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Corporate Presentation

September 2019

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Cautionary note regarding forward-looking statements: This presentation contains forward-looking statements, including, but not limited to, statements regarding plans with respect to commercializing our product and product candidates, our translational research program, 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, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of our regulatory filings 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: Rare by Design, 9 Years from Founding

Exceptional Rare Disease Company	▪ Forging new approaches ▪ 14+ indications ▪ Multiple modalities
Gene Therapy Platform	▪ 6+ programs ▪ Clinical POC in 2 ▪ Strong manufacturing
Global Commercial	▪ 2 approved therapies ▪ Third potential therapy filed ▪ N. America, S. America, Europe and Turkey

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The RARE Formula for Effective Pipeline Development

Science We Choose

Potent & Clear Disease & Drug Biology

The Need We Solve

- Serious Unmet Medical Need: Often First Drug Ever
- Disease-Modifying Therapeutic

The Development We Plan

- Fast to Clinic and Speed: Dynamic Development Model
- Creative, Adaptive Clinical and Regulatory Strategy
- Rapid Global Submissions Long-Term Follow-up in DMP

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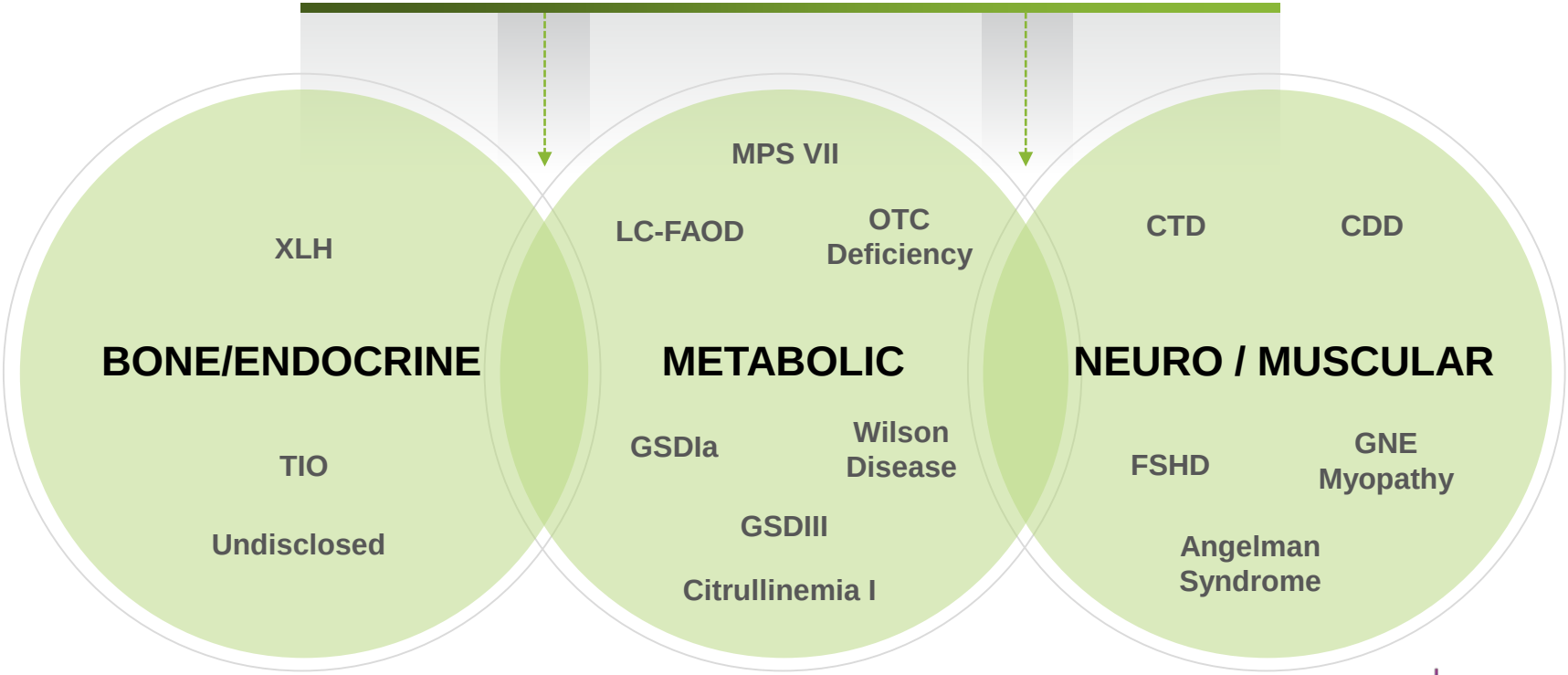
Current Focus on Therapeutic Areas with Rare Genetic Disease

Clinical and Commercial Synergies



Pipeline Driving Next Opportunities Across 4 Modes

Picking the best mode for each indication

	TRADITIONAL BIOLOGICS	SMALL MOLECULE	AAV GENE THERAPY	mRNA / ASO
Commercial	CRYSVITA burosumab; Mepsevii (vestronidase alfa-vjbk) injection	LC-FAOD UX007		
Clinical	TIO Crysvita		OTC DTX301; GSDIa DTX401; Hem A DTX201 (Bayer)	
Research	Undisclosed UX064; Undisclosed UX032; Undisclosed UX008	Creatine Transporter Deficiency UX068; FSHD UX018; GNE Myopathy UX001P	Wilson UX701; CDD UX055; 3 Additional Targets	GSDIII UX053; Angelman GTX-102; Up to 11 Additional Targets

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Diverse Clinical Pipeline Across Metabolic Indications

Candidate	Description	Pre-Clinical	IND	Phase 1	Phase 2	Phase 3	Approved*	Est'd Patients in Dev. World
CRYSVITA® burosumab KYOWA KIRIN	Anti-FGF23 monoclonal antibody	XLH						~48,000
		TIO						~2,000 - 4,000
Mepsevii™ (vestronidase alfa-vjbk) injection	Enzyme replacement	MPS 7						~200
UX007	Substrate replacement	LC-FAOD						~8,000-14,000
DTX301	AAV8-OTC Gene Transfer	OTC						~10,000
DTX401	AAV8-G6Pase Gene Transfer	GSDIa						~6,000
BAYER DTX201	AAV-FVIII Gene Transfer	Hemophilia A						~144,000

Protein Biologic | Gene Therapy | Small Molecule

14+ Translational Research Programs | Advancing One into the Clinic Every 1-2 Years

* Crysvita is approved in the U.S., Canada, EU, and Brazil
* Mepsevii is approved in the U.S., EU, and Brazil

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Commercial and Clinical Catalysts

Candidate	Disease	2019	2020
Mepsevii *Enzyme Replacement*	MPS7	Commercial Updates	
Crysvita *Anti-FGF23 monoclonal antibody*	XLH	Commercial Updates ✓ 64-week pediatric data	
	TIO	❑ Finalize registrational plan (Q3)	
UX007 *Substrate Replacement*	LC-FAOD	✓ Long-term extension data ✓ NDA submission	
DTX301 *AAV8 gene therapy*	OTC Deficiency	❑ Ph 1/2 Cohort 3 data (Q4)	❑ Potential Ph 3 Initiation
DTX401 *AAV8 gene therapy*	GSDIa	✓ Ph 1/2 Cohort 1 data ✓ Ph 1/2 Cohort 2 data	❑ Ph 1/2 Exp Cohort Data ❑ Potential Ph 3 Initiation
UX701 *Gene Therapy*	Wilson		❑ IND Submission
UX053 *mRNA*	GSDIII	IND Enabling Nonclinical Studies, CMC Process Optimization, and Clinical Protocol Development	❑ IND Submission
UX068 *Small Molecule*	CTD		❑ IND Submission
GTX-102* *ASO*	Angelman Syndrome		❑ IND Submission

*Partnered with GeneTx

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Commercial Update

CRYSVITA® burosumab-twza

Mepsevii™ (vestronidase alfa-vjbk) injection

Presence in Three Major Rare Disease Markets

Less than 18 Months Post-Launch

	North America	Europe	Latin America
CRYSVITA® burosumab-twza	APPROVED	APPROVED	APPROVED
		NAMED PATIENT / PENDING DECISIONS	NAMED PATIENT / PENDING DECISIONS
Mepsevii (vestronidase alfa-vjbk) injection	APPROVED	APPROVED	APPROVED
	PLANNED	PLANNED	NAMED PATIENT / PENDING DECISIONS

Note: Crysvita in North America is profit shared with Kyowa Kirin International (KKI); in Europe (excluding Turkey), KKI is responsible for commercialization; and in Latin America Ultragenyx is responsible for commercialization.

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U.S. Patient Access Model

Unique model to support and accelerate growth

CRYSVITA burosumab-twza

Patient Diagnosis Liaisons (~30)

Find new doctors with XLH patients

Hand off leads

UltraCare Liaisons (~30)

Assist identified XLH doctors in placing patients on therapy

Start forms sent

UltraCare Guides (~15)
Patient Access Liaisons (5)

Support treatment or reimbursement needs

Market Access Support

Medical Science Liaisons

Educate HCPs and payers throughout the process

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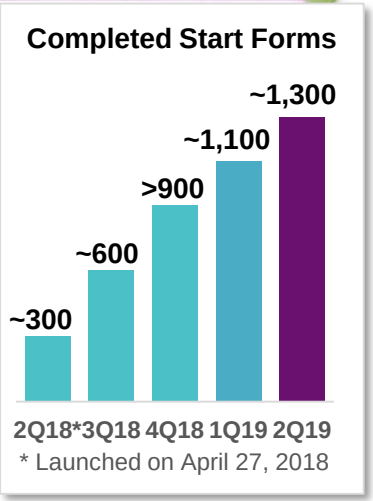
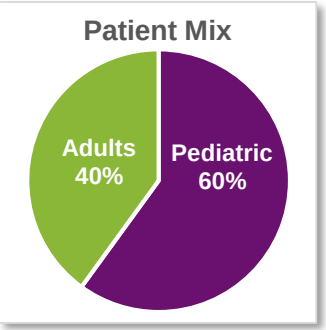
Strong Crysvita U.S. Launch

Key U.S. Commercial Launch Metrics

As of June 30, 2019

- ~ 1,300 completed start forms
- ~ 580 unique prescribers
- ~ 960 patients on reimbursed, commercial therapy
- In 2Q19, policies (60% private / 40% gov't), nearly full coverage of lives in the U.S.





Crysvita Clinical Data Supports Launch

Pediatric

Crysvita Superiority Over Conventional Therapy

Substantial Rickets Healing after 64 Weeks on Treatment

- 86.2% on Crysvita
- 18.8% on oral phosphate, vitamin D regimen

Adult

Significant Clinical Improvement with Crysvita Treatment

Substantial Fracture Healing

- Serum phosphorus normal
- Improvements in stiffness, pain, physical functioning

Untreated Adult XLH

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UX007 for Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD)

Phase 2 substrate replacement therapy
(oral liquid)

UX007 for LC-FAOD
NDA submitted July 2019

- **LC-FAOD:** Inability to convert fat into energy
- **Key symptoms/prognosis:**
  - Hypoglycemia, muscle rupture, heart failure
  - Mortality ~50%[1]; a cause of SIDS (newborn screened in U.S.)
- **Standard of care:** Diet and MCT[2] oil
- **UX007 Phase 2 data**:
  - Clinically meaningful reduction in frequency and duration of major medical events
- **U.S. prevalence:** ~2,000 – 3,500
- **Status:**
  - ✓ Submitted NDA to FDA

[1] J Inherit Metab Dis 2013;36:795-803
[2] Medium chain triglycerides

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UX007 NDA Submitted

NDA submission includes:

- Company-sponsored Phase 2 (n=29)
- Long-term extension study (n=75)
- Retrospective medical review (n=20)
- Expanded access (n=70)
- Investigator-sponsored study (n=32)

NDA submitted July 2019

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Extension Study Supports Sustained Clinically Meaningful Impact of UX007

	Original Data: Phase 2 Study	New Data: Extension Study	
	Phase 2 (n=29) 78 Weeks of UX007 Tx	**Ph2 Rollover** (n=24) 156 Weeks of UX007 Tx	**UX007 Naïve** (n=20) Median 63 Weeks of UX007 Tx
Median Annualized **Event** Rate (events/yr)	↓ 51% 1.3 pre-UX007 to 0.7 after 78 weeks of Tx	↓ 67%* 1.5 pre-UX007 to 0.0 at data cut-off**	↓ 70% 2.3 pre-UX007 to 0.7 at data cut-off**
Median Annualized **Event-Day** Rate (days/yr)	↓ 77% 5.3 pre-UX007 to 1.2 after 78 weeks of Tx	↓ 66%* 5.3 pre-UX007 to 0.0 at data cut-off**	↓ 80% 10.0 pre-UX007 to 2.0 at data cut-off**

* Percent reductions based on total UX007 treatment period (Phase 2 + Ext periods)
** 156 weeks on Tx for Ph2 rollover patients and median of 63 weeks for naïve patients

Safety profile in the long-term extension study (n=75) consistent with what has been previously observed with UX007

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AAV Gene Therapy Platform

Gene Therapy Platform Supported by People, Pipeline, and Manufacturing

People

- Dimension Therapeutics provided technology base
- Ultragenyx Gene Therapy has built in-house process discovery, definition, and development
- Internal knowledge de-risks scale up and tech transfer

Deep and Focused Pipeline

- 2 clinical-stage programs
  - OTC, GSDIa
- 1 partnered clinical program
  - Hem A
- 1 late-stage research
  - Wilson
- 4 early-stage research
  - CDD, PKU, Citrullinemia type I, Undisclosed

Scalable Mammalian Manufacturing

- HEK293
- HeLa producer cell line
- Internally controlled process development
- Scalable up to 2,000L

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Gene Therapy Pipeline: Deep and Focused

Candidate	Description	Pre-Clinical	IND	Phase 1	Phase 2	Phase 3	Est'd Patients in Dev. World
DTX301	AAV8-OTC Gene Transfer	Ornithine Transcarbamylase Deficiency					~10,000
DTX401	AAV8-G6Pase Gene Transfer	Glycogen Storage Disease Type Ia					~6,000
DTX201	AAV-FVIII Gene Transfer	Hemophilia A					~144,000
UX701	AAV-ATP7B Gene Transfer		Wilson Disease				>50,000
UX055	AAV9-CDKL5 Gene Transfer		CDKL5 Deficiency Disorder				~30,000
UX501	AAV8-PAH Gene Transfer		PKU				~50,000
UX601	AAV8-ASS1 Gene Transfer		Citrullinemia type I				~2,000
UX067 (Partnered)	Undisclosed						>10,000

Combination Liver Metabolic Diseases (OTC, GSDIa, PAH, ASS1 +1, Wilson) and Neurology (CDKL5)

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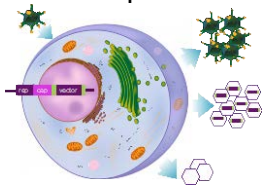
Ultragenyx Gene Therapy AAV Vector Production

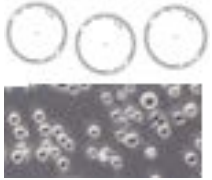
Vector Discovery to GMP Manufacturing

PD & manufacturing across 15 ml to 2,000L continuum – scaling factor > 130,000

HeLa PCL suspension/Adeno helper



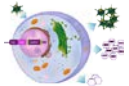
HEK293 suspension/Transfection



15mL Ambr

50L

200L



2,000L

4 x 200L

- Cell line cloning
- Early development

- Bioprocess development
- Preclinical & tech transfer Center of Excellence
- Large scale reference tox vector manufacturing

Clinical & commercial manufacturing at partner CMOs

Product yield consistency maintained across scale

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DTX401 Program for Glycogen Storage Disease Type Ia (GSDIa)

Phase 1/2 study of adeno-associated virus serotype AAV8-G6Pase Gene Transfer

DTX401 AAV8 for GSDIa

- **GSDIa:** Autosomal recessive, inborn error of glucose metabolism; deficient glucose-6-phosphatase (G6Pase)

- **Key symptoms/prognosis**
  - Hypoglycemia leading to significant morbidity and mortality
  - Long-term liver and renal disease
  - Impaired growth and delayed puberty
  - Severe long-term complications (70-80% patients)

- **Treatment limited; only curative approach is liver transplantation**

- **WW prevalence:** 6,000

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DTX401 Cohort 2 Update: Improved Glucose Control and Other Metabolic Parameters in all Patients

- Improved glucose production and control across Cohorts 1 and 2
  - Higher hyperglycemia in Cohort 2 suggests greater transgene expression at higher dose
  - Cornstarch reduction trends well aligned between cohorts
- Cohort 2 glucose control supported by greater improvements in other key metabolic measures
  - Lower lactate levels after treatment compared to baseline
  - Consistent early reductions in liver fat fraction (representative of glycogen storage) as measured by MRI across all Cohort 2 patients

	Liver fat fraction (%), (change from baseline)					
	Cohort 1			Cohort 2		
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
W12	8.2 (-6%)	7.2 (-20%)	15.1 (-37%)	7.4 (-40%)	4.3 (-39%)	5.0 (-32%)

Moving to Expansion Cohort to Confirm 6e12 GC/kg dose; Data Expected 1H 2020

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DTX401 Phase 1/2 Study: Demographics

Cohort 2 patients generally heavier and received more than 3x GC total dose

	Cohort 1 (2e12 GC/kg)			Cohort 2 (6e12 GC/kg)		
	Pt 1	**Pt 2**	**Pt 3**	**Pt 4**	**Pt 5**	**Pt 6**
Study Site	UCONN	UMICH	UCONN	UT	UMICH	UCONN
Gender	Male	Female	Male	Male	Male	Male
Age (yrs)	28	57	51	31	19	39
Genotype	c.247C>T c.1039C>T	c.1039C>T (homozygous)	c.247C>T c.1039C>T	c.379_380dup (homozygous)	c.247C>T c.323C>T	c.79del c.189G>A
Weight (kg)	57	59	80	114	74	93
Total GC	1.14e14	1.19e14	1.60e14	6.00e14	4.47e14	5.58e14
Baseline Treatment	Cornstarch	Cornstarch + Continuous Feed	Cornstarch	Cornstarch	Cornstarch	Cornstarch
On Study (wks)	52	52	52	34	25	19

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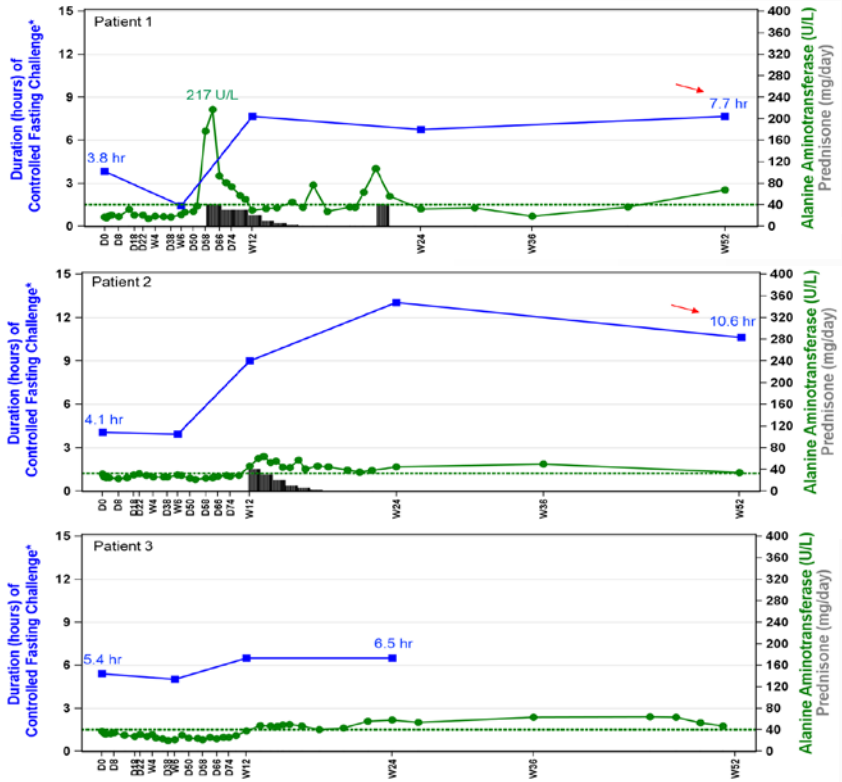
DTX401 Cohort 1 Long-term Data Demonstrates Improvement in Time to Hypoglycemia

Cohort 1 (2e12 GC/kg)
Controlled Fasting Challenge



Cohort 1, Patient 1

- 103% improvement in time to hypoglycemia
- 100% reduction in daily cornstarch (off cornstarch completely)

Cohort 1, Patient 2

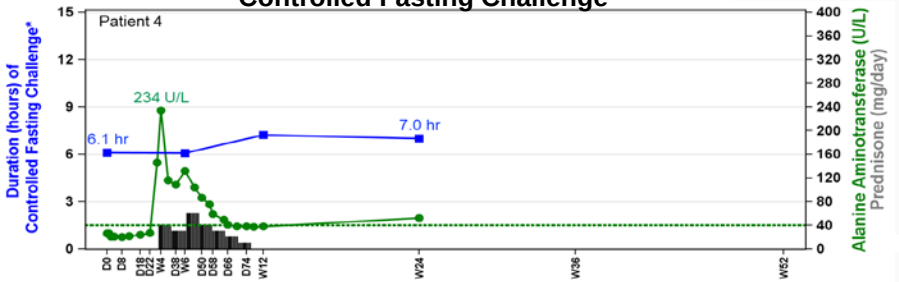
- 159% improvement in time to hypoglycemia
  - Terminated fasting challenge due to hunger as opposed to blood glucose levels
- 56% reduction in daily cornstarch

Cohort 1, Patient 3

- 20% improvement in time to hypoglycemia
- 79% reduction in daily cornstarch (wk 52)

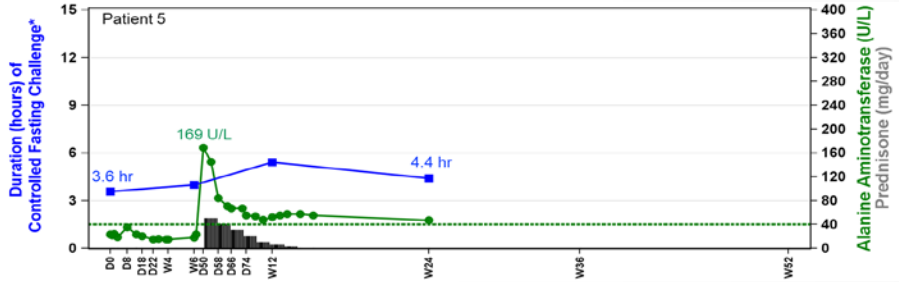
DTX401 Cohort 2 Data Demonstrates Improvement in Glucose Control

Cohort 2 (6e12 GC/kg)
Controlled Fasting Challenge



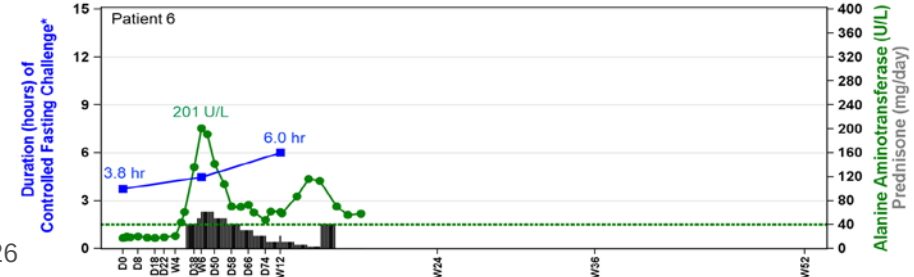
Cohort 2, Patient 4

- 15% improvement in time to hypoglycemia
- 69% reduction in daily cornstarch



Cohort 2, Patient 5

- 22% improvement in time to hypoglycemia
- 16% reduction in daily cornstarch

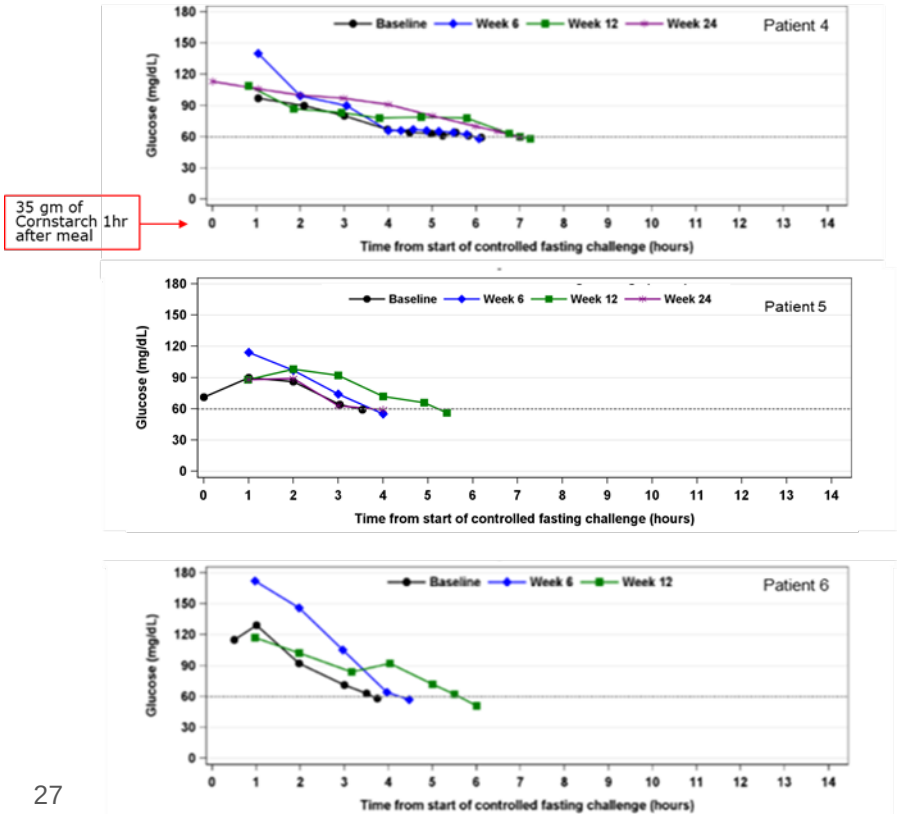


Cohort 2, Patient 6

- 58% improvement in time to hypoglycemia
- 68% reduction in daily cornstarch (Wk 18)

DTX401 Cohort 2: Insulin Surges Drove Hypoglycemia

Cohort 2 (6e12 GC/kg)
Glucose curve



~ 20x insulin surges in Patients 5 & 6 during fasting challenge at Week 6, one hour after cornstarch consumption

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DTX401: Clinically Significant Reduction of Daily Cornstarch Use Across Both Cohorts

	Cornstarch Consumption (grams)					
	Cohort 1 (2e12 GC/kg)			Cohort 2 (6e12 GC/kg)		
Visit	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Baseline	405	171	269	325	268	329
W6	355	165	255	270	268	341
W12	160	165	138	265	270	253
W24	94	96	76	100 *(-69%)*	224 *(-16%)*	105 *(-68%)**
W52	0 *(-100%)*	76 *(-56%)*	57 *(-79%)*	NR	NR	NR

**Cornstarch level at week 18*

NR=Not yet reached

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DTX401: No Safety Issues Observed in Cohort 1 or 2

- Mild asymptomatic elevation in ALT levels in 4 patients
  - Successfully treated with a tapering course of steroids
- No infusion-related adverse events
- All adverse events have been Grade 1 or 2
- No treatment related SAEs

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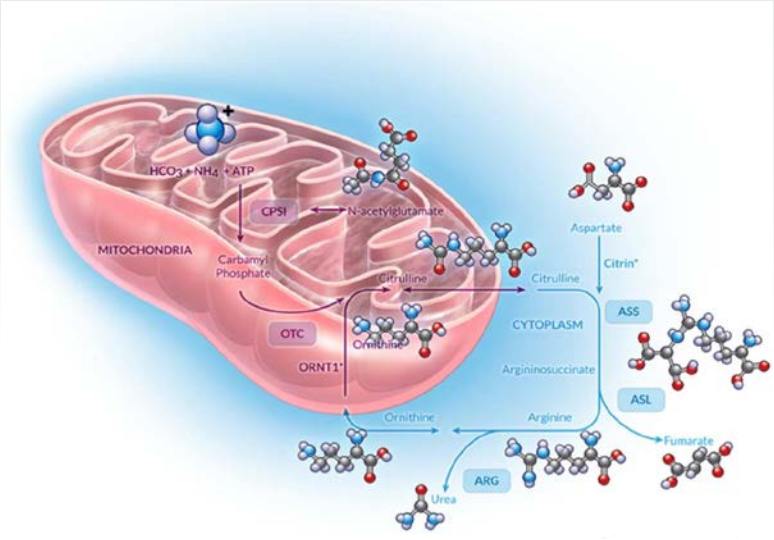
DTX301 Program for Ornithine Transcarbamylase (OTC) Deficiency

Phase 1/2 study of adeno-associated virus serotype AAV8 vector encoding human OTC

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 that can lead to hospitalization, adverse cognitive & neurological effects, death
- **Treatment limited; only curative approach is liver transplantation**
- **WW prevalence:** ~10,000, 80% late-onset



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DTX301: Two Patients Continue to Demonstrate Long-term Normalization of Ureagenesis

- Sustained normalization of ureagenesis at 52-78 weeks
- Clinically and metabolically stable, while discontinuing all alternate pathway medications
- Liberalized protein-restrictive diet without hyperammonemia concerns
- One patient had proven Influenza illness without hyperammonemia episode

Cohort 3 (1e13 GC/kg dose) update Q4 2019

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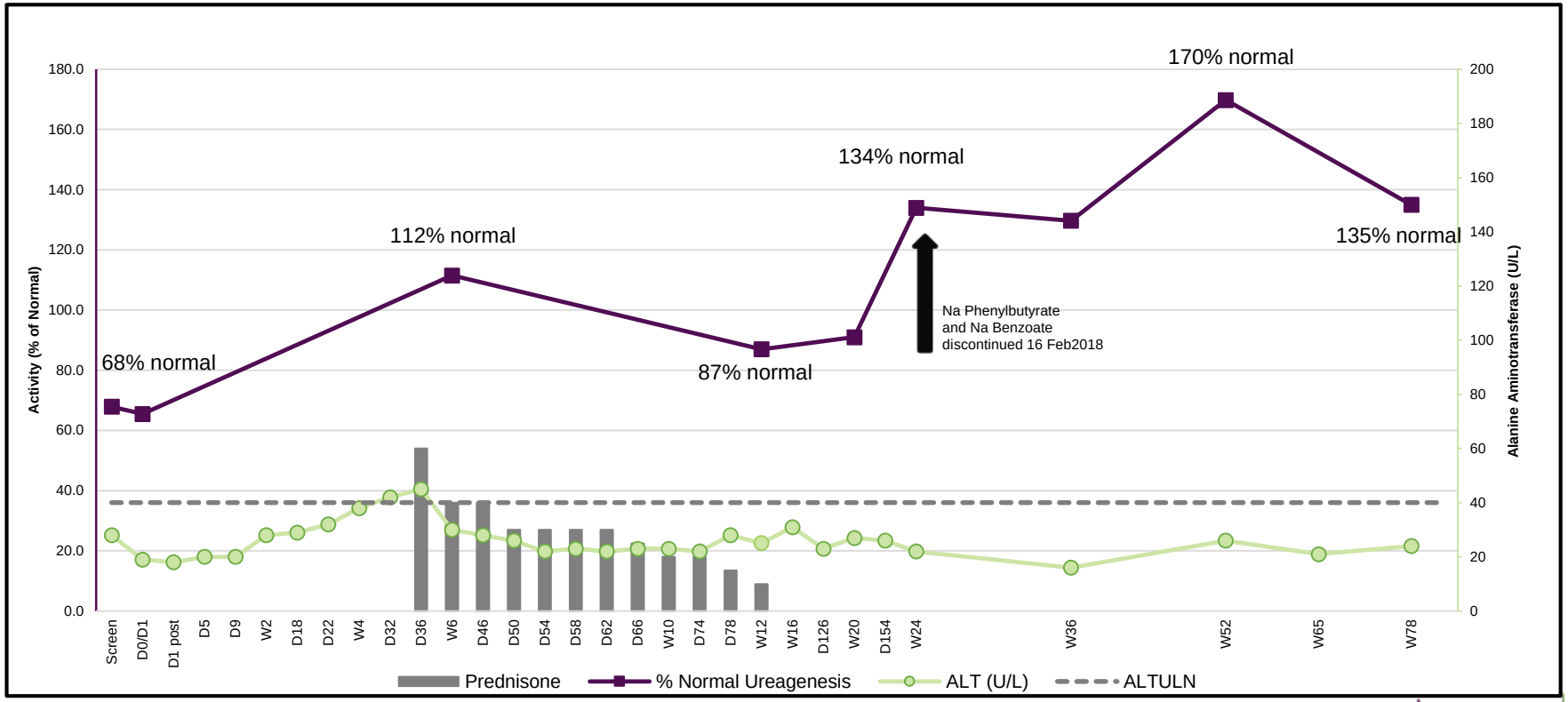
Cohort 1, Patient 1 – Durable Normalization of Ureagenesis

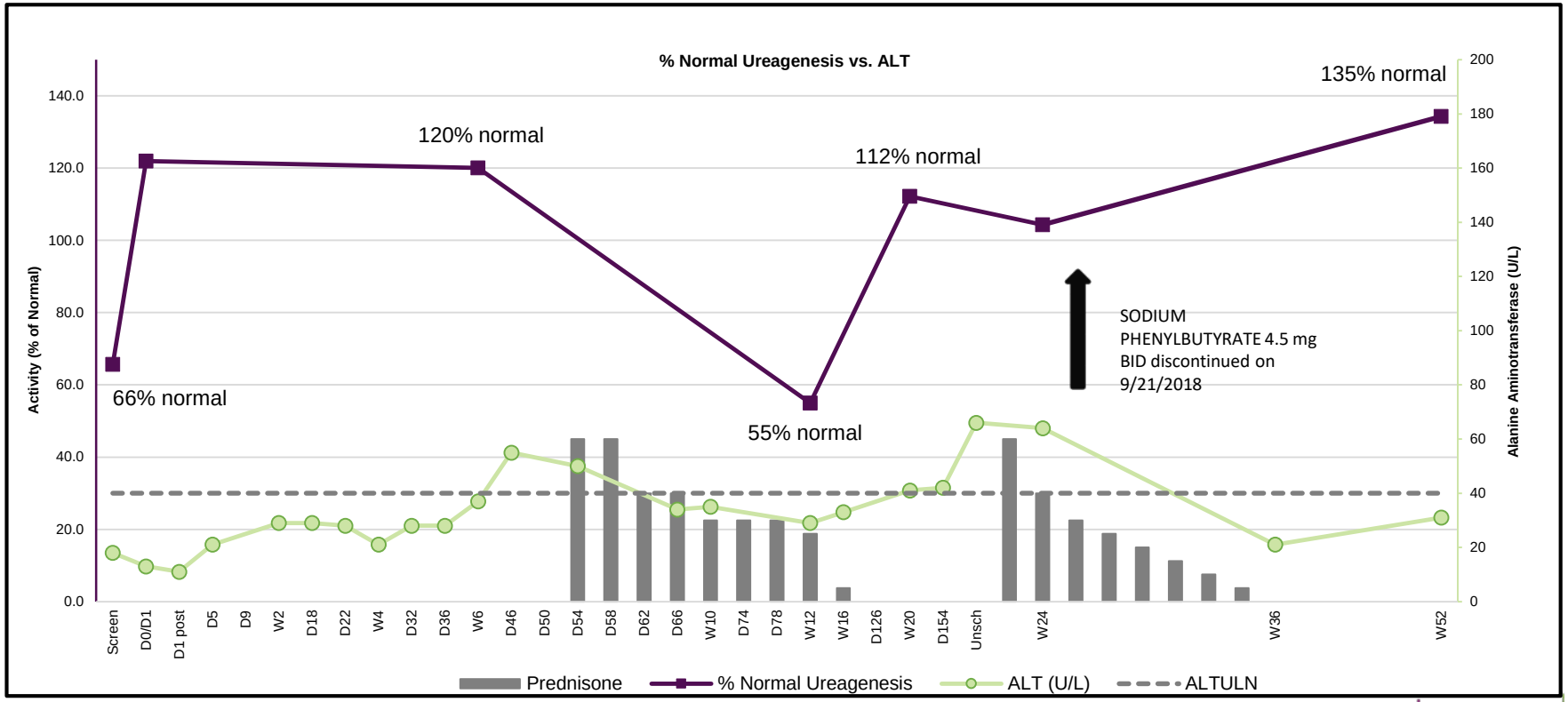
Liberalized diet and clinical stability off medications since ~Week 24



* Patient entered long-term extension study after week 52

Cohort 2, Patient 4 – Durable Normalization of Ureagenesis

Liberalized diet and clinical stability off medications since ~Week 24



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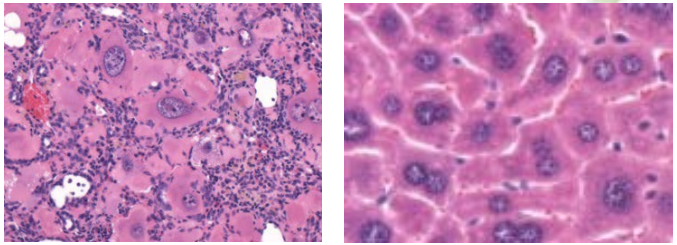
UX701 for Wilson Disease

UX701 for Wilson Disease

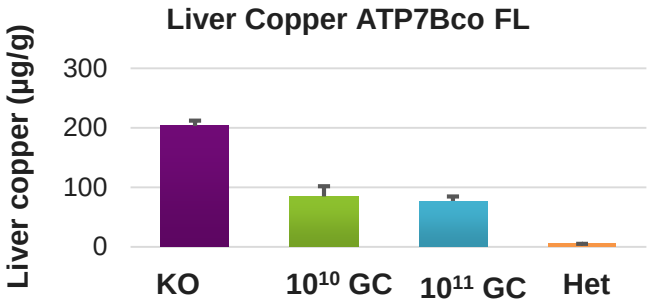
Next Gene Therapy program, entering the clinic in 2020

- **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/neurological deterioration
- **WW prevalence:** >50,000
- **Initial preclinical studies completed**
  - Novel version of ATP7B developed
  - Capsids from REGENXBIO
  - IND filing expected 2020



Untreated KO Mice **1x10^{11} GC Treated Mice**

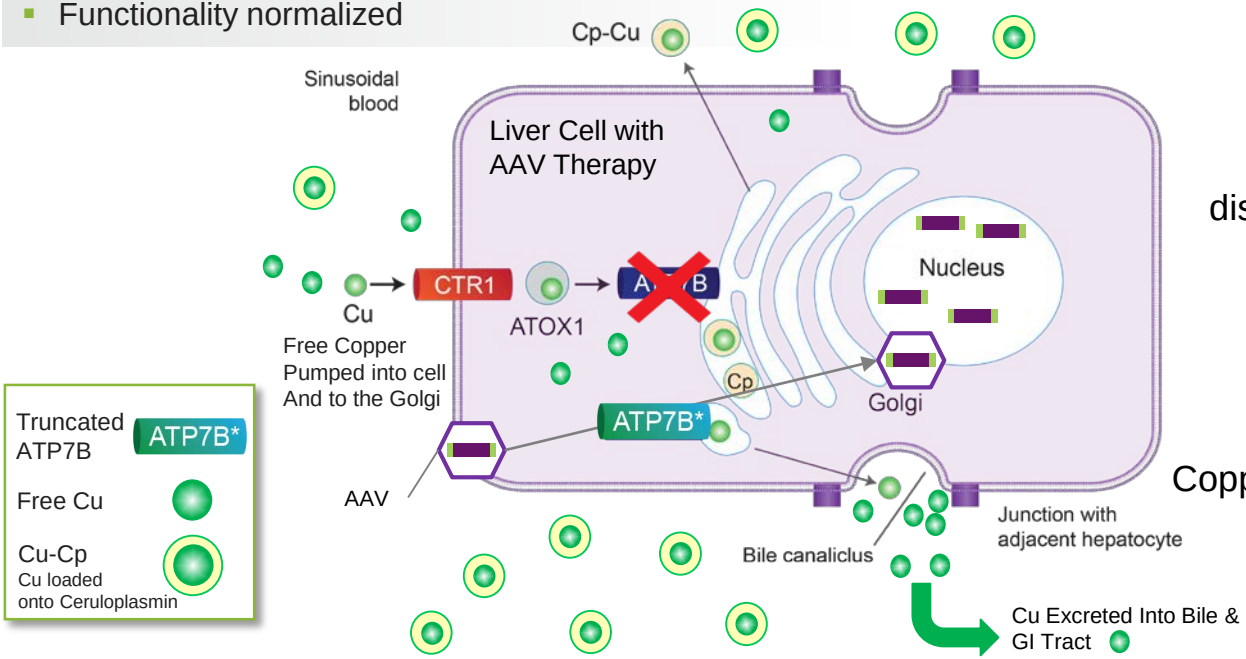
Reduced liver copper accumulation leading to improved liver pathology in preclinical models

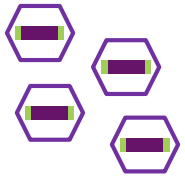


AAV Therapy Pumps Copper from the Liver into Blood and Bile

With AAV Therapy

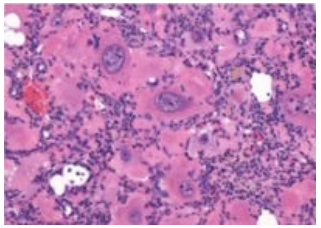
- ATP7B* is formed and pumps copper from cytoplasm into the Golgi
- Loads copper onto ceruloplasmin to secrete into the serum
- Excretes excess copper into the bile to exit the body
- Functionality normalized



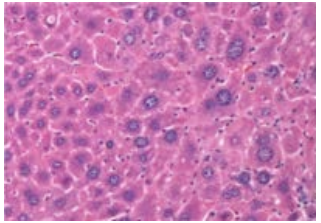


AAV ATP7B*

Wilson disease liver



Copper toxicity treated



After AAV GT with ATP7B*

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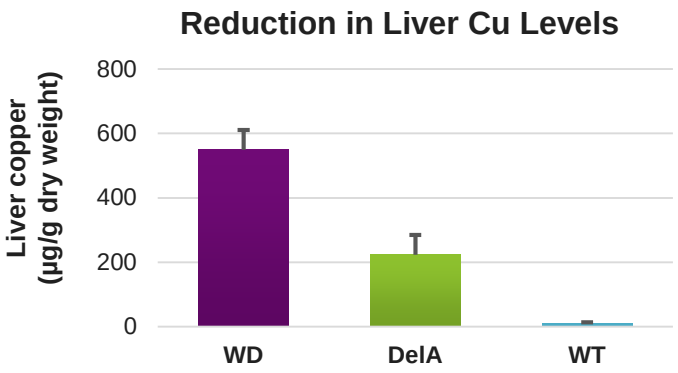
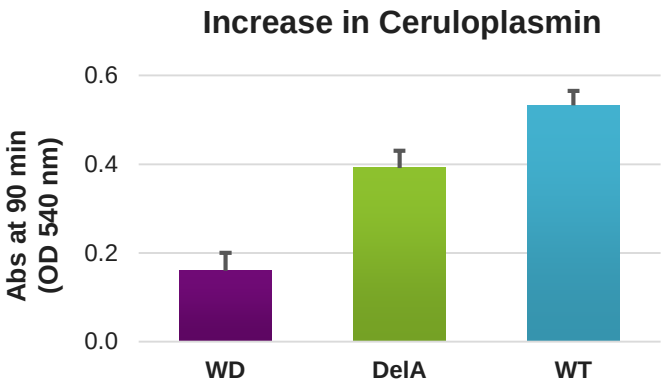
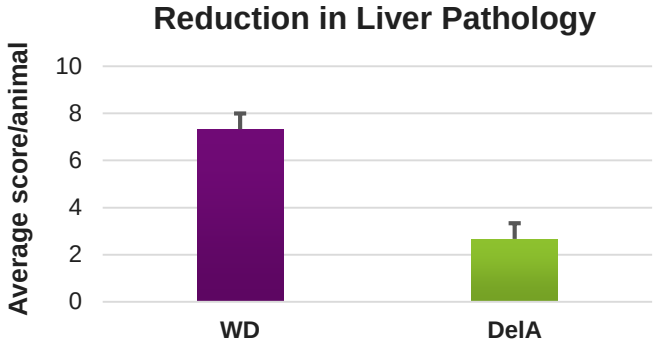
ATP7B Deletion A – Key Therapeutic Properties

Rapid reduction in free liver copper, increased copper ceruloplasmin and reduced liver pathology







Study Design

- Vector: DelA
- At T_0 mice = 6 - 8 weeks old
- Duration of study: 4 weeks

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UX053 Program for Glycogen Storage Disease III

UX053 for Glycogen Storage Disease III

Lead mRNA preclinical program, entering the clinic in 2020

Genetics

Autosomal recessive mutation in the AGL gene leading to glycogen accumulation in the liver and muscle

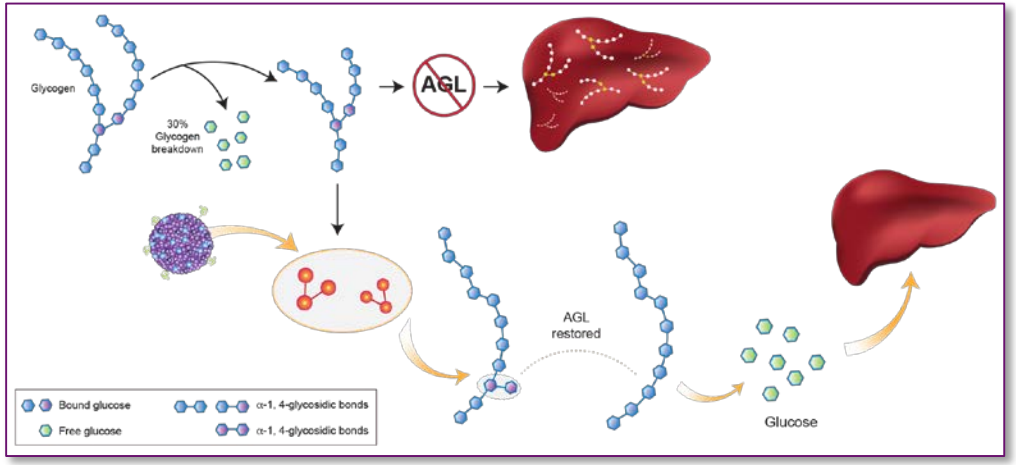
Clinical Presentation (based on literature)

- Beginning in infancy:
  - Hypoglycemia, hyperlipidemia, increased LFTs, hepatomegaly
- Later in Life
  - Fibrosis and cirrhosis
  - Cardiomyopathy, hypotonia, myopathy

Current Management

- High protein, cornstarch, fructose / galactose
- Hypoglycemia prevention
- Liver transplant

WW prevalence: ~10,000



IND-Enabling Studies Underway
IND Filing Expected 2020

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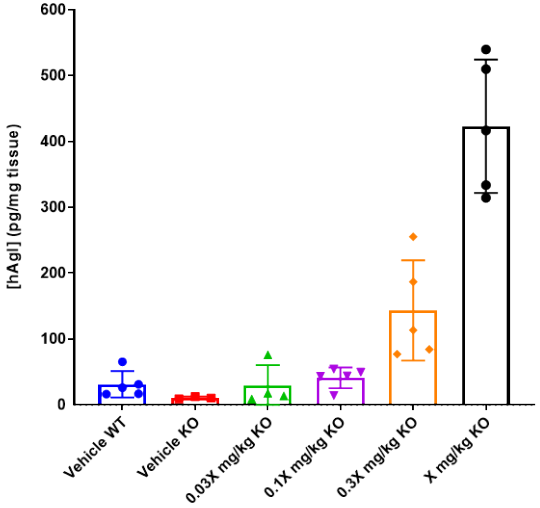
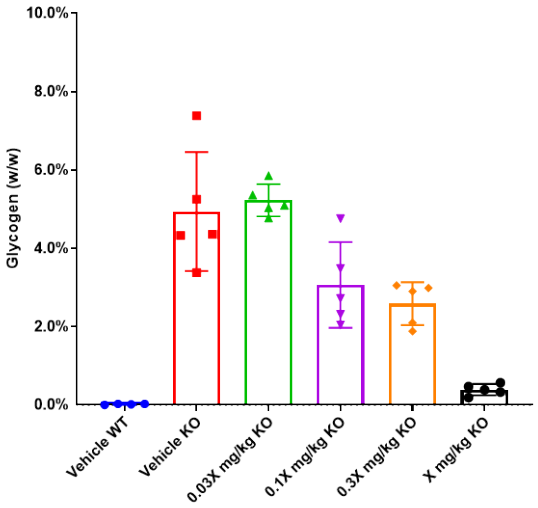
Dose-Response for AGL mRNA-LNP in GSDIII Mouse Model

Reduction in liver glycogen, and an increase in blood glucose

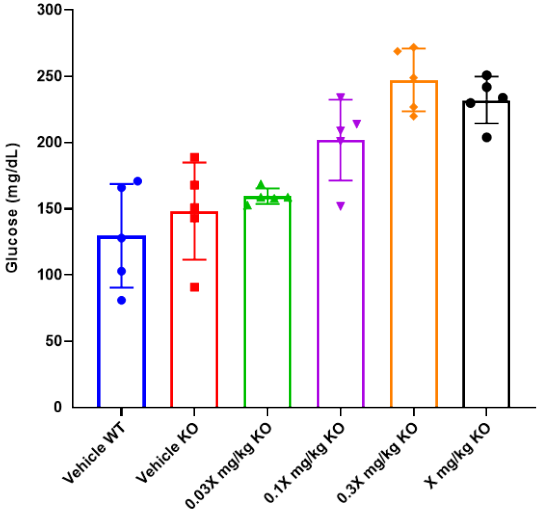
Liver human AGL Protein (hGDE)
24 hours Post-Dose



Liver Glycogen Content
24 hours Post-Dose



Serum Glucose
24 hours Post-Dose



X= dose undisclosed

Dose-response after a single dose of AGL-mRNA to reduce liver glycogen and stimulate increase in serum glucose (24 hours post-dose shown)

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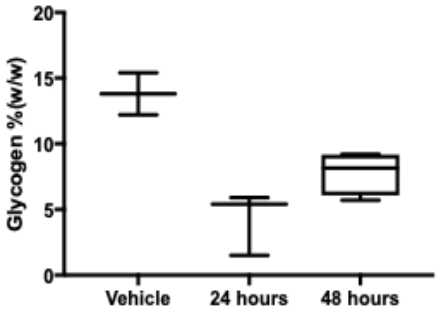
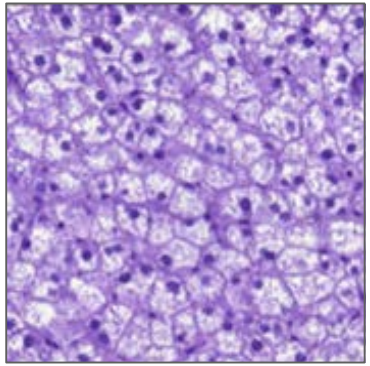
AGL mRNA-LNP Reduces Liver Glycogen in Single Dose

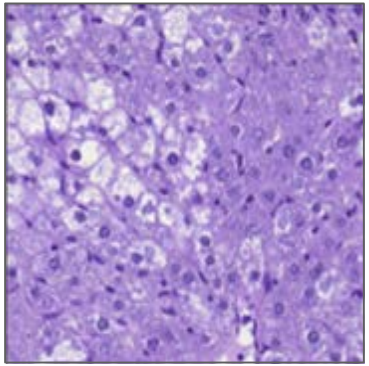
Levels approach normal and are maintained for 48 hours in mouse model

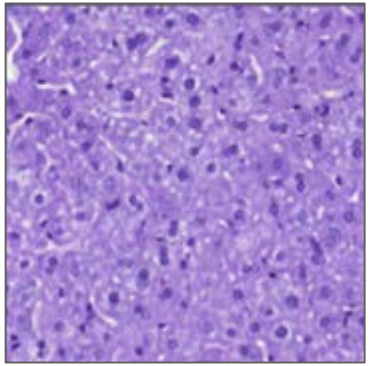
Liver Glycogen
GSDIII Fasted Mice



Vehicle | AGLmRNA/24 hours | AGLmRNA/48 hours







Protein levels:

WT | Vehicle | AGLmRNA/24 hours | AGLmRNA/48 hours

Glycogen levels are reduced and hepatocyte hypertrophy is completely resolved after a single dose, and maintained for 48 hours. PD Response correlates with liver delivered protein levels.

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UX068

Double-Trigger Prodrug for Creatine Transporter Deficiency

UX068 for Creatine Transporter Deficiency

Lead small molecule preclinical program, entering the clinic in 2020

Genetics: X-linked recessive disorder due to mutations in SLC6A8

- Leading cause of X-linked intellectual disability in males
- Females can have mild to severe phenotype

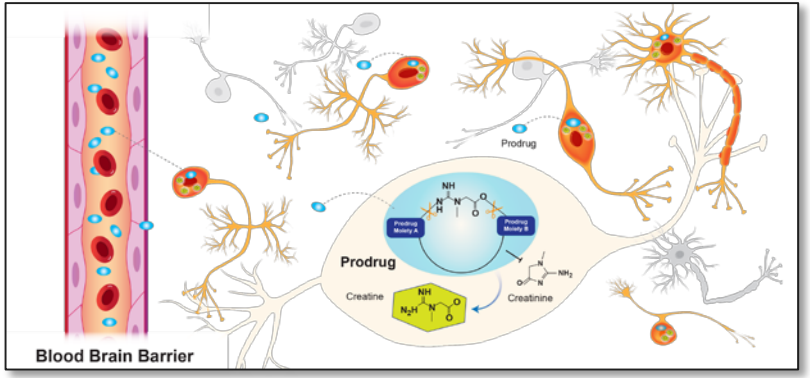
Clinical Presentation (based on literature)

- Neurological deficits
  - Autism, speech/language developmental delays
  - Cognitive / developmental impairment
  - Motor skill delays, extrapyramidal symptoms
  - Seizures
  - Brain Cr levels range from undetectable to ~20 % of normal
    Non-CNS deficits
  - Muscle hypotonia and hypotrophy

Current Management: No SOC, only supportive care, AEDs effective for seizures

WW prevalence: >50,000

Mechanism of Action: Prodrug traverses the BBB and cell membrane and releases creatine to neurons



IND-Enabling Studies Underway
IND Filing Expected 2020

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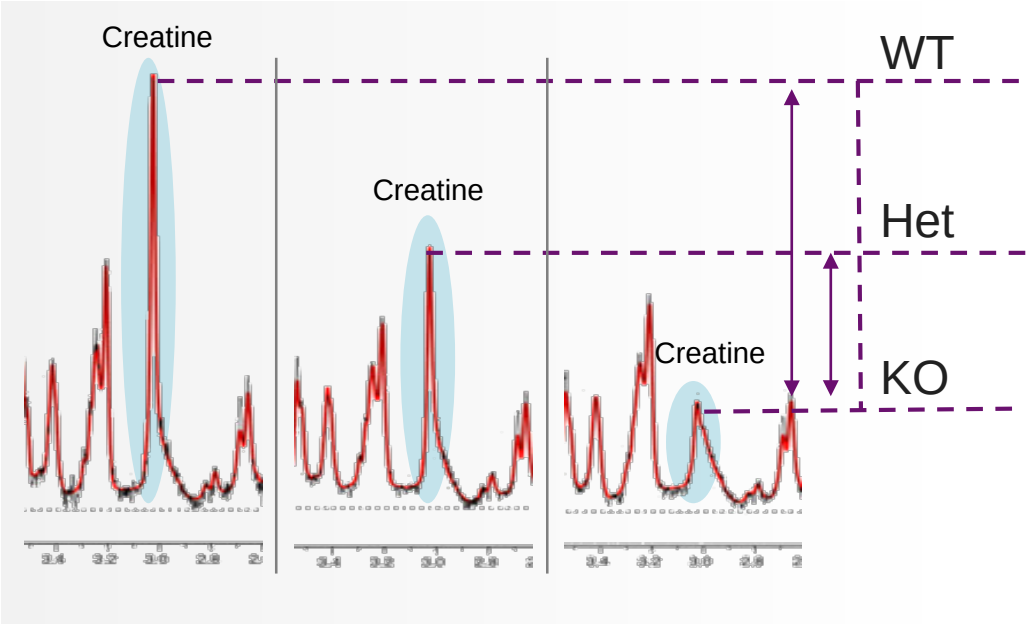
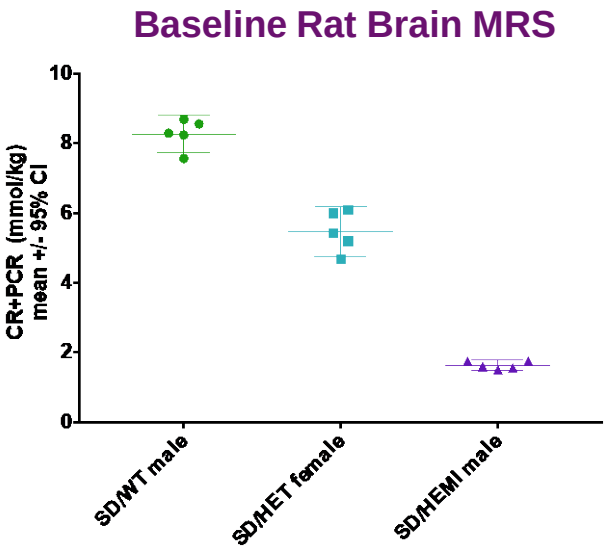
UGX-developed Rat KO Model using CRISPR-technology

MR Spectroscopy, a clinically relevant biomarker, is used to characterize creatine in this animal model



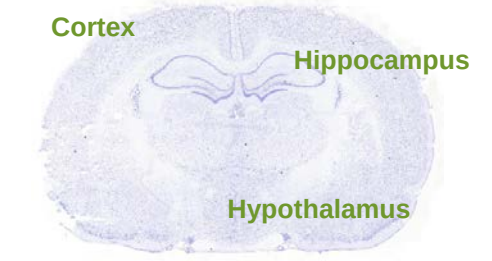
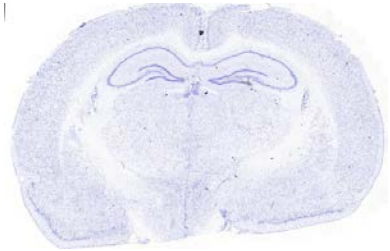
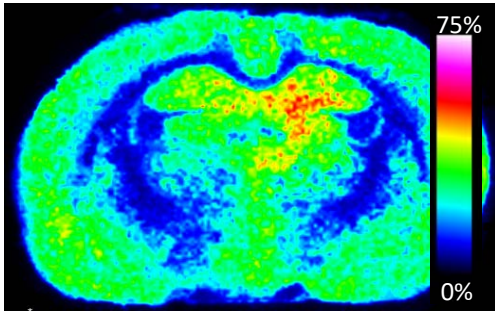
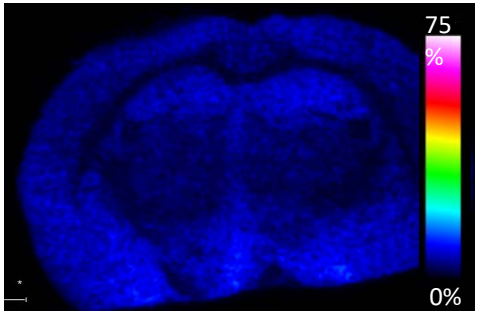
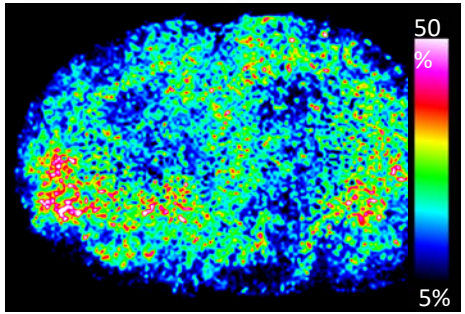


MR Spectroscopy discriminates total brain creatine by genetic phenotype

Widespread Prodrug-derived Brain Creatine Distribution

Creatine is delivered throughout the brain, including cortex and hippocampus

Imaging Mass-Spec for d3-Creatine (prodrug derived)

	Wild Type Rat Endogenous creatine	CrT KO rat Endogenous creatine	CrT KO rat Prodrug derived d3-Creatine
Nissl staining			
d3-Cr imaging Mass Spec			

40 mg/kg dosed over 8 hours to SLC6A8 KO-rat, brains harvested after 24 hours

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GTX-102 Program for Angelman Syndrome

Partnership to develop GeneTx's antisense oligonucleotide (ASO)

New Partnership to Advance GTX-102 for Angelman Syndrome

- **Significant unmet need:** ~60k patients WW, ~22k in U.S., serious disease with no approved treatment options
- **Clear biology of disease:** Disease mechanism well understood, ASO treatment validated and targets disease directly
- **Promising preclinical work** completed by GeneTx
  - IND expected 1H 2020
  - Orphan Drug Designation and Rare Pediatric Disease Designation Granted

Deal terms:

- $20M upfront payment for exclusive option to acquire GeneTx
- Option begins after IND acceptance; Can be extended with $25 million payment to earlier of 30 months from first patient dosing in Phase 1/2 study or 90 days after study results available
- During exclusive option period, GeneTx funds development; Ultragenyx provides strategic guidance, clinical expertise, staff support

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Angelman Syndrome

Debilitating disease with no treatment options

- Serious neurogenetic disorder
  - Estimated prevalence: 1 in 15,000
- Significant unmet need
  - Lack of speech
  - Cognitive impairment
  - Motor dysfunction
  - Seizures
  - Sleep disorder
- No currently approved therapies
  - Not neurodegenerative, potential for reversal of symptoms

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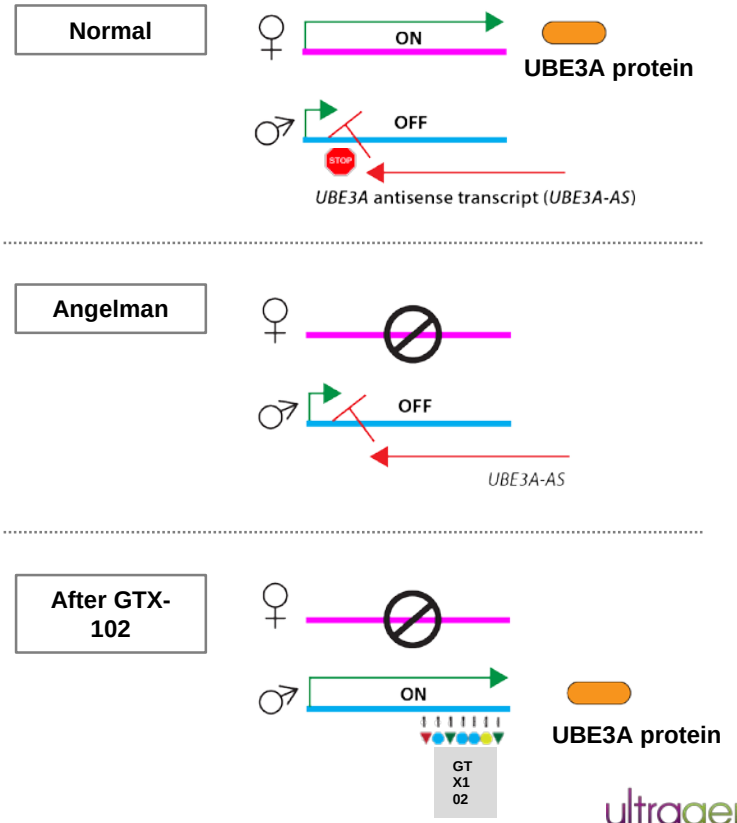
GTX-102
ASO designed to activate the paternal gene

- Angelman defined by loss of expression of single gene UBE3A
  - Paternal UBE3A gene silenced in all mammals, but protein expressed by maternal allele
  - Angelman patients have deletion or mutation preventing maternal expression
- GTX-102 ASO reactivates the paternal UBE3A gene
  - Knocks down paternal UBE3A-antisense transcript (UBE3A-AS)
  - GTX-102 unique in targeting all implicated antisense regions

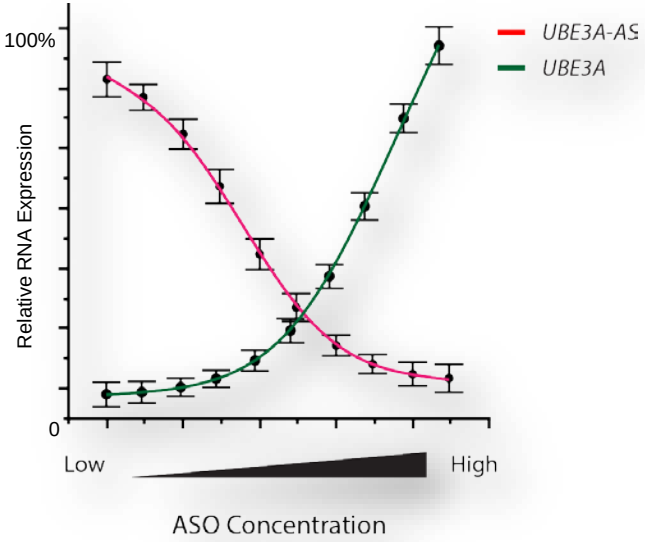


Preclinical Proof of Concept: Specific ASO Discovered with Potent Impact on Releasing Paternal Gene Expression

Human Neuronal Stem Cells

UBE3A-AS knockdown by nearly 100% in human AS neurons after treatment with GTX-102 in vitro. Direct correlation with UBE3A RNA supporting robust reactivation of the paternal UBE3A gene.

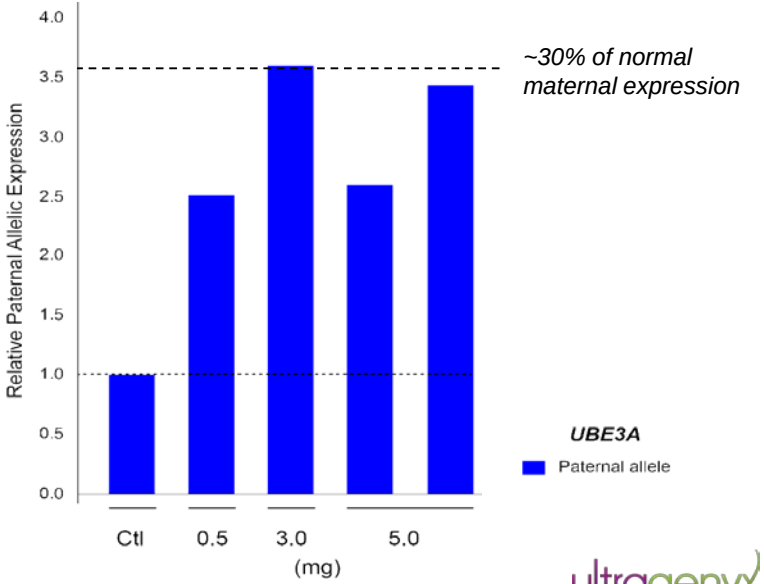
Relative Expression of RNA after GTX-102 Exposure in Cultured AS Neurons



Non-Human Primates

Single-dose of GTX-102 in wild type monkeys demonstrates substantially increased paternal UBE3A gene expression in key brain region. Additional NHP data show broad brain distribution of antisense knockdown.

Relative Increase of Paternal UBE3A Expression in Motor Cortex after Single Dose of GTX-102



Dindot et al., manuscript in preparation

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Finance and Business Summary

Financial Overview
as of June 30, 2019

- **Total Revenue (2Q19): $24.1 million**
- **Total RARE Crysvita Revenue (2Q19): $20.2 million**
- **Cash[1]: $618.3 million**
- **Cash Used in Operations (1H19): $184.8 million**
- **No Debt**

[1]Cash, cash equivalents, and available-for-sale investments as of June 30, 2019

2019 Will Fuel Continued Value Expansion

2010 – 2018

- 2 commercially approved products in 3 major geographic regions
- 34 active or completed clinical studies
- 14+ programs in the development pipeline

2019

- Continue successful global launches of Crysvita and Mepsevii
- UX007 NDA submitted
- DTX301 and DTX401 data readouts
- Begin building our AAV GMP manufacturing facility
- Prepare for up to 3 INDs to be filed in 2020
- Active on BD front

2020+

- Phase 3 gene therapy studies
- Launch UX007 for LC-FAOD if approved
- Initiate clinical trials for Wilson, GSDIII, and CTD programs
- Incorporate other BD deals into the pipeline

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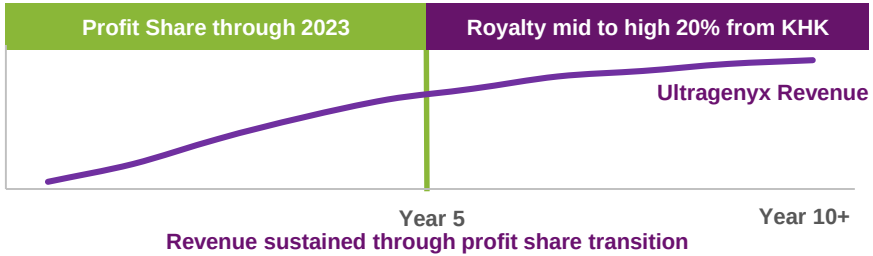
Appendix

Review of KHK Co-Promotion and Profit Share

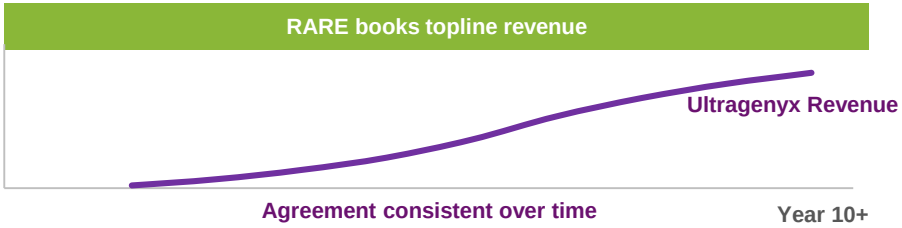
	U.S. AND CANADA	EUROPE	LATIN AMERICA
Commercialization	▪ Ultragenyx launches ▪ KHK books sales ▪ 50/50 profit share for 5 years then tiered revenue share ▪ Shared commercial activities over time	KHK commercializes and books sales	Ultragenyx commercializes and books sales
Royalties	After 5 years, tiered revenue share in mid to high 20% range to Ultragenyx after profit share period	Up to 10% royalty to Ultragenyx	Low single-digit royalty to KHK
Commercial supply	KHK supplies; price is double-digit percentage of net sales	NA	KHK supplies; price is double-digit percentage of net sales

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

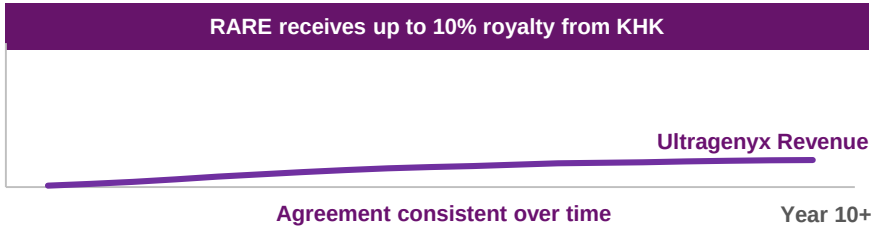
U.S.
Prevalence:
12,000



LatAm
Prevalence:
18,000



EU5
Prevalence:
13,000



Note: charts are for illustrative purposes only

Key Licenses & Intellectual Property

Product	License	Intellectual Property/Royalties
Burosumab (XLH, TIO)	KHK	▪ Shared rights to U.S. patents to generic and specific antibodies and use for treatment of XLH (2022-2032)[1] ▪ See summary of collaboration
Vestronidase Alfa (MPS 7)	St. Louis University	▪ Composition and use for treatment of MPS 7 (2035) ▪ Low single-digit royalty
UX007 (LC-FAOD)	Baylor Research Institute (BRI)	▪ Composition (2020-2029/30)[1] ▪ Use for treatment of LC-FAOD (2020) ▪ Mid single-digit royalty
DTX301 (OTC Deficiency)	Sub-License from REGENXBIO of UPENN IP	▪ Composition and use for treatment of OTC Deficiency (2022-2035) ▪ Low to mid single-digit royalty
DTX401 (GSDIa)	Sub-License from REGENXBIO of UPENN IP	▪ Composition for treatment of GSDIa (2022-2024) ▪ Low to mid single-digit royalty
	NIH (Non-Exclusive)	▪ Composition for treatment of GSDIa (2034) ▪ Low single-digit royalty

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

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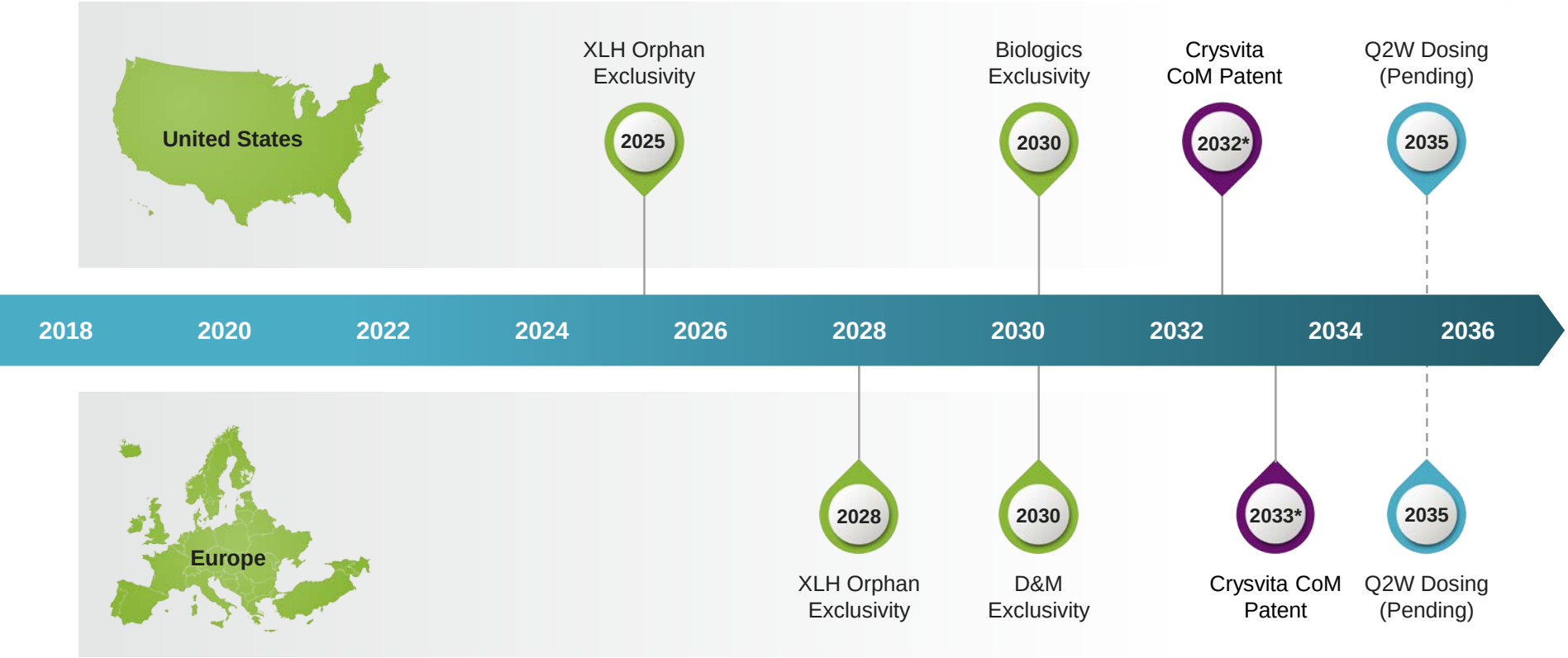
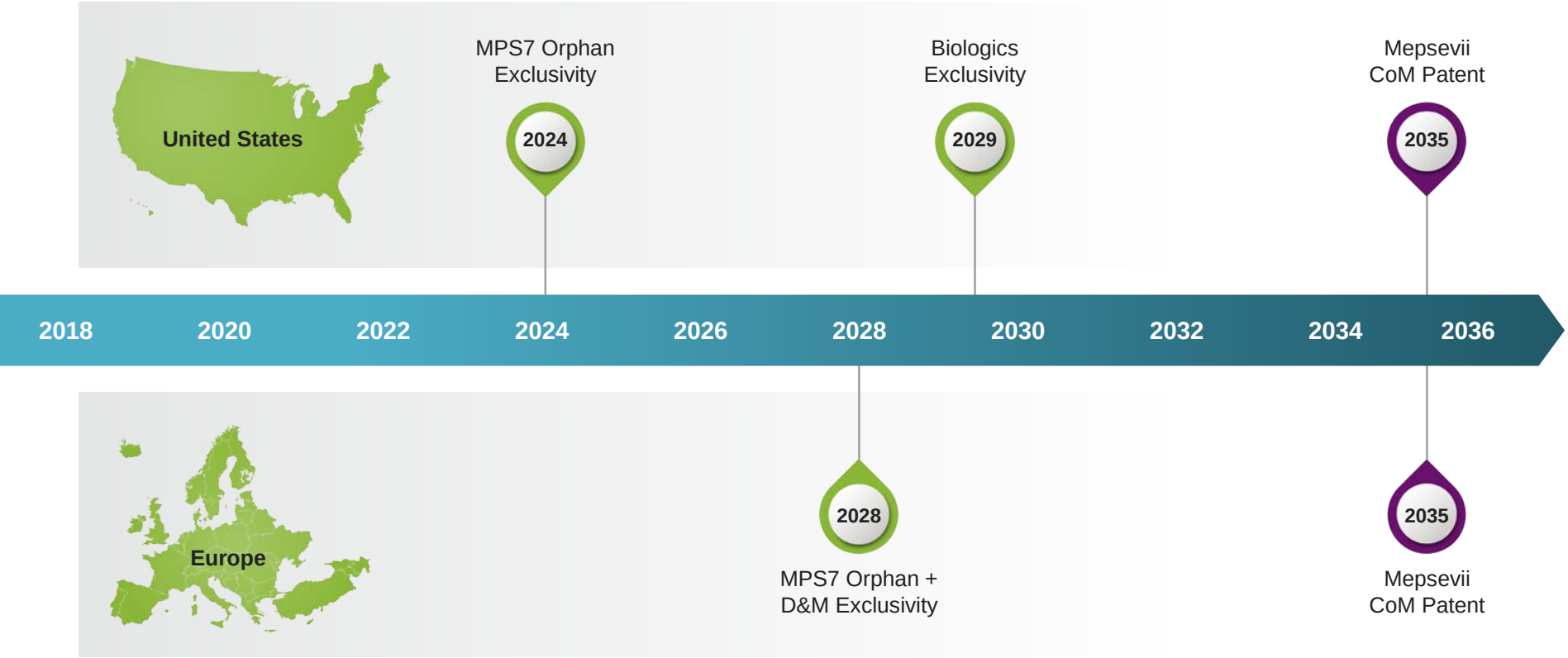
Crysvita® Exclusivity Summary



*Includes projected US PTE and EU SPC awards

Mepsevii™ Exclusivity Summary

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



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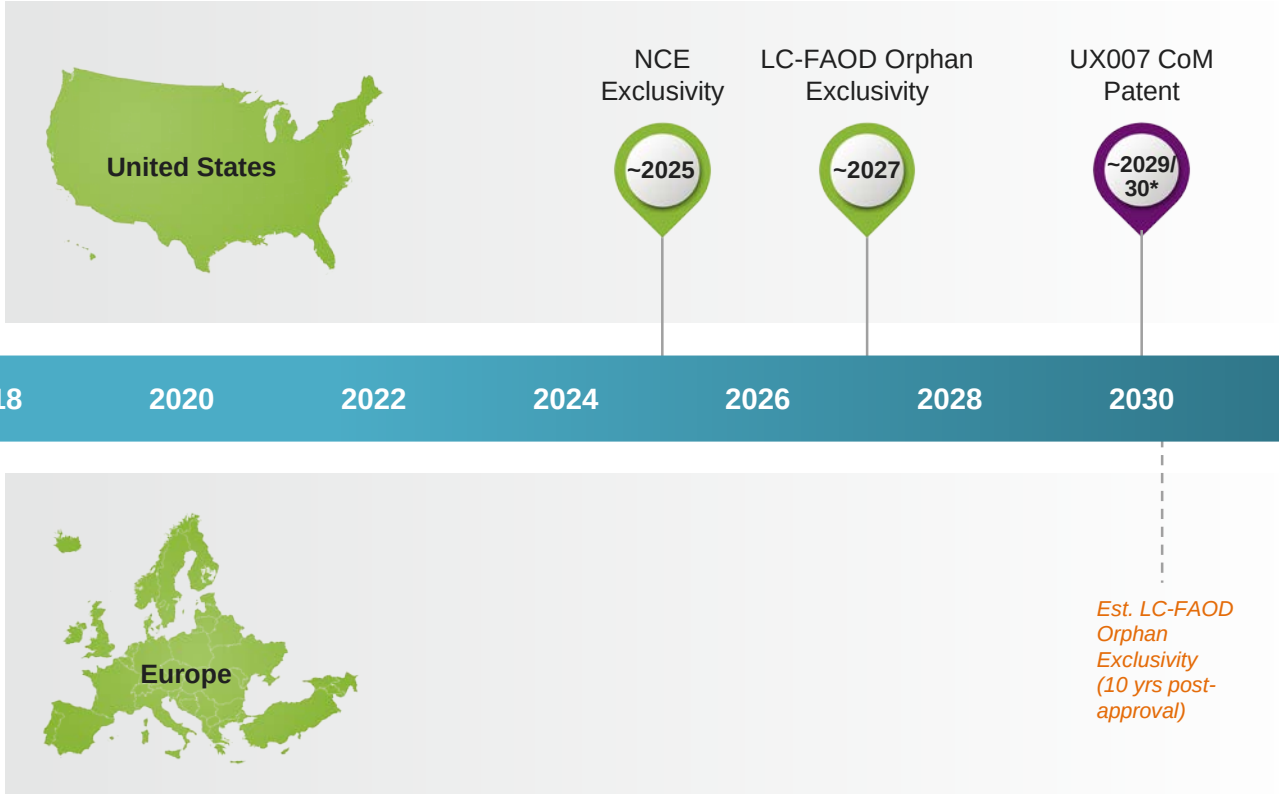
UX007 Exclusivity Summary



*Includes projected U.S. PTE award