

Corporate Deck

December 2021

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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, 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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Ultragenyx, Ultragenyx Pharmaceutical, Ultragenyx Gene Therapy, Mepsevii, Dojolvi and our logo are our trademarks. Any other trademarks appearing in these slides are 2^{the property of their respective holders.} Building an Exceptional Rare Disease Company with Value Drivers Across Commercial, Clinical, and Platforms

Commercial Expansion

- Continued Crysvita growth
- Strong Dojolvi launch for LC-FAOD

Clinical Development Catalysts

- Initiate four pivotal studies (including three gene therapy)
- Data catalysts and study initiations

Gene Therapy Manufacturing

- PCL Platform: High quality, commercial scale
- Supports larger indications with reduced COGS



2017-2020: Completing Four Approvals and Launches Refilling the pipeline through efficient business development



Three Therapeutic Areas Approaching \$1 Billion of **Product Revenue in the Next Five Years**



Diverse Clinical Pipeline with Larger Indications to Drive Long-Term Growth



1: Ultragenyx has an option to acquire GTX-102 from GeneTx

Commercial Performance and Strong Capital Position Drive Future Growth

3Q21 Revenue (\$M)		
Crysvita in Ultragenyx Territories ¹	\$50.3	
Dojolvi	10.7	
Mepsevii	3.9	
Daiichi Sankyo	12.0	
Crysvita royalty in EU territory	4.7	
Total Revenue	\$81.6	

Strong Capital Position: Strategic Investments and Financial Discipline

- Cash balance² as of 3Q21 approximately \$941.4 million
 - Modest YoY OpEx growth in 2021 to support advancing clinical pipeline and commercial launches, excluding the \$50M upfront payment to Mereo in 1Q21

1: Crysvita in Ultragenyx Territories, which excludes royalty in the European territory 2: Cash, cash equivalents, and marketable debt securities as of September 30, 2021



2021 Clinical Milestones Initiating Four Pivotal Clinical Studies

GENE THERAPY			1H21	2H21
DTX401	GSDIa	Longer-Term Phase 1/2 Data	 Image: A second s	
AAV8 Gene Therapy		Phase 3 Initiation		
DTX301 AAV8 Gene Therapy	отс	Longer-Term Phase 1/2 Data	 Image: A second s	
		Phase 3 Initiation		
UX701	Wilson Disease	IND Cleared	 Image: A second s	
AAV9 Gene Therapy		Phase 1/2/3 Initiation		 Image: A second s
ASO/mRNA			1H21	2H21
GTX-102 ASO	Angelman Syndrome	Resume Phase 1/2 Study		✓
		Updated Phase 1/2 Data		
UX053 GSDIII:	GSDIII:	IND Cleared	 Image: A second s	
mRNA/LNP Debrancher Deficienc		Phase 1/2 Initiation		 Image: A second s
			1H21	2H21
Setrusumab (UX143) Monoclonal Antibody	Osteogenesis Imperfecta	Phase 2/3 Initiation		
				ultra



Setrusumab (UX143) for Osteogenesis Imperfecta

Phase 2/3 monoclonal antibody in large genetic bone disease

Setrusumab for Osteogenesis Imperfecta (OI) Large genetic bone disorder with positive Phase 2b adult data

- OI: Reduced or abnormal collagen causes increased bone breakdown and decreased bone mass and strength
- Setrusumab: Fully human anti-sclerostin antibody that increases bone formation and density
- **Key symptoms:** Bone fragility, fractures, deformities, stiffness, pain, short stature, loss of mobility
- No approved treatments; bisphosphonates antiresorptive treatments are standard of care off-label
- WW prevalence: ~60,000 (targeting types I/III/IV)
- Partnership: Ultragenyx leads development and has commercial rights ex-EU (receives royalty in EU)
- Development: Phase 2b completed in adult OI; pivotal study in pediatric and young adult patients planned





Setrusumab: Phase 2b Data in Adults with OI

- Open-label study (n=90) with 3 escalating dose cohorts, dosed monthly for 12 months
 - Studied types I, III, and IV (~90% of prevalent population)
- Bone mineral density increases observed across multiple measures
 - Dose dependent and across anatomical sites
- P1NP biomarker of collagen formation and bone production improvements
 - Seen consistently across disease sub-types
- Bone strength and stiffness potential benefits
 - Improvements in wrist bone failure load and trend to improvement in ankle bone failure load at highest dose
- Setrusumab well-tolerated
 - No cardiac-related safety issues



Setrusumab: Next Steps

Planning Phase 2/3 study in patients with OI

- Phase 2 portion: determine optimal dose based on increases in collagen production using serum P1NP levels
- Phase 3 portion: evaluate fractures over 15-24 months
- Aim to initiate study around the end of 2021, pending regulatory feedback

Development program to be led by development organization that achieved rapid approval for Crysvita in XLH and TIO





GTX-102 Program for Angelman Syndrome

Positive interim Phase 1/2 efficacy data from ASO program in Angelman syndrome

GTX-102 for Angelman Syndrome Large neurodevelopmental disorder

- Angelman syndrome: Neurogenetic disorder caused by loss of expression of UBE3A gene
- GTX-102: Antisense oligonucleotide (ASO) that targets regulatory RNA to activate paternal UBE3A expression
- Key symptoms/prognosis: Motor dysfunction, lack of speech, cognitive impairment, sleep disorder
- No approved treatments
- WW prevalence: ~60,000
- Partnership: Ultragenyx has option to acquire collaborator GeneTx after Phase 1/2 completion
- Phase 1/2 study design: Intrathecal intra-patient dose escalating, open-label study in deletion patients (most common genotype and most severe phenotype)





GTX-102 Efficacy and Safety Summary

- Five patients treated with GTX-102 in open label, intra-patient dose escalation safety and efficacy Phase 1/2 study
- All five patients showed substantial improvements in multiple domains
- All five patients had a grade 1 or 2 serious adverse event of lower extremity weakness
 - SAE has fully resolved in all patients



CGI-I-AS* Ratings of Change by Patient at Day 128 Mean global score of +2.4 across patients (scale of -3 to +3)



*CGI-I-AS: Clinical Global Impression of Improvement-Angelman Syndrome; domains are fine motor, gross motor, communication, behavior sleep

(1) Patients 2, 3, and 4 had gross motor impairment at time of assessment due to ongoing SAE



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Summary of US and ex-US Protocols Initial clinical data expected YE 2021

	US ¹	Canada / UK	
	Active Group	Cohort 4	Cohort 5
Age	4 to 7 y/o	4 to 7 y/o	8 to 17 y/o
Number of Patients	4	6	6
Monthly Loading Dose	2 0 mg	3.3 mg	5.0 mg
(up to 4 doses)	2.0 mg	Can escalate following 2 doses	
Dose Escalation Criteria	n/a	Individually titrated until at least 2 CGI-I-AS domains of much improved or very much improved	
Maximum Dose	2.0 mg	14.0 mg	
Maintenance Dose Frequency	Every 3 months	Every 3 months	
Administration Modifications	n/a	Trendelenburg and 10 mL artificial CSF flush	

1: The US site will enroll 4, age matched patients into a comparator group and will have limited assessments at Baseline and Day 128. These patients would then be eligible to receive GTX-102 under the same dosing strategy as the active group.



Gene Therapy Program, Platform and Partnerships

Gene Therapy Overview



Ultragenyx PCL Manufacturing Platform



Version 2.0

Higher fill ratio, 10x yield, better speed via refined high throughput screening

UX701 for Wilson



Further improved yield, speed, and lower COGS

Version 3.0

UX810 for Duchenne

Expected to open in 2023

Large Scale Plant Under Construction



DTX401: AAV8 for Glycogen Storage Disease Type Ia

- GSDIa: Defect in liver's ability to release glucose to the circulation due to G6Pase deficiency
- Key symptoms/prognosis
 - Severe life-threatening hypoglycemia
 - Significant morbidity and mortality
 - Long-term liver and renal disease
 - Impaired growth and delayed puberty
 - Severe long-term complications (70-80% patients)
- **Treatment:** Diet and cornstarch only
 - Keeps patients alive but not normal
 - Only curative approach is liver transplantation
- WW prevalence: 6,000

Patient 3 Cornstarch when Travelling



"I don't think people can understand how fast the blood sugars fall. And the stress that these families have, knowing that if you oversleep or you miss your alarm clock, your child can die or have a seizure." -David Weinstein, former Director-Glycogen Storage Disease Program, Connecticut Children's Medical Center



All Patients Reduced Cornstarch Therapy While Maintaining or Improving Time in Euglycemia



Cohorts 3/4: Cornstarch reduced 64-73%, while time in euglycemia increased or remained essentially flat

DTX401: Regulatory Status and Phase 3 Design

Regulatory Status

- EOP2 and Scientific Advice meetings held with both FDA and EMA, respectively
- Expect to initiate around the end of 2021

Planned Phase 3 Study Design

- 50 patients, randomized 1:1 DTX401 (1.0 x 10¹³ GC/kg) to placebo
 - Patients on placebo will cross over to gene therapy arm
- 48-week duration
 - Longer-term Phase 1/2 data to be included in submission to support durability
- Primary endpoint: reduction in oral glucose replacement therapy (cornstarch) while maintaining or improving glucose control by CGM



DTX301: AAV8 for OTC Deficiency AAV8 gene therapy for stable expression of OTC

- OTC Deficiency: X-linked urea cycle disorder, genetic defect in ammonia detoxification
- Key symptoms/prognosis:
 - Acute hyperammonemic episodes
 - Adverse cognitive & neurological effects
 - Hospitalizations
 - Death
- Treatment limited: Liver transplantation only curative, ammonia scavengers, protein restricted diet
- WW prevalence: ~10,000, 80% late-onset



S. Harris, et al., Obstetrics and Gynecology Clinics of North America (2018)



Durable Metabolic Control and Sustained Responses Lasting More than 3 Years Post-Treatment

Overall Response

- 6 of 9 patients in reactive steroid cohorts of Phase 1/2 responded to DTX301
 - Includes all 3 patients in highest dose cohort
- First of 2 patients in prophylactic steroid cohort of Phase 1/2 is a responder
 - Second patient is in the process of modifying ammonia-scavenging drugs and diet
- 3 complete responders who have discontinued alternative medications and protein-restricted diets without ammonia issues
 - 3 other responders with stable ammonia; all started tapering medications and 2 liberalizing diets

Prophylactic Steroid Cohort Update

- Both patents dosed and doing well
 - First patient has demonstrated a response
 - Second patient responder status will be evaluated after patient finishes steroid regimen



DTX301: Regulatory Status and Phase 3 Design

Regulatory Status

- EOP2 and Scientific Advice meetings held with FDA and EMA, respectively
- Expect to Expect to initiate around the end of 2021

Phase 3 Study Design

- 50 patients, randomized 1:1 DTX301 (1.7 x 10¹³ GC/kg) to placebo
 - Patients on placebo will cross over to gene therapy arm
- 64-week duration
 - Longer-term Phase 1/2 data to be included in submission to support durability
- Co-primary endpoints
 - Change in 24-hour plasma ammonia levels
 - Percent of patients who achieve a response as measured by discontinuation or reduction in baseline disease management



UX701: AAV9 for Wilson Disease Second clinical program to utilize PCL manufacturing system

- Wilson Disease: Causes copper to accumulate in liver, brain and other vital organs
- Key symptoms/prognosis: Liver failure, neurological deterioration, death
- Standard of Care: Chelation therapy and dietary restriction
 - Many patients still experience liver and neurological deterioration
- WW prevalence: >50,000
- Status: Seamless single-protocol Ph1/2/3 initiated with patients in baseline monitoring period





Untreated KO Mice

1x10¹¹ GC Treated Mice

Reduced liver copper accumulation leading to improved liver pathology in preclinical models



Positive, Clinically Effective Hem A Data from the PCL Platform Out-licensed program to Bayer validates Ultragenyx PCL manufacturing system



- Positive data from first three dose cohorts
- Data from nine patients, five at third dose level
- Clinically meaningful Factor VIII levels in five of six patients
 - Sustained FVIII levels up to >23 months with no evidence of loss of expression
 - No spontaneous bleeds were reported after achieving protective FVIII levels (>11 IU/dL)
- Favorable safety results
 - ALT/AST elevations observed in one patient in Cohort 2 and three of five patients in Cohort 3, managed with tapering course of corticosteroids
 - One SAE related to corticosteroids managed with H2receptor antagonists
- Following DMC review, escalation to dose cohort 4 (4e13 GC/kg) is planned

Factor VIII Expression Levels

(Chromogenic assay; % normal)





Building a Commercial Rare Disease Company with Accelerating Growth







Appendix

Key Licenses & Intellectual Property

Product	License	US Intellectual Property Rights/Royalties		
CRYSVITA® (XLH, TIO)	Kyowa Kirin Co. (KKC)	 Anti-FGF23 antibodies and use for treatment of XLH and TIO (2022-2032)¹ Q2W dosing for treatment of FGF23-associated hypophosphatemic disorders (2035) See discussion of KKC license and collaboration in annual report for royalty summary 		
MEPSEVII® (MPS 7)	St. Louis University (Know-How)	 Low single-digit royalty until expiration of orphan drug exclusivity 		
	N/A (IP Owned by Ultragenyx)	 Recombinant human GUS (rhGUS) and use for treatment of MPS7 (2035) 		
DOJOLVI® (LC-FAOD)	Baylor Research Institute (BRI)	 Compositions comprising triheptanoin (2025-2029)¹ Mid single-digit royalty 		
DTX301 (OTC Deficiency)	Sub-License from REGENXBIO of UPENN IP	 AAV8 Capsid (2022-2024) Recombinant vectors comprising codon-optimized OTC gene (2035) Low to mid single-digit royalty 		
DTX401 (GSDIa)	Sub-License from REGENXBIO of UPENN IP	 AAV8 Capsid (2022-2024) Low to mid single-digit royalty 		
	NIH (Non-Exclusive)	 Recombinant vectors comprising codon-optimized G6Pase gene (2034) Low single-digit royalty 		
UX143 (Osteogenesis Imperfecta)	Mereo Biopharma	 Setrusumab antibody (2028) Use of anti-sclerostin antibodies including setrusumab for treatment of OI (Pending; 2037) Tiered double-digit royalty on ex-EU sales 		
DTX201 (Hemophilia A)	Sub-License from REGENXBIO of UPENN IP	 Hu37 Capsid (2024) Recombinant vectors comprising codon-optimized Factor VIII gene (2037) Low to mid single-digit royalty 		
GTX-102 (Angelman Syndrome)	Option to Acquire GeneTx (Exclusive Licensee of TAMU's GTX-102 IP)	 UBE3A-ATS antisense oligonucleotides including GTX-102 and their use in treatment of AS (Pending; 2038) Development and commercial milestones plus royalties 		



1: Includes projected U.S. patent term extension

Revenue to Ultragenyx Maintained After Transition from Profit Share to Royalty in U.S.					
U.S. Prevalence: 12,000	TO AS	Profit Share through 2023	Royalty mid to high 20% from H Ultragenyx R ar 5 Yes	KKC Revenue ar 10+	
	U.S. AND CANADA			EUROPE	
Commercialization	 KKC books sales 50/50 profit share for 5 years then tiered revenue share Shared commercial activities over time 		Ultragenyx commercializes and books sales	KKC commercializes and books sales	
Royalties	After 5 years, tiered revenue share in mid to high 20% range to Ultragenyx after profit share period		Low single-digit royalty to KKC	Up to 10% non-cash revenue ¹ to Ultragenyx after Royalty Pharma transaction	
Commercial supply	KKC supplies: 35% of net sales through 2022, 30% thereafter		KKC supplies: 35% of net sales through 2022, 30% thereafter	NA	

1: Beginning January 1, 2020, the company no longer receives cash payments from the EU territory royalty until the respective threshold amount is met pursuant to the Royalty Pharma transaction. The company remains, however, contractually entitled to the royalties from KKC and will continue recognizing the Crysvita EU territory royalties in total revenues as "non-cash revenue" since the associated cash proceeds will be remitted to Royalty Pharma.



CRYSVITA[®] Exclusivity Summary







MEPSEVII[®] Exclusivity Summary

Mepsevii[™] (vestronidase alfa-vjbk) injection, for intravenous use





DOJOLVI[®] Exclusivity Summary

DOJOLVI[®] TRIHEPTANOIN



