Corporate Deck

May 2022

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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.

Any forward-looking statements made by us in this presentation speak only as of the date of this presentation and represent our estimates and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation, and we disclaim any intent, to update these statements to reflect actual results.

This presentation concerns commercial products as well as discussion of investigational drugs that are under preclinical and/or clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). They are currently limited by Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated.

Building an Exceptional Rare Disease Company with Value Drivers Across Commercial, Clinical, and Platforms

Global Commercial Growth

- Continued Crysvita growth and strong Dojolvi launch
- Licensed ex-US rights from Regeneron for Evkeeza (evinacumab) in HoFH

Robust Development Pipeline

- 7 clinical programs, 5 in pivotal studies across modalities and therapeutic areas
- 2 programs with clinical data in 2022

Advanced Technology Platforms

- Gene Therapy: AAV platform with high-quality, commercial-scale manufacturing
- mRNA: Emerging platform with first program now in clinical development

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Evolution of Commercial and Clinical Portfolio

Expanding through efficient business development

Pipeline Approvals

Mepsevii™ (vestronidase alfa-vjbk) injection — MPS VII

CRYSVITA® burosumab — XLH

CRYSVITA® burosumab — TIO

DOJOLVI® TRIHEPTANOIN Oral Liquid — LC-FAOD

2017 | 2018 | 2019 | 2020 | 2021 | 2022+

Pipeline Build

Gene Therapy

- DIMENSION THERAPEUTICS → OTC AAV8 DTX301 → GSDIa AAV8 DTX401
- Wilson AAV UX701
- CDKL5 AAV UX055
- SOLID BIOSCIENCES → Duchenne UX810
- Abeona THERAPEUTICS → MPS IIIA UX111

Nucleic Acid

- ARCTURUS therapeutics → GSDIII mRNA/LNP UX053
- genetx → Angelman-ASO GTX102

MAb

- Mereo BioPharma → OI UX143
- REGENERON → HoFH Evkeeza

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Building Franchises Across Three Rare Disease Therapeutic Areas

DEVELOPMENT

COMMERCIAL

BONE ENDOCRINE

Ph 2/3

Setrusumab
for OI

CRYSVITA® burosumab

XLH

CRYSVITA® burosumab

TIO

METABOLICS

Ph 1/2

UX053
for GSDIII

Ph 1/2/3

UX701
for Wilson

Ph 3

DTX401
for GSDIa

Ph 3

DTX301
for OTC

Mepsevii™ (vestronidase alfa-vjbk) injection

MPS VII

DOJOLVI® TRIHEPTANOIN Oral Liquid

LC-FAOD

Evkeeza® (evinacumab-dgnb) Injection

HoFH

CNS / MUSCLE

Ph 1/2

GTX-102
for Angelman

Ph 3

UX111
for MPS IIIA

Preclinical
(Disclosed)

UX810
for Duchenne

UX055
for CDKL5

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

Candidate	Description	Pre-Clinical / IND / Phase 1 / Phase 2 / Phase 3 / Approved	Est'd Patients in Dev. World
KYOWA KIRIN / CRYSVITA® burosumab	Anti-FGF23 Monoclonal Antibody	X-Linked Hypophosphatemia (XLH) & Tumor-Induced Osteomalacia (TIO)	~50,000
Mepsevii® (vestronidase alfa-vjbk) injection	Enzyme Replacement	Mucopolysaccharidosis Type VII (MPS VII)	~200
REGENERON / Evkeeza® (evinacumab-dgnb) Injection	Anti-ANGPTL3 Monoclonal Antibody[1]	Homozygous Familial Hypercholesterolemia (HoFH)	~3,000 - 5,000[2]
Mereo BioPharma UX143 (setrusumab)	Anti-Sclerostin Monoclonal Antibody	Osteogenesis Imperfecta (OI)	~60,000
DOJOLVI® TRIHEPTANOIN Oral Liquid	Substrate Replacement	Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD)	~8,000 - 14,000
UX111 (ABO-102)	AAV9 Gene Therapy	Mucopolysaccharidosis Type IIIA (MPS IIIA)	~3,000 - 5,000
DTX401	AAV8-G6Pase Gene Therapy	Glycogen Storage Disease Type Ia (GSDIa)	~6,000
DTX301	AAV8-OTC Gene Therapy	Ornithine Transcarbamylase (OTC) Deficiency	~10,000
BAYER DTX201	AAVhu37-FVIII Gene Therapy[3]	Hemophilia A	~144,000
UX701	AAV9-ATP7B Gene Therapy	Wilson Disease (WD)	~50,000
UX810	Microdystrophin Gene Therapy	Duchenne Muscular Dystrophy	~40,000
genetX GTX-102[4]	Antisense Oligonucleotide	Angelman Syndrome (AS)	~60,000
UX053	mRNA/LNP	Glycogen Storage Disease Type III (GSDIII)	~10,000

Protein Biologic | Small Molecule | Gene Therapy | ASO / mRNA

1: Ultragenyx licensed ex-US rights to Evkeeza from Regeneron
2: Excludes the US, where Regeneron has rights
3: In collaboration with Bayer
4: Ultragenyx has an option to acquire GTX-102 from GeneTx

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First Quarter 2022 Financials

1Q22 Select Product Revenue	
Crysvita in Ultragenyx Territories[1]	$54.6M
Dojolvi Global	$12.4M

2022 Product Revenue Guidance	
Crysvita in Ultragenyx Territories[1]	$250M to $260M
Dojolvi Global	$55M to $65M

Strong Capital Position

- Cash balance[2] as of March 31, 2022: ~$814 million
- Strong capital position to execute on 2022 priorities
- Net cash use in 2022 driven by 4 late-stage clinical studies and construction of gene therapy manufacturing plant

1: Crysvita in Ultragenyx Territories, which excludes royalty revenue in EU
2: Cash, cash equivalents, and available-for-sale investments as of March 31, 2022

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2022 Clinical Milestones

Data from 2 programs and execution across 5 pivotal studies

ASO/mRNA			1H22	2H22
GTX-102 ASO	**Angelman Syndrome**	Phase 1/2 Data in 12 Ex-US Patients	☐ *Mid-2022*	
UX053 mRNA/LNP	**GSDIII: Debrancher Deficiency**	Phase 1/2 Single-Dose Stage Preliminary Data		☐
		Phase 1/2 Repeat-Dose Stage Initiation		☐

PROTEIN BIOLOGIC			1H22	2H22
UX143 (setrusumab) Monoclonal Antibody	**Osteogenesis Imperfecta**	Phase 2/3 Pivotal Study Initiation (Age 5-25)	✓	
		Phase 2/3 Dosing Update & Phase 3 Transition		☐
		Study Initiation (Age <5)		☐

GENE THERAPY			1H22	2H22
UX111 AAV9 Gene Therapy	MPS IIIA	Pivotal Transpher A Regulatory Update		☐ *Around Year End*
DTX401 AAV8 Gene Therapy	GSDIa	Phase 3 Enrolling	*Throughout 2022*	
DTX301 AAV8 Gene Therapy	OTC	Phase 3 Enrolling	*Throughout 2022*	
UX701 AAV9 Gene Therapy	Wilson Disease	Phase 1/2/3 Enrolling	*Throughout 2022*	

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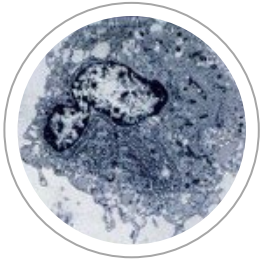
UX111 (ABO-102) for
Sanfilippo Syndrome Type A (MPS IIIA)

Encore pivotal data from Transpher A pivotal study presented at ASGCT 2022

Sanfilippo Syndrome Type A (MPS IIIA)

Lysosomal Storage Disease Leading to Early Neurocognitive Decline & Death

- **MPS IIIA:** Inherited monogenic disease, causing abnormal accumulation of heparan sulfate (HS)
- **Key symptoms/prognosis**
  - Progressive language and cognitive decline
  - Behavioral abnormalities
  - Seizures, sleep disturbances
  - Rapid cognitive decline by age 3; 70% do not reach age 18
- **No current therapies**
  - UX111 uses self-complementary AAV9 expressing a functional copy of SGSH under the control of the murine U1 promoter
- **WW prevalence:** ~3,000 - 5,000
- **Ultragenyx assumes full responsibility for UX111; Abeona to receive tiered royalties up to 10% on net sales and commercial milestones**



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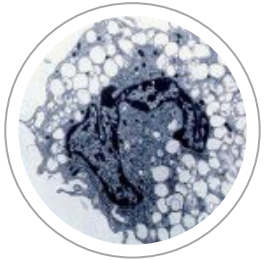

Cell with lysosome deficiency showing vacuolization

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Transpher A Pivotal Study for MPS IIIA

transpher B study

Study Description	▪ Single-dose ABO-102 for MPS IIIA ▪ Open-label, dose-escalation trial ▪ Comparator group: Natural history studies ▪ 9 follow up visits within 24 months after gene transfer
Intravenous Dosing	▪ Cohort 1: 5 x 10^{12} vg/kg (n=3) ▪ Cohort 2: 1 x 10^{13} vg/kg (n=3) ▪ Cohort 3: 3 x 10^{13} vg/kg (n=18)*
Primary Endpoints	▪ Age-equivalent developmental score (Mullen Scales of Early Learning or Kaufman Assessment Battery for Children) vs natural history study data ▪ Product safety
Secondary Endpoints	▪ Behavior evaluations, quality of life, Biomarkers (e.g., HS and GAG levels, enzyme activity), heparan sulfate levels, and brain and liver volume

* <2 years old or DQ ≥60, n=10

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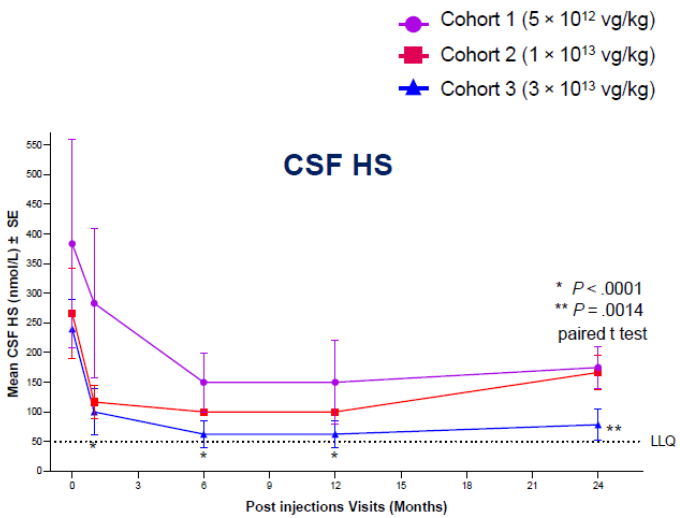
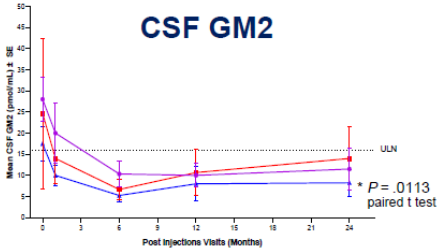
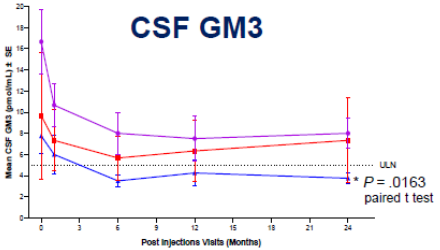
Preliminary Biomarker Results

Sustained and Statistically Significant Reduction in CNS and Systemic Biomarkers

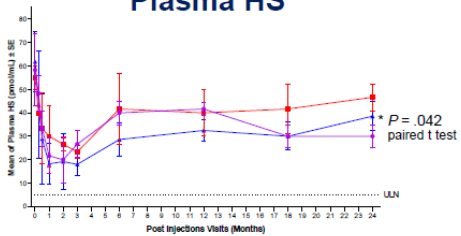


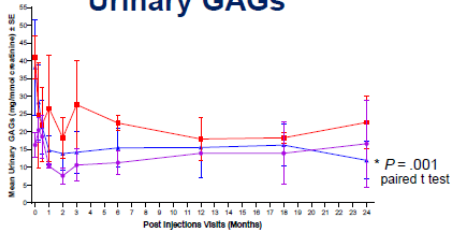
No. Patients	Screening	Month 1	Month 6	Month 12	Month 24
Cohort 1	3	3	3	2	2
Cohort 2	3	3	3	3	3
Cohort 3	15	14	12	8	7





No. Patients	Screening	Month 1	Month 6	Month 12	Month 24
Cohort 1	3	3	3	2	2
Cohort 2	3	3	3	3	3
Cohort 3	4	4	4	4	4



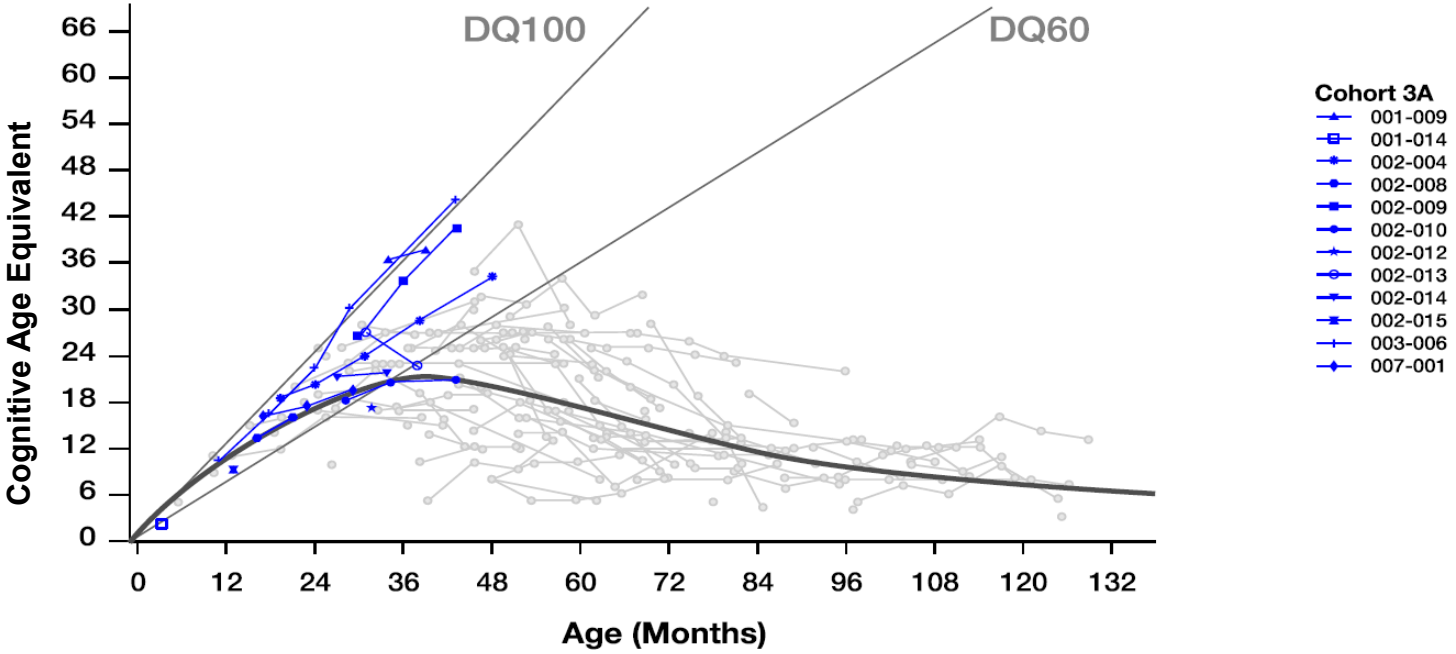


No. Patients	Screening	Day 7	Day 14	Day 30	Day 60	Day 90	Month 6	Month 12	Month 18	Month 24
Cohort 1	3	3	3	3	3	3	3	3	3	3
Cohort 2	3	3	3	3	3	3	3	3	3	3
Cohort 3	13	10	9	14	13	10	11	8	8	7

No. Patients	Screening	Day 7	Day 14	Day 30	Day 60	Day 90	Month 6	Month 12	Month 18	Month 24
Cohort 1	3	2	3	3	3	3	3	3	3	3
Cohort 2	3	3	3	3	3	3	2	3	3	3
Cohort 3	12	11	10	12	9	11	12	8	7	7

Mullen Cognitive Age-Equivalent Data

Patients treated at an early age track along normal development range



- **Black solid line and gray data points:** Typical developmental pattern for children with MPS IIIA per natural history data
- **DQ60 and DQ100 lines:** Expected development for children without disease. Development Quotient (DQ): ratio between age equivalent and actual age (chronological)
- **Cognitive age equivalent:** Functional age of the child, calculated by comparison with the age at which a child in the normal population develops similar skills

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Summary of Transpher A Results

Pivotal study data with ABO-102

- Based on MSEL and VABS-II assessments: patients treated at an early age track along normal development range and showed continuous improvements by 30-36 months post-administration
- In the 10 patients in Cohort 3, some have reached 24 months post-treatment; stabilization or increase in cortical gray matter, total cerebral, and amygdala volumes
- Statistically significant reduction in liver volume

Sustained, and statistically significant reductions in biomarkers 2 years post-administration

- CSF levels of HS were significantly reduced in Cohort 3
- Statistically significant reduction in CSF GM2 and GM3 levels in patients treated in Cohort 3
- Statistically significant reductions of plasma HS and urinary GAGs in Cohort 3

ABO-102 was well tolerated

- Drug-related AEs have been grade 1 or 2 (mostly mild, grade 1) and all resolved within 2 months
- Subclinical ALT and AST elevations, low and transient AAV9-positive responses (8 patients), and mild thrombocytopenia (5 patients)

Evkeeza (evinacumab) for Homozygous Familial Hypercholesterolemia (HoFH)

Ex-US rights to monoclonal antibody approved in Europe

Evkeeza® (evinacumab-dgnb) Injection

Collaboration Adds Potent Approved Product with Novel MOA to our Ex-US Commercial Portfolio with Potential for Expansion

Potent Late-Stage Product	• Approved traditional biologic • First-in-class with novel mechanism of action • Significant clinical impact in challenging disease
Commercial Infrastructure	• Leverages strong LATAM/Canada capabilities • Scales and leverages EU before other launches • Accelerates company's APAC expansion
Strategic Partnership	• Establishes complementary collaboration • Potential for expansion: (1) other evinacumab indications; (2) exclusive option to negotiate for FOP product[1]

1: Fibrodysplasia Ossificans Progressiva (FOP) an ultra-rare genetic bone disease

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Evkeeza Commercial Collaboration Overview

REGENERON

- Discovered, developed, & obtained approval in US and EU for patients 12+ with HoFH
- Commercializing in US
- Manufactures product for global use
- Developing any additional genetic indications
  - Phase 2 in adults with severe hyper-triglyceridemia for the prevention of recurrent acute pancreatitis

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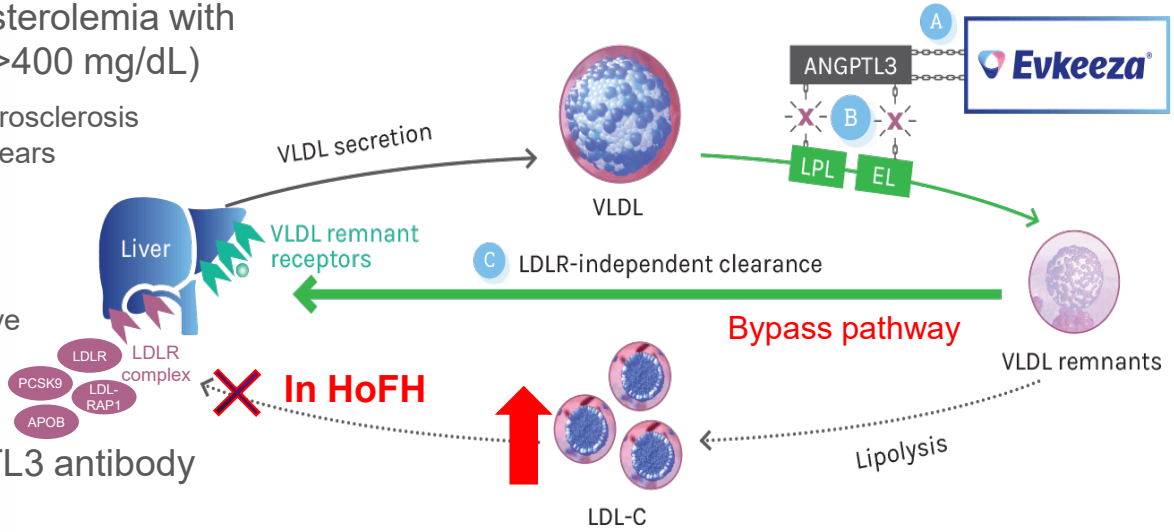
- Exclusive license to commercialize outside the US
- $30M upfront, $63M in milestones
  - Tiered payments percentage on cumulative net sales
- Plan to submit for reimbursement in 2022 and launch in Europe in 2023, where approved for HoFH
- Will seek regulatory approval in other countries/regions
- Manage regional post-marketing requirements

Homozygous Familial Hypercholesterolemia (HoFH)

Severe and typically refractory inherited high LDL-C

- **HoFH:** Form of familial hypercholesterolemia with dangerously high levels of LDL-C (>400 mg/dL)
  - **Key symptoms:** Risk for premature atherosclerosis and cardiac events as early as teenage years
  - **Current treatment:** Most have inadequate response or poorly tolerate other agents
    - Most other treatments largely ineffective in patients with virtually absent LDL receptor function (~20% of total)
- **Evkeeza:** Fully human anti-ANGPTL3 antibody that increases lipid metabolism
  - **Mechanism:** ANGPTL3 broad role in cholesterol regulation and atherosclerosis, as well as triglycerides, validated by Regeneron Genetics Center
    - Evkeeza mechanism does not rely on LDL receptor, enabling response in most severe HoFH patients (i.e., null-null LDLR)



A Evkeeza binds to and blocks ANGPTL3, an inhibitor of LPL and EL

B By blocking ANGPTL3, LPL and EL are active and convert VLDL into easily processed VLDL remnants that are rapidly cleared by VLDL remnant receptors in the liver instead of being converted to LDL-C particles

C By enhancing VLDL remnant clearance and reducing LDL-C precursors, Evkeeza reduces cholesterol levels in an LDLR-independent manner

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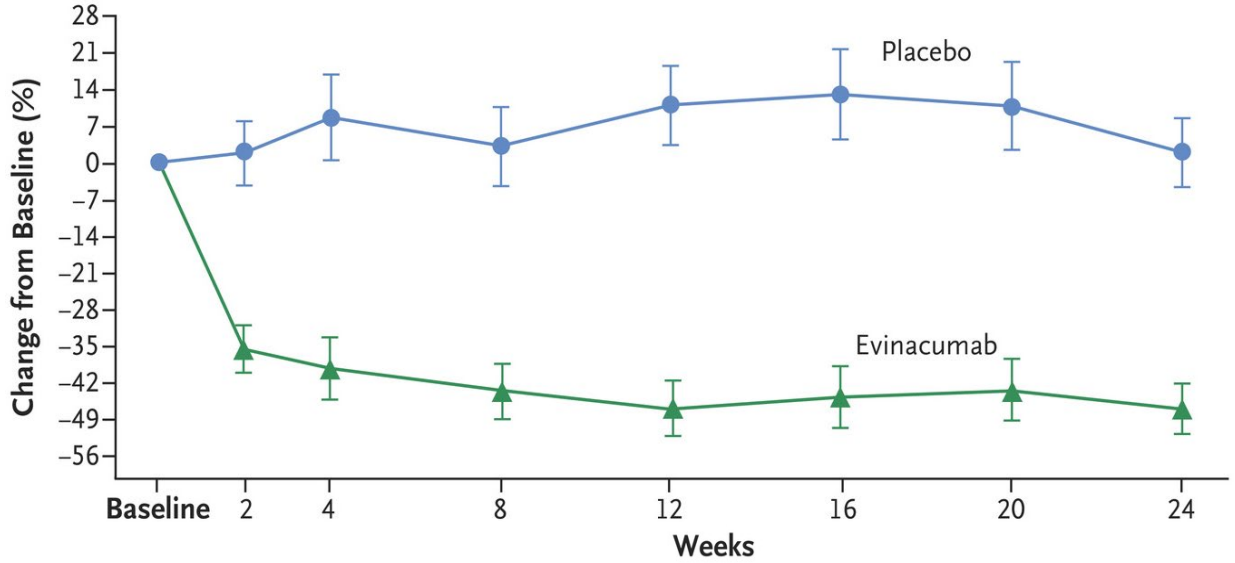
Evkeeza Approved for HoFH by EMA

Based on significant LDL reductions on top of existing therapies

Phase 3 Study

Double-blind, placebo-controlled (n=65; 2:1 drug:placebo)

- **LDL-C reduced 49% relative to placebo** in all patients
  - Reduction was on top of maximum current therapy (e.g. statins, PCSK9 inhibitors, ezetimibe, lomitapide, apheresis)
- **LDL-C reduced 72% relative to placebo in patients with <2% LDLR activity**
- **Triglycerides also reduced by 50%** across study participants



Raal *et al.* New England Journal of Medicine, August 2020

Evkeeza Well-Positioned in High Unmet Need HoFH

- **Prevalence** of 3,000 to 5,000 in Ultragenyx key target markets
  - Approximately 1,600 in EU
- **Competition** for HoFH with low LDLR activity
  - Juxtapid/Lojuxta (lomitapide) approved in US and EU
    - Tolerability issues leading to persistence/compliance issues but is administered orally
  - Apheresis to remove LDL
    - Challenging for patients and requires frequent procedures
  - Evkeeza with high potency and monthly dosing compares well
- **Market research** with 10 top KOLs indicate strong interest in Evkeeza profile

"I'm extraordinarily excited about evinacumab for HoFH. It's going to be way more convenient than current interventions and its big advantage is that it works independently of LDLR"

– Italian KOL

"I will try to get all of my HoFH patients on evinacumab. It's got to be first line."

– Canadian KOL

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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)

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Summary of Amended US and Ex-US Protocols

	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 (up to 4 doses)	2.0 mg	3.3 mg	5.0 mg
		Can escalate following 2 doses	
Dose Escalation Criteria	n/a	Individually titrated until at least 2 CGI-I-AS[2] 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.
2: CGI-I-AS: Clinical Global Impression of Improvement-Angelman Syndrome

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Update on Amended Protocols

Still early in process, but encouraging so far

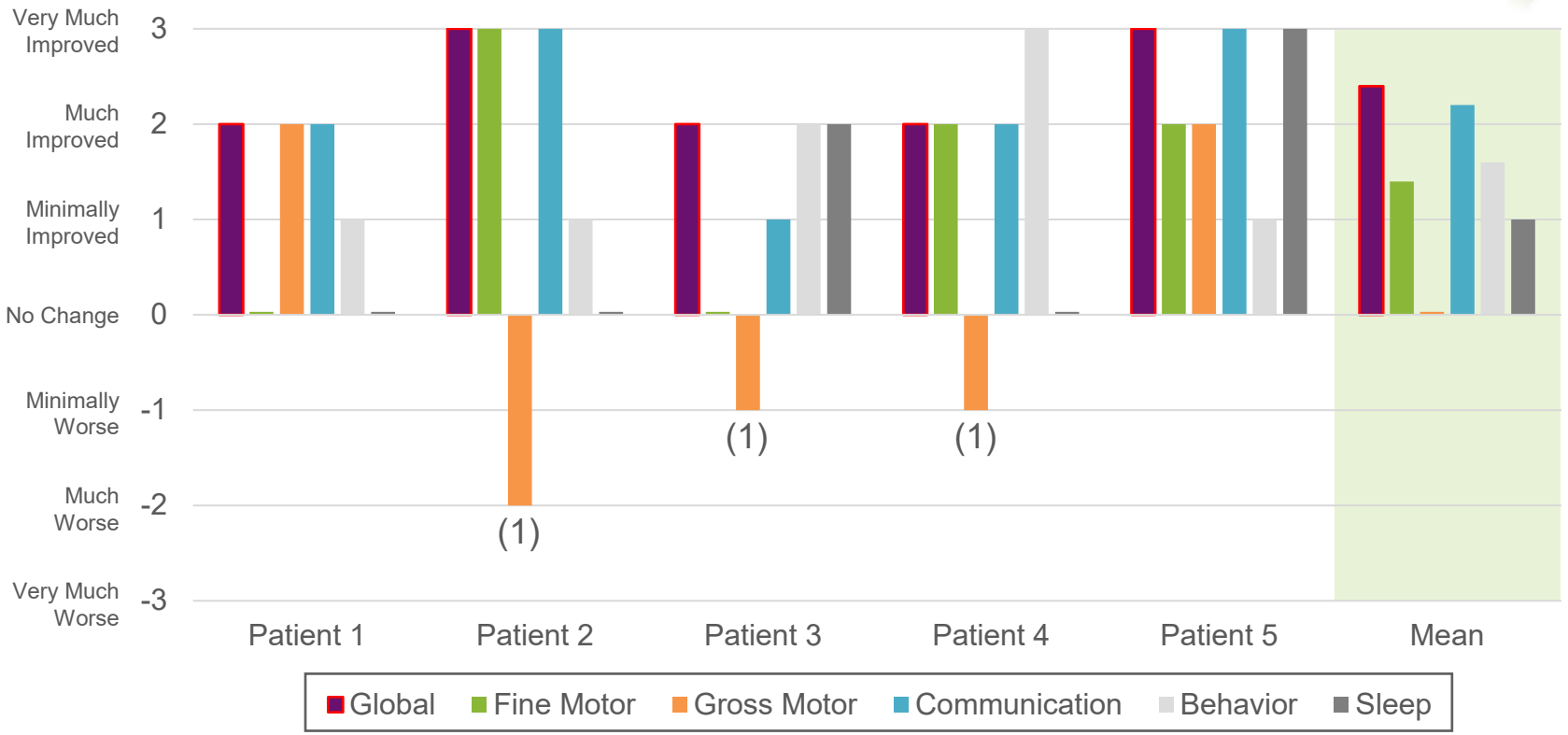
- Across Cohorts 4 and 5, no reported lower extremity (LE) weakness to date
  - DSMB recommended expansion of both cohorts
- Initial assessments, including CGI-I-AS[1], indicate early and encouraging signs of activity in multiple domains
  - Similar to activity seen at these doses under original protocol
- Once safe dose determined for efficacy, additional new patients beyond these 12 patients are expected to enroll at the new dose
- Dosing in the U.S. cohort has begun

Next data update expected in mid-2022

(1) CGI-I-AS: Clinical Global Impression of Improvement-Angelman Syndrome

Reminder of Prior Data on CGI-I-AS* Ratings in Initial 5 US Patients

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

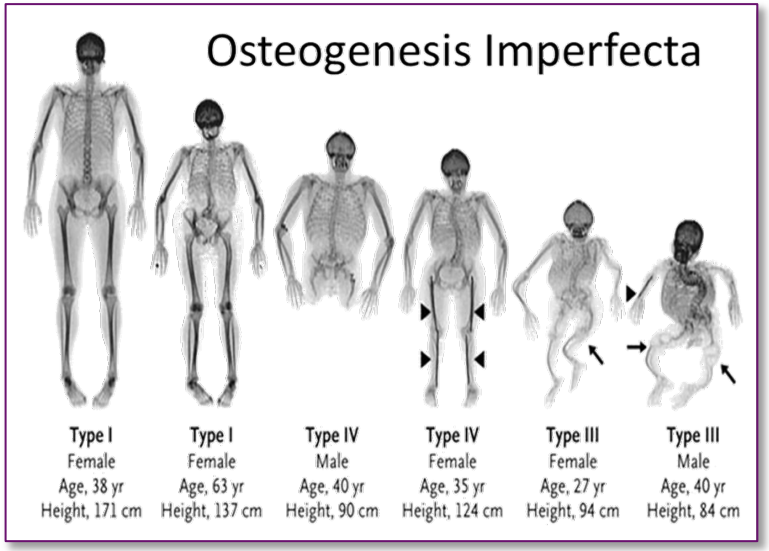
UX143 (setrusumab) for Osteogenesis Imperfecta

Phase 2/3 monoclonal antibody in large genetic bone disease

UX143 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
- **UX143 (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 anti-resorptive 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 Phase 2/3 study in pediatric and young adult patients initiated



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UX143: 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
- UX143 (setrusumab) well-tolerated
  - No cardiac-related safety issues

UX143: Next Steps

- Phase 2/3 Orbit study in patients 5-25 years old initiated in April 2022
  - Phase 2 portion: determine optimal dose based on increases in collagen production using serum P1NP levels
  - Phase 3 portion: expected to initiate in second half of 2022; evaluate fractures over 15-24 months
- Additional study in patients <5 years old expected to be initiated in second half of 2022

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


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Gene Therapy Programs,
Platform, and Partnerships

Gene Therapy Overview

Programs

Clinical
- UX111 for MPS IIIA
- DTX401 for GSDIa
- DTX301 for OTC
- UX701 for Wilson

Preclinical
- UX810 for Duchenne
- UX055 for CDKL5 Deficiency

Partnerships

Program

BAYER

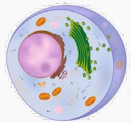
DTX201 for Hem A

Manufacturing

Daiichi-Sankyo

Platform License

Ultragenyx PCL Manufacturing Platform



Producer Cell Line (PCL) Platform

Higher fill ratio, 10x yield, better speed via refined high throughput screening. Continuing to improve scale, productivity, and quality.

DTX201 for Hem A **UX701 for Wilson** **UX810 for Duchenne**

Expected to open in 2023

Large-Scale Plant Under Construction

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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

Before | After

"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

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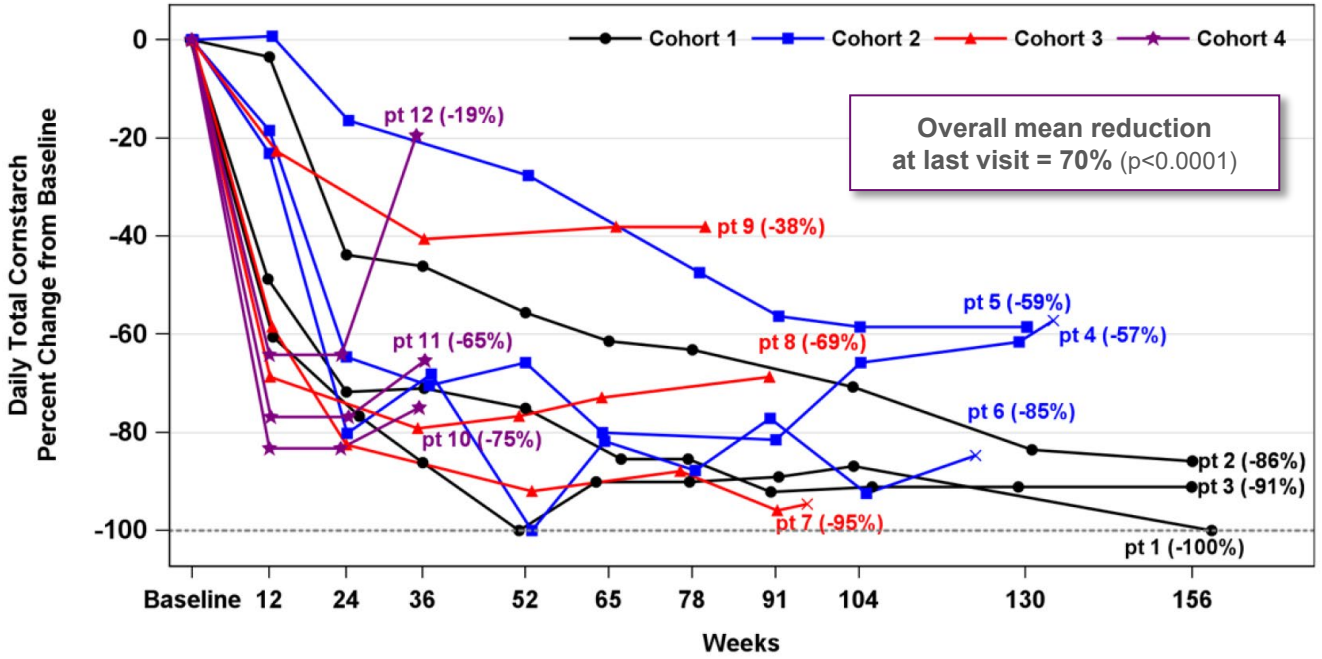
All Patients Reduced Cornstarch Therapy While Maintaining or Improving Time in Euglycemia



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

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DTX401: Phase 3 Status and Design

Study Status

- EOP2 and Scientific Advice meetings held with both FDA and EMA, respectively
- Patients in screening and have been dosed

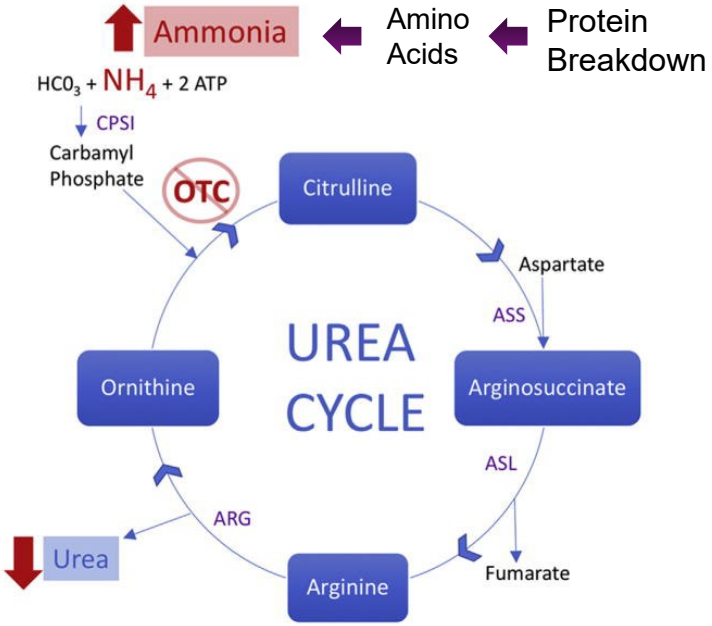
Phase 3 GlucoGene Study Design

- 50 patients, randomized 1:1 DTX401 (1.0×10^{13} 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
- Secondary endpoints include time to hypoglycemia during fasting challenge, GSD Functional Assessment Diary (FAD)

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)

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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

Study Status

- EOP2 and Scientific Advice meetings held with FDA and EMA, respectively
- Expect to initiate in mid-2022

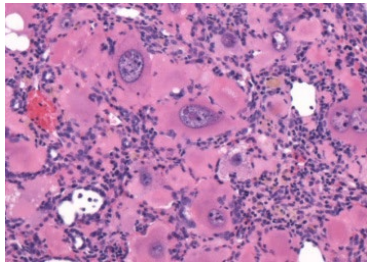
Phase 3 Enh3ance Study Design

- 50 patients, randomized 1:1 DTX301 (1.7 x 10^{13} GC/kg) to SOC/placebo
  - Patients on SOC/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 and percent of patients who achieve a response as measured by discontinuation or reduction in baseline disease management
- Secondary endpoints include Hyperammonemia Indicator Question (HI-Q), Cogstate Cognitive Assessment, rate of hyperammonemic crises

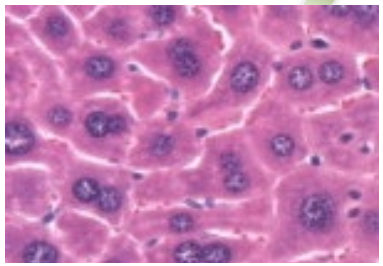
UX701: AAV9 for Wilson Disease

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 Ph 1/2/3 is screening and enrolling

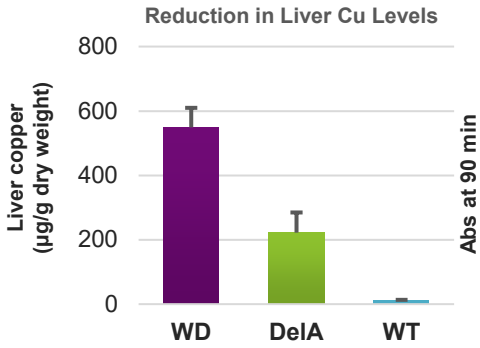


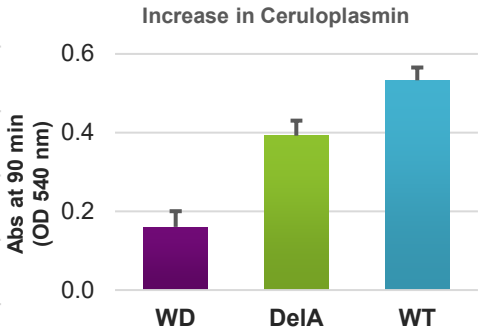
Untreated KO Mice



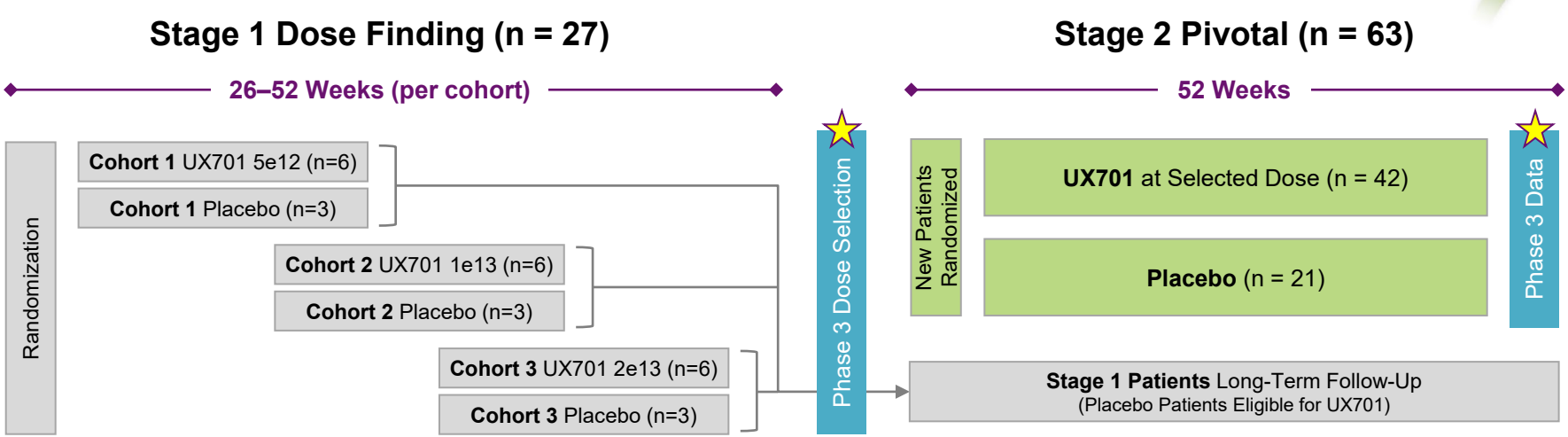
1x10^{11} GC Treated Mice

Reduced Liver Copper Accumulation Leading to Improved Liver Pathology in Preclinical Models



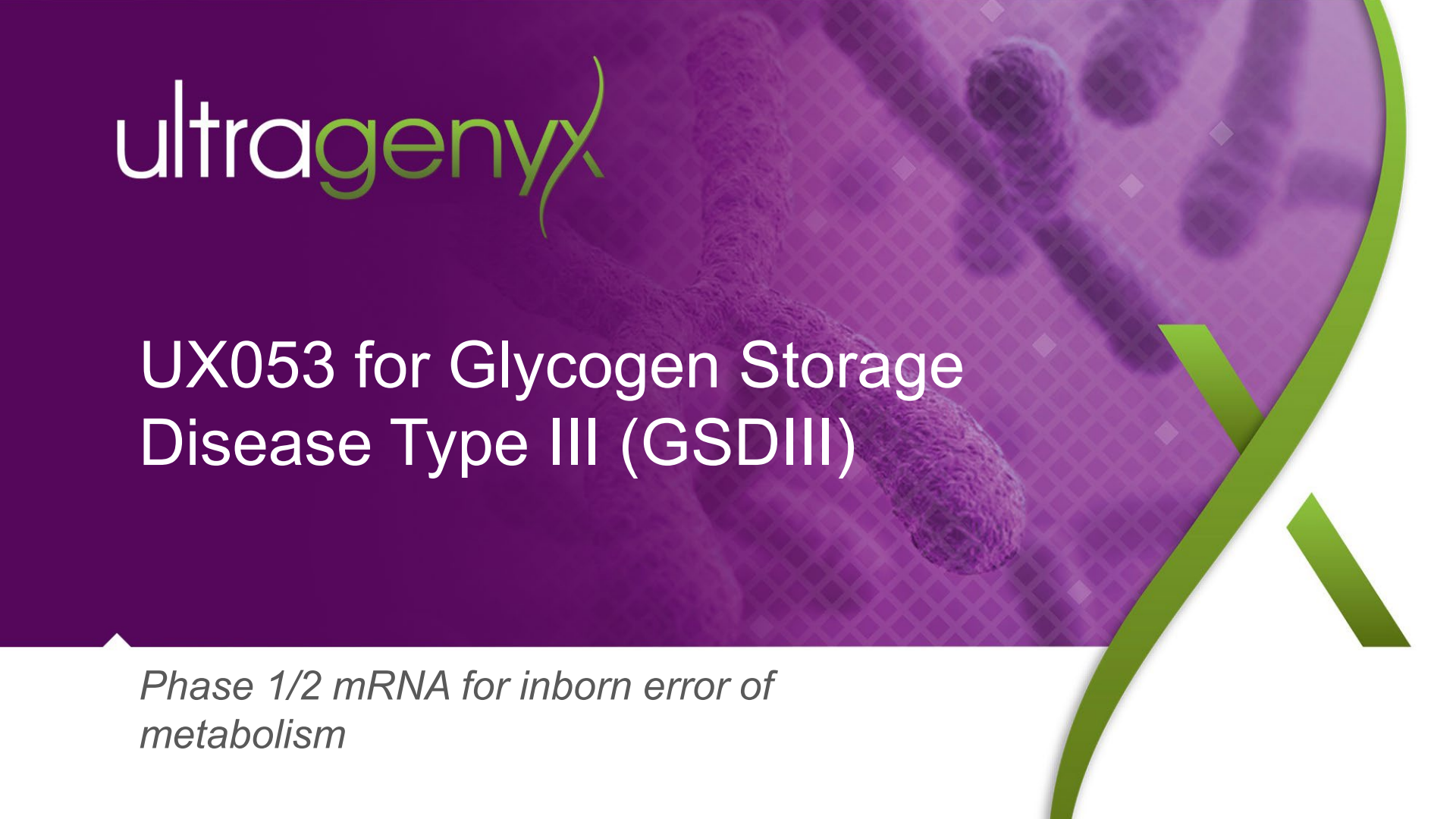


UX701: AAV9 for Wilson Disease
Seamless Phase 1/2/3 Study Design



- Safety profile
- Changes in copper (CU) metabolism
  - 24-hr urinary CU, ceruloplasmin concentration, ceruloplasmin activity, non-ceruloplasmin bound copper, total serum copper
- Reduction in the use of copper chelator and/or zinc (SoC)

- Co-primary endpoints
  - CU regulation based on 24-hr urinary CU concentration
  - Percent reduction in SoC at Week 52
- Key secondary endpoints: additional biomarkers of CU metabolism and patient- and clinician-reported outcomes from a modified Wilson Disease Functional Rating Scale



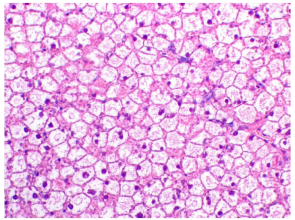
UX053 for Glycogen Storage Disease Type III (GSDIII)

Phase 1/2 mRNA for inborn error of metabolism

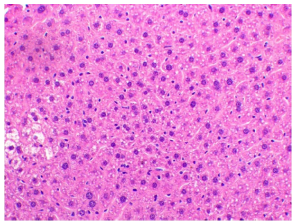
UX053: mRNA for Glycogen Storage Disease Type III

First clinical program from emerging mRNA platform

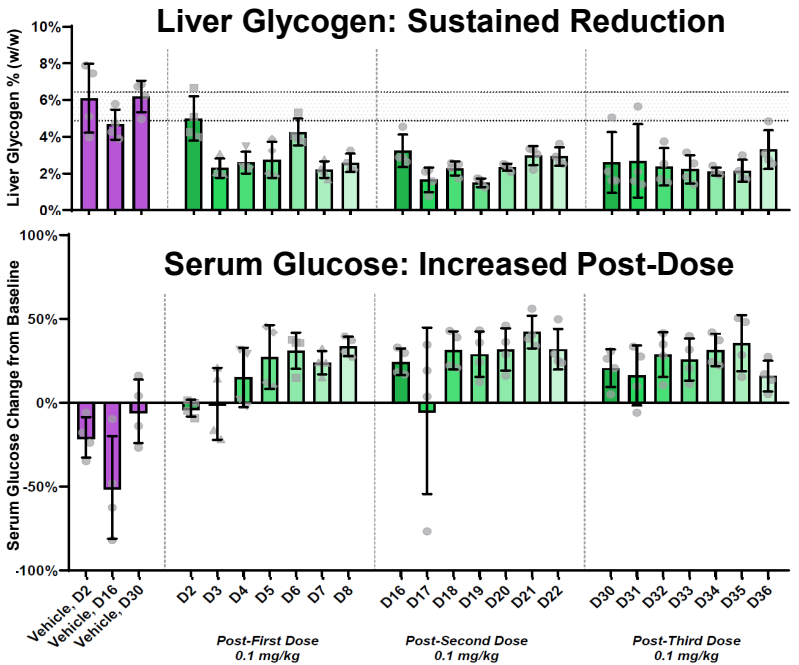
- **GSDIII:** Deficiency of glycogen debranching enzyme (GDE) causes accumulation of partially metabolized glycogen in liver and muscle
- **Key symptoms/prognosis:** Hypoglycemia, enlarged liver, cirrhosis, skeletal myopathy, cardiomyopathy, growth impairment
- **Standard of Care:** Diet and cornstarch only
- **WW prevalence:** 10,000
- **Status:** Enrolling and dosing in single-ascending dose portion of Phase 1/2 study
  - Preliminary data expected 2H 2022



Vehicle in KO Mouse
Substantial liver cell glycogen storage



UX053 Single Dose in KO Mouse
Significantly reduced glycogen storage



Broad and Diverse Clinical Pipeline to Build on Strong Commercial Foundation

Stable & Growing Revenue Base

>$300M revenue in 2022 from current commercial portfolio

CRYSVITA® burosumab — XLH & TIO

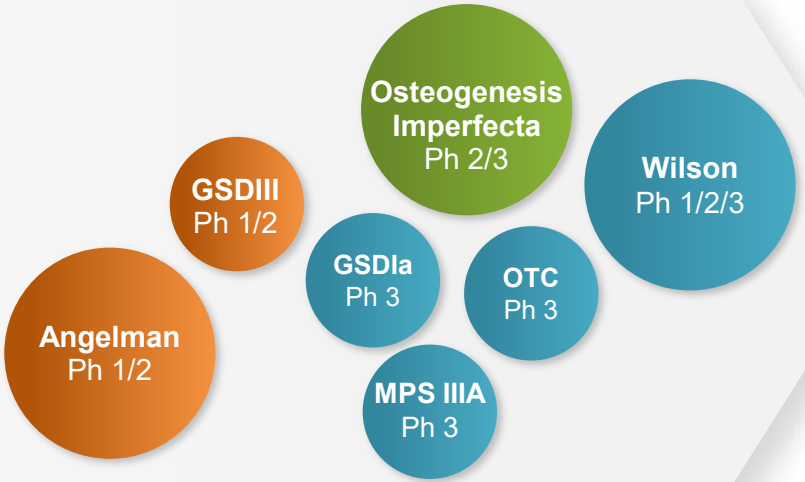
DOJOLVI® TRIHEPTANOIN Oral Liquid — LC-FAOD

Evkeeza® (evinacumab-dgnb) Injection — HoFH (ex-US)

Mepsevii™ (vestronidase alfa-vjbk) injection — MPS VII

Significant Clinical Catalysts over Next Few Years

Diversified across modalities and smaller and larger indications



Protein Biologic | Small Molecule | Gene Therapy | ASO / mRNA

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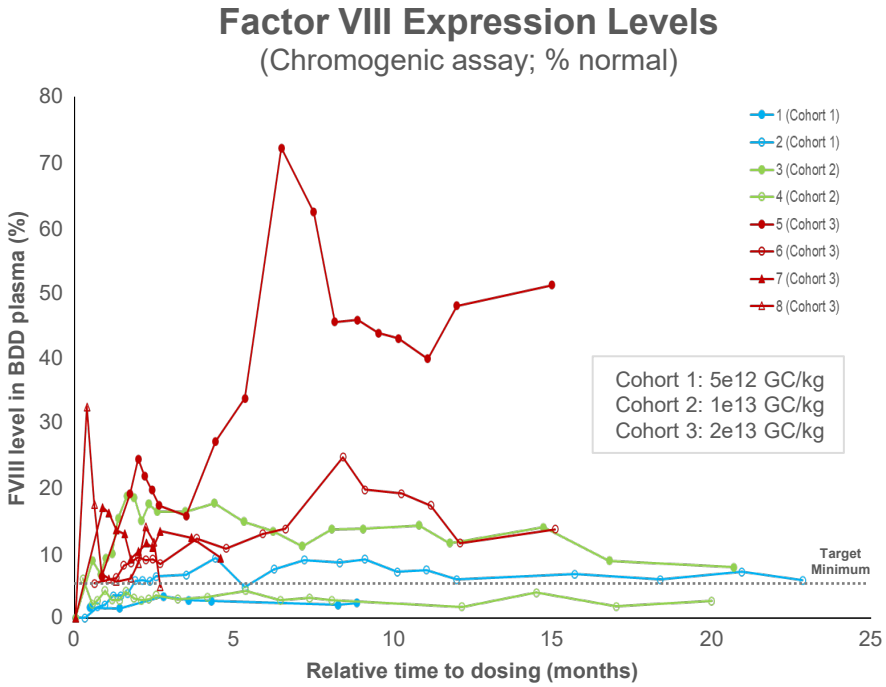
Appendix

Positive, Clinically Effective Hem A Data from the PCL Platform
Out-licensed program to Bayer validates 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 H2-receptor antagonists
- Following DMC review, escalation to dose cohort 4 (4e13 GC/kg) is planned



Pipe *et al.* International Society on Thrombosis and Haemostasis (ISTH), June 2021

Key Licenses & Intellectual Property – Commercial Products

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)[2] ▪ Mid single-digit royalty
	N/A (IP Owned by Ultragenyx)	▪ Ultrapure triheptanoin and use in treatment of FAOD (Pending; 2034)

[1]Includes granted U.S. patent term extension
[2]Includes projected U.S. patent term extension

Product	License	EU Intellectual Property Rights/Royalties
EVKEEZA® (HOFH)	Regeneron	▪ Evkeeza antibody and use for treatment of HOFH (2036)[3] ▪ Evkeeza antibody in combination with other agents for treatment of HOFH (Pending: 2037) ▪ Stabilized formulations of Evkeeza (Pending: 2041) ▪ Regeneron supplies product and charges Ultragenyx a transfer price from the low 20% range up to 40% on net sales

[3]Includes projected extension via supplementary protection certificates (SPCs)

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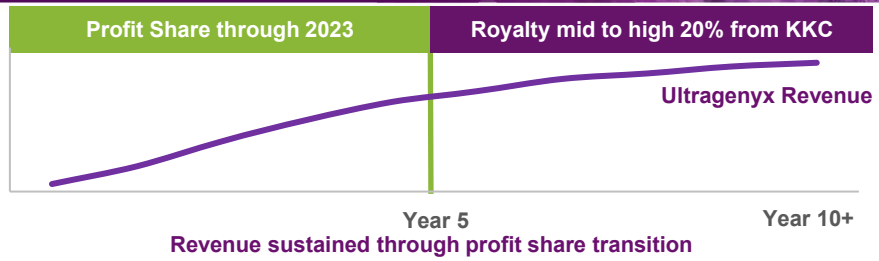
Key Licenses & Intellectual Property – Clinical Programs

Product	License	US Intellectual Property Rights/Royalties
UX143 (Osteogenesis Imperfecta)	Mereo Biopharma	▪ Setrusumab antibody (2028) ▪ Use of anti-sclerostin antibodies including setrusumab for treatment of OI (2037) ▪ Tiered double-digit royalty on ex-EU sales
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
UX111 / ABO-102 (MPS IIIA)	Nationwide Children's Hospital (NCH)	▪ Recombinant vectors comprising SGSH gene (Pending; 2032) ▪ Development and commercial milestones plus royalties
	Abeona Therapeutics	▪ Development and commercial milestones plus royalties
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
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
UX701 (Wilson Disease)	Sub-License from REGENXBIO of UPENN IP	▪ AAV9 Capsid (2024-2026) ▪ Mid to high single-digit royalty
	UPENN	▪ Recombinant vectors comprising certain regulatory and coding sequences packaged in UX701 (Pending; 2037) ▪ Development and commercial milestones plus low to mid single-digit royalty
	N/A (IP Owned by Ultragenyx)	▪ Recombinant vectors expressing a novel truncated version of ATP7B protein produced by UX701 (Pending; 2040)
GTX-102 (Angelman Syndrome)	Option to Acquire GeneTx (Exclusive Licensee of TAMU's GTX-102 IP)	▪ Use of UBE3A-ATS antisense oligonucleotides including GTX-102 for treatment of AS (2038) ▪ Development and commercial milestones plus royalties
UX053 (GSDIII)	Arcturus Therapeutics	▪ Various cationic lipids including the lipid used in UX053 (2034-2038) ▪ Various codon-optimized mRNA sequences encoding AGL including the codon-optimized version expressed by UX053 (Pending; 2038) ▪ Development and commercial milestones plus low to mid single-digit royalty

Revenue to Ultragenyx Maintained After Transition from Profit Share to Royalty in U.S.

CRYSVITA® burosumab

U.S. Prevalence: 12,000



	U.S. AND CANADA	LATIN AMERICA	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.

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CRYSVITA® Exclusivity Summary

XLH Orphan Exclusivity — 2025

TIO Orphan Exclusivity — 2027

Biologics Exclusivity — 2030

Crysvita CoM Patent — 2032*

Q2W Dosing Patent — 2035

2018 2020 2022 2024 2026 2028 2030 2032 2034 2036

2028 — XLH Orphan + D&M Exclusivity

2033* — Crysvita CoM Patent

2035 — Q2W Dosing Patent

*Includes projected US PTE and EU SPC awards

MEPSEVII® Exclusivity Summary

Mepsevii®
(vestronidase alfa-vjbk)
injection, for intravenous use
10 mg/5 mL (2 mg/mL)

MPS7 Orphan Exclusivity
2024

Biologics Exclusivity
2029

Mepsevii CoM Patent
2035

2018 2020 2022 2024 2026 2028 2030 2032 2034 2036

2028
MPS7 Orphan + D&M Exclusivity

2035
Mepsevii CoM Patent

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DOJOLVI® Exclusivity Summary

DOJOLVI® TRIHEPTANOIN Oral Liquid

NCE Exclusivity — 2025

LC-FAOD Orphan Exclusivity — 2027

Dojolvi CoM Patent — 2029*

Ultrapure Dojolvi (Pending) — 2034

2018 2020 2022 2024 2026 2028 2030 2032 2034 2036

2034 — Ultrapure Dojolvi (Pending)

*Includes projected US PTE award

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EVKEEZA® Exclusivity Summary

Evkeeza® (evinacumab-dgnb) Injection

Data & Marketing Exclusivity

2031

Evkeeza Ab Patent

2036[1]

Exemplary additional patent applications pending:

- Evkeeza w/ PCSK9 Ab
- Evkeeza w/ statins
- Evkeeza formulations

Projected expiration dates between **2037-2041**

2022 2024 2026 2028 2030 2032 2034 2036 2038 2040

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