosing three of original five U.S. patients

- Clinical responses at lower loading doses (Cohorts 4-7)
- Continuing dose exploration with higher loading doses
- Patients showing clinical activity and further improvements during maintenance dosing of 10-14 mg

Original U.S. cohort of five patients

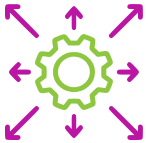
- Two patients re-dosed in Canada
  - Patients doing well, no signs of lower extremity weakness
- One patient re-dosed under Early Access Protocol in U.S.
  - Received two doses of 3.3 mg and doing well
  - Now sleeping through the night
  - FDA allowed dosing up to 7.5 mg for this patient

> For the first time in their life, Patient was able to sleep through the night, feed themself, play with their sister... problem solve, follow directions, learn new skills, and demonstrate that they know so much more than AS ever allowed them to show us. All of that is gone now. They have lost every single skill they gained in the short amount of time they were on GTX-102.
>
> -Letter excerpt from family requesting Early Access for re-dosing with GTX-102

GTX-102 program next steps

In discussions with FDA to harmonize U.S. study with U.K. / Canada

Enrolling Phase 1/2 expansion cohorts



Phase 3 planning and endpoints

Next program update based on a larger number of patients in the program

Our gene therapy franchise

Leading clinical and manufacturing expertise

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Large advanced gene therapy portfolio in rare disease

Candidate	Description	Pre-Clinical	IND	Phase 1	Phase 2	Phase 3	Approved
UX111 (ABO-102)	AAV9 Gene Therapy	**Mucopolysaccharidosis Type IIIA (MPS IIIA)**					
DTX401	AAV8-G6Pase Gene Therapy	**Glycogen Storage Disease Type Ia (GSDIa)**					
DTX301	AAV8-OTC Gene Therapy	**Ornithine Transcarbamylase (OTC) Deficiency**					
UX701	AAV9-ATP7B Gene Therapy	**Wilson Disease (WD)**					
UX055	AAV9 Gene Therapy		CDKL5 deficiency disorder				
UX810	Microdystrophin Gene Therapy		Duchenne Muscular Dystrophy				

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Four pivotal gene therapy programs

DTX401 for GSDIa

- WW prevalence: 6,000
- Phase 3 fully enrolled
- Data anticipated by 1H24

UX111 for MPS IIIA

- WW prevalence: 3,000-5,000
- Phase 1/2/3 ongoing
- Meeting with FDA to discuss filing path 1H23

DTX301 for OTC

- WW prevalence: 10,000
- Phase 3 FPI in 1Q23

UX701 for Wilson disease

- WW prevalence: 50,000
- Open-label dose-finding stage
- Enrolling cohorts by mid-year & data by early 2024

Our gene therapy technology & manufacturing facility provide control over quality and COGS

Pinnacle PCL™ platform

- Efficient, reliable production of AAV
- Improved product quality and yield
- Lower cost and increased speed of production
- Potentially improved safety of AAV therapy at higher doses

Manufacturing facility in Bedford, MA

Foundation for value generation

Three parallel opportunities to meaningful value

			2023 milestones	Expected data generation
	Angelman Syndrome	~60,000 patients	• FPI for expansion cohorts	• Phase 1/2 data in 2023
	Osteogenesis Imperfecta	~60,000 patients	• Phase 3 transition • Initiate young pediatric study	• Phase 2 data mid-2023
	Wilson disease	~50,000 patients	• Stage 1 LPI	• Stage 1 safety and initial efficacy data in early 2024

We are leading the future of rare disease medicine

One of the most robust and diverse clinical pipelines in rare

Broad global commercial footprint and expertise

History of strong clinical and commercial execution

Inspired and urgent mission to transform as many lives as possible

Thank you

IR@ultragenyx.com