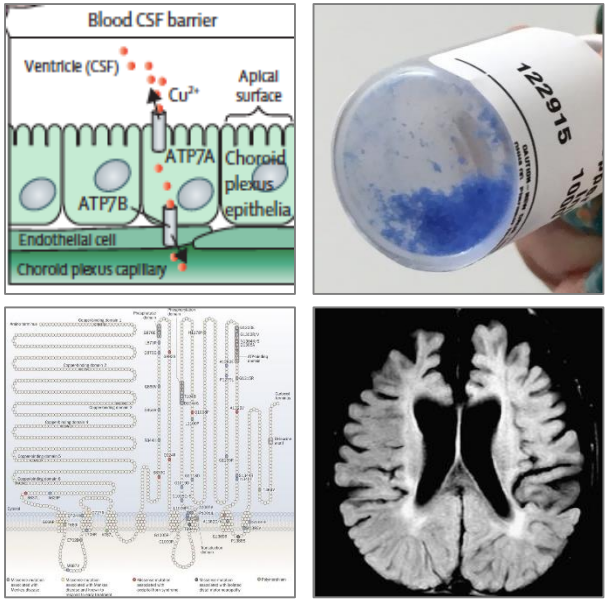


CYPRIUM THERAPEUTICS

A subsidiary company of FORTRESS BIOTECH

Corporate Presentation

November 2018

Forward Looking Statements

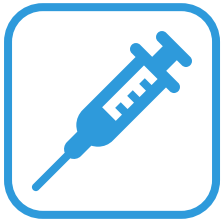
This presentation may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, as amended. Such statements include, but are not limited to, any statements relating to our growth strategy and product development programs and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock price. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; government regulation; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; uncertainties relating to preclinical and clinical testing; risks relating to the timing of starting and completing clinical trials; our dependence on third-party suppliers; our ability to attract, integrate, and retain key personnel; the early stage of products under development; our need for substantial additional funds; patent and intellectual property matters; competition; as well as other risks described in our SEC filings. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.

Cover Page Image Source: Kaler SG

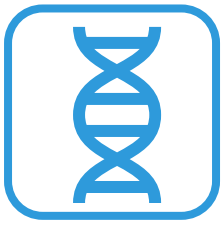
Company Highlights

- **Cyprium Therapeutics** is a company majority-owned by Fortress Biotech (Nasdaq: FBIO) with a focus on the development and commercialization of novel therapies for Menkes disease, a rare and fatal pediatric disease in copper metabolism.

- In March 2017, Cyprium acquired the World-Wide development and commercial rights to the Menkes program at NIH/NICHD through CRADA and licensing agreements with NICHD.



- **CUTX-101 (Copper Histidinate Injections):**
  - Already reported compelling Phase 1/2 data; Phase 3 study ongoing
  - Orphan Drug and Fast Track Designations granted by FDA
  - Natural History Study of untreated Menkes patients ongoing
  - Meetings with FDA to discuss regulatory pathway
  - **Potential NDA filing in 2019 – would be the first FDA-approved treatment for Menkes Disease**



- **AAV-ATP7A Gene Therapy:**
  - Preclinical and already has Orphan Drug Designation from FDA
  - **Expects to nominate candidate for clinical development in 2019**

Copper in Human Development and Health

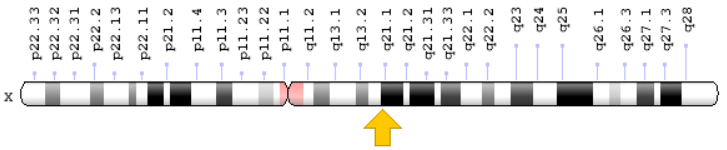
Biological Functions	Copper Containing Proteins
Brain Development	
Catecholamine production	Dopamine β-hydroxylase
Mitochondrial respiration	Cytochrome C oxidase
Iron and copper transport	Ceruloplasmin
Peptide amidation	Peptidylglycine α-amidating monooxygenase
Antioxidant defense	Superoxide dismutase
Connective tissue formation	Lysyl oxidase
Pigment formation	Tyrosinase

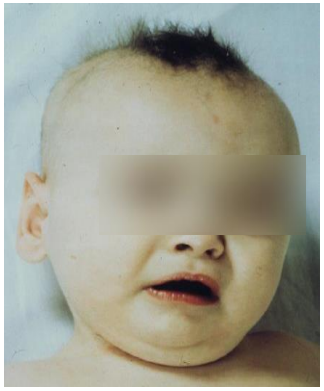
Source: de Bie, et al, 2007; Image source: freepik.com

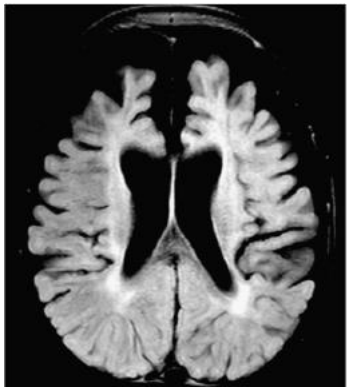
Menkes Disease

Menkes Disease

- First described by Dr. John Menkes in 1962
- X-linked recessive disease: affecting mostly boys
- Ultra-rare at 1: 50,000 - 100,000 live births per year
- Disorder of copper metabolism
- Mutations in the Copper transporter ATP7A
- **If untreated, premature death ~ 3 years**







Distinctive clinical phenotypes

- Sparse, depigmented hair (“kinky hair”)
- Neurodegeneration/Neurodevelopment delays
- Failure to thrive
- Connective tissue problems

Distinctive biochemical phenotypes

- Low copper in blood and brain
- Abnormal catecholamine levels

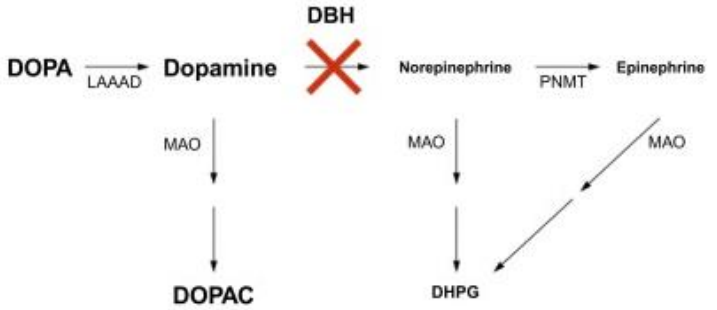
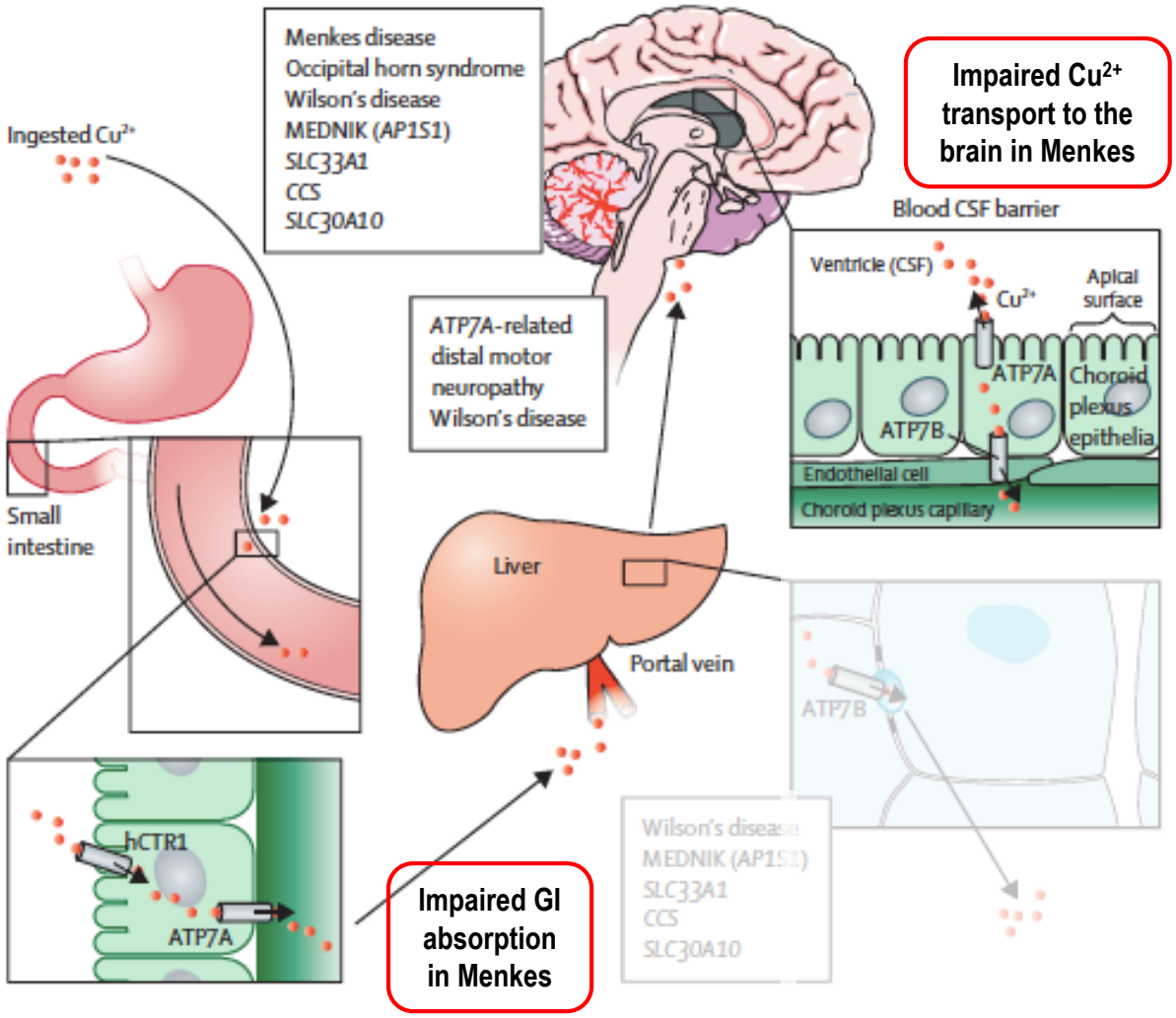


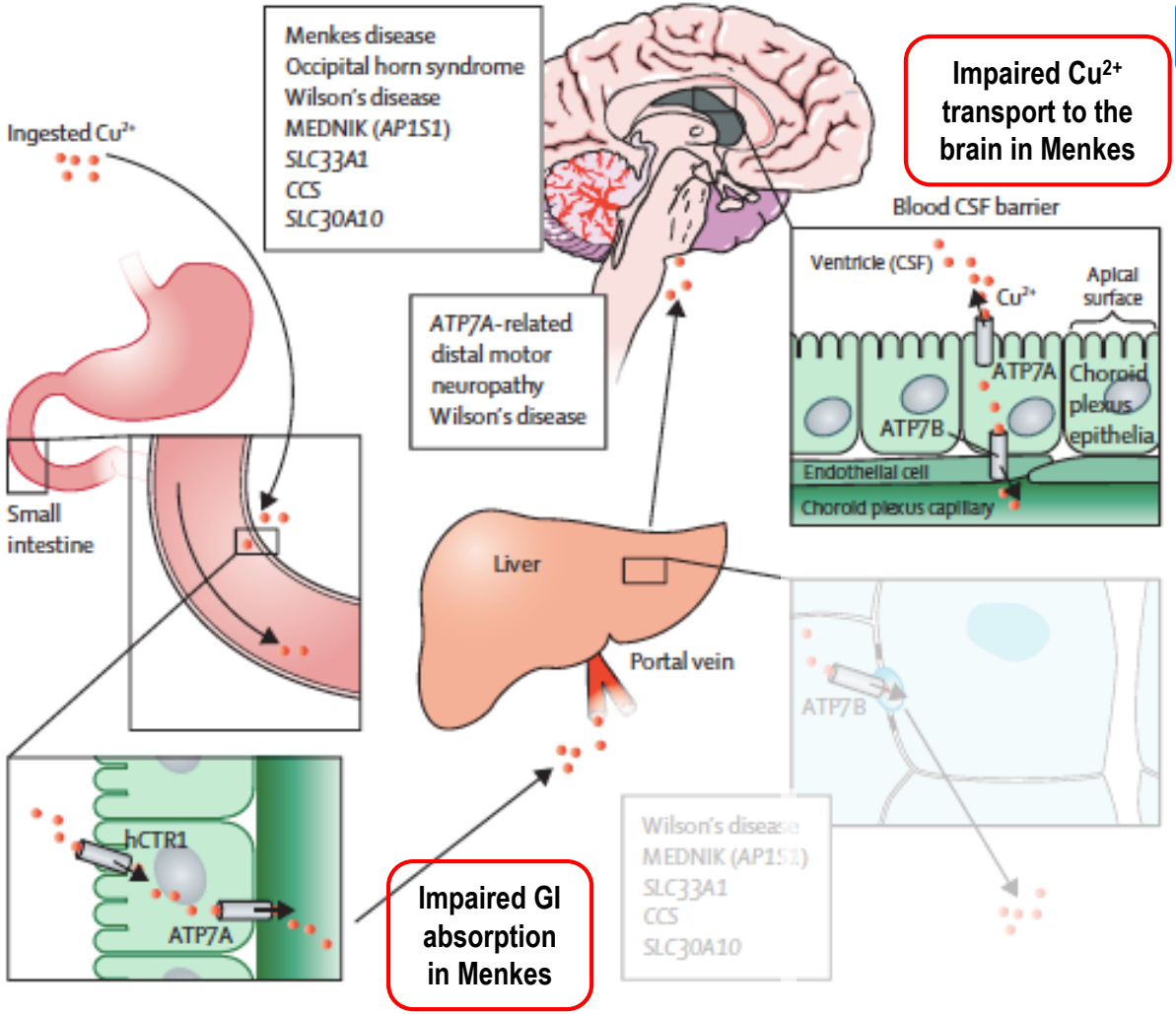
Image Source: Stephen G. Kaler, MD; NCBI;

ATP7A Critical for Copper Transport to the Brain & GI



Bandmann et al, Lancet Neuro 2015

Therapeutic Strategy for Menkes Disease



Bandmann et al, Lancet Neuro 2015

1

CUTX-101 Copper Histidinate

- SC injection to replenish Cu^{2+}
- Bypass GI absorption of Cu^{2+} (impaired in Menkes patients)
- Better tolerability (pH 7.4)
- May not be sufficient alone in some Menkes patients

Phase 1/2 efficacy data published;
Phase 3 Study ongoing;
Natural History Study ongoing

2

AAV-ATP7A Gene Therapy

- Codon-optimized reduced-sized ATP7A to be delivered via AAV vector (Preclinical)
- May restore Cu^{2+} transport
- Will require Cu^{2+} injections

Preclinical

Partnership with NICHD/NIH

- **Menkes disease program at *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD):**
  - Led by Stephen G. Kaler, MD, Senior Investigator and Head, Section on Translational Neuroscience, Molecular Medicine Branch, NICHD
- **Cooperative Research And Development Agreement (CRADA)**
  - Executed and announced in March 2017
  - Research Plan describes the responsibilities of both parties
  - NIH granted Cyprium Authorization to file NDA for CUTX-101
  - Dr. Kaler remains the PI of Menkes clinical study at NICHD
  - Cyprium continues GMP manufacturing of CUTX-101 for clinical studies at NICHD
  - Cyprium provides research support to Dr. Kaler's lab based on milestones
- **Licensing Agreement for AAV-ATP7A Gene Therapy**
  - Executed and announced in March 2017
  - Cyprium obtained World wide exclusive rights to develop and commercialize codon-optimized AAV-ATP7A Gene Therapy program for the treatment of Menkes disease and related disorders

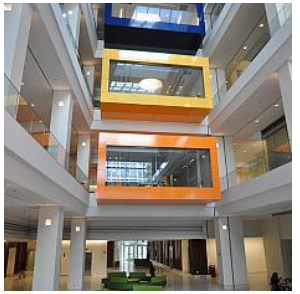


Image Source: NIH.gov

Phase 1/2 Study of CUTX-101 in Menkes Patients

- **Phase 1/2 Study (NCT00001262)**
- **Status: Completed**

Primary Endpoint:
Denver Developmental Screening Test
- Gross Motor
- Fine Motor
- Personal-Social
- Language

Other Outcomes: Weight, Length, Head Circumference, **3-Year Mortality Rate**

Classic Menkes Disease Dx
- Neurochemical levels
- ATP7A mutation analysis

57

NICHD

Pre-specified Categories

Group I: Late Treatment
CuHis treatment begins:
- After 1 month of age
- After onset of symptoms

22

CUTX-101 Injections
- **Age < 1 Yr** 250ug SC BID
- **Age > 1 Yr** 250ug SC QD

Group II: Early Treatment
CuHis treatment begins:
- Within 1 month of age
- Before onset of symptoms

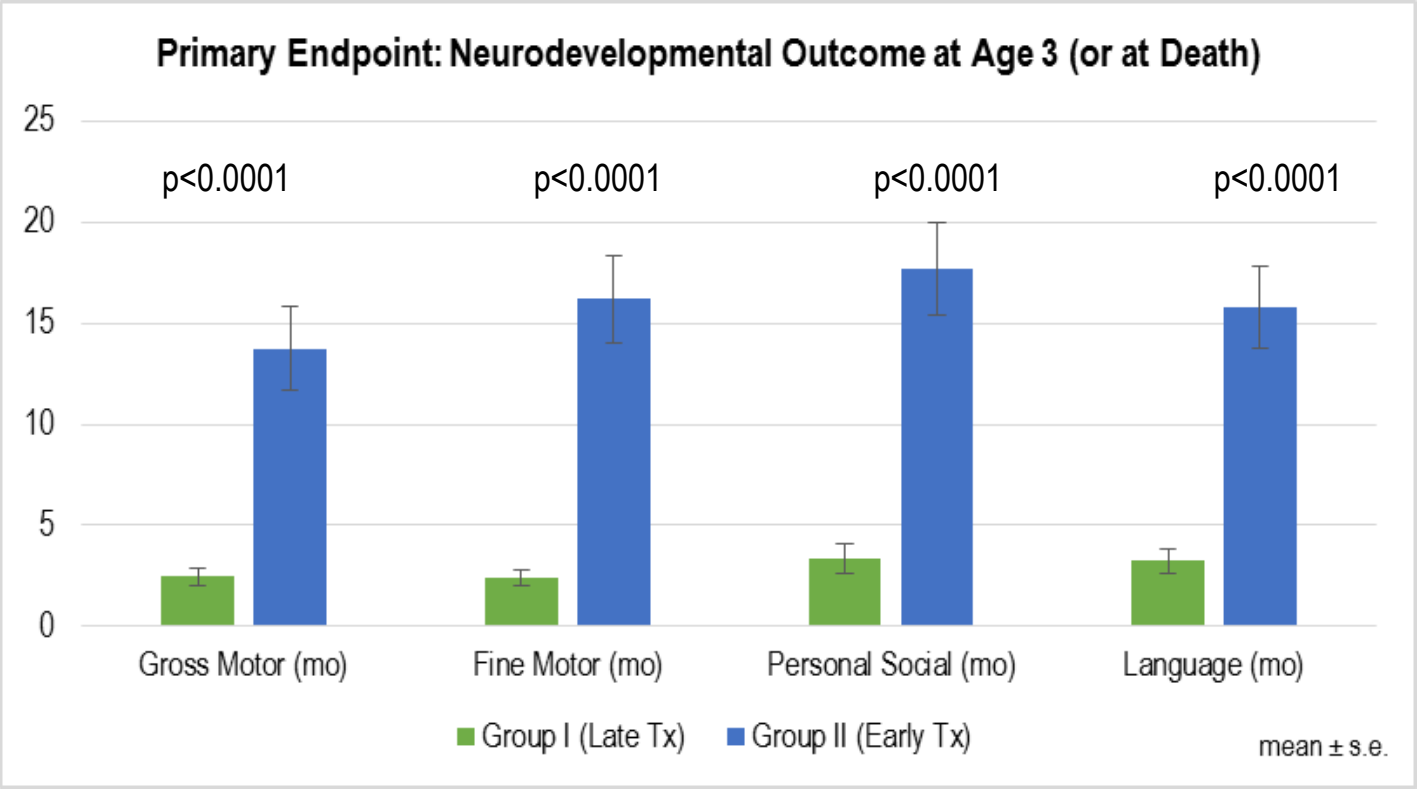
35

CUTX-101 Injections
- **Age < 1 Yr** 250ug SC BID
- **Age > 1 Yr** 250ug SC QD

Kaler et al, NEJM 2008; Kaler SG, JTEMB 2014

CUTX-101 improved neurodevelopment outcomes

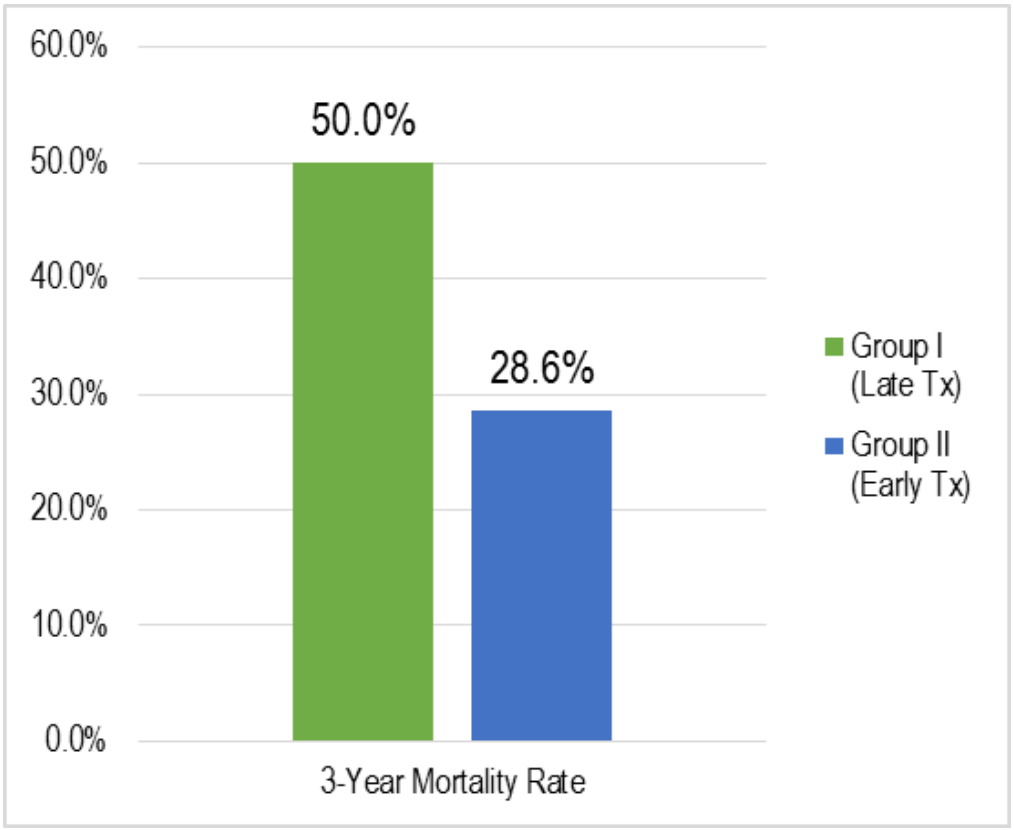
- Early Treatment with CUTX-101 significantly improved all four scales of Denver Developmental Screening Test in Menkes patients (p<0.0001).



Kaler et al, NEJM 2008; Kaler SG, JTEMB 2014

Early Treatment of CUTX-101 Improved 3-Year Mortality Rate

- Menkes patients who received early treatment of CUTX-101 had a lower 3-Year Mortality rate compared to late treatment.



Kaler et al, NEJM 2008; Kaler SG, JTEMB 2014

Clinical Summary for CUTX-101

- Early treatment with CUTX-101 significantly improved Denver Developmental Screening Test in all 4 scales (gross motor, fine motor/adaptive, personal-social, and language).
- Menkes patients who received early treatment of CUTX-101 had a lower 3-Year mortality rate (28.6%) compared to late treatment (50%). Importantly, 3-Year mortality rate for Menkes patients treated with CUTX-101 was significantly lower than untreated historical control (preliminary data not yet reported).
- CUTX-101 appears to be safe and well tolerated. Low incidence of renal tubular dysfunction was observed, which was reversible upon drug discontinuation.
- NICHD is conducting a natural history study of Menkes disease patients who have not been treated with copper supplements. Data from this natural history study may serve as a historical control to demonstrate the efficacy of CUTX-101.

CUTX-101: Current Status & Next Steps

Regulatory:

- FDA has been very helpful in providing guidance for regulatory pathway towards NDA submission for CUTX-101. FDA recommended Cyprium/NICHD to continue frequent communications.
- FDA acknowledged Cyprium would submit NDA based on data from NICHD studies and historical control, using survival as primary endpoint.
- FDA granted Fast Track Designation
- Additional regulatory activities in US and other territories

Clinical:

- Continue Phase 3 Study of CUTX-101 in Menkes patients (NICHD) (NCT00811785)
- Continue Natural History Study of Untreated Menkes Patients (NICHD)

CMC:

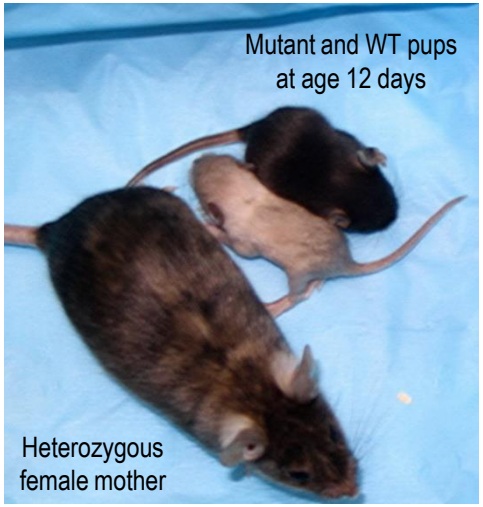
- Continue GMP manufacturing of CUTX-101
- Additional CMC and product development activities

Others:

- Additional nonclinical studies will be planned based on FDA communications.

AAV-ATP7A Gene Therapy for Menkes Disease

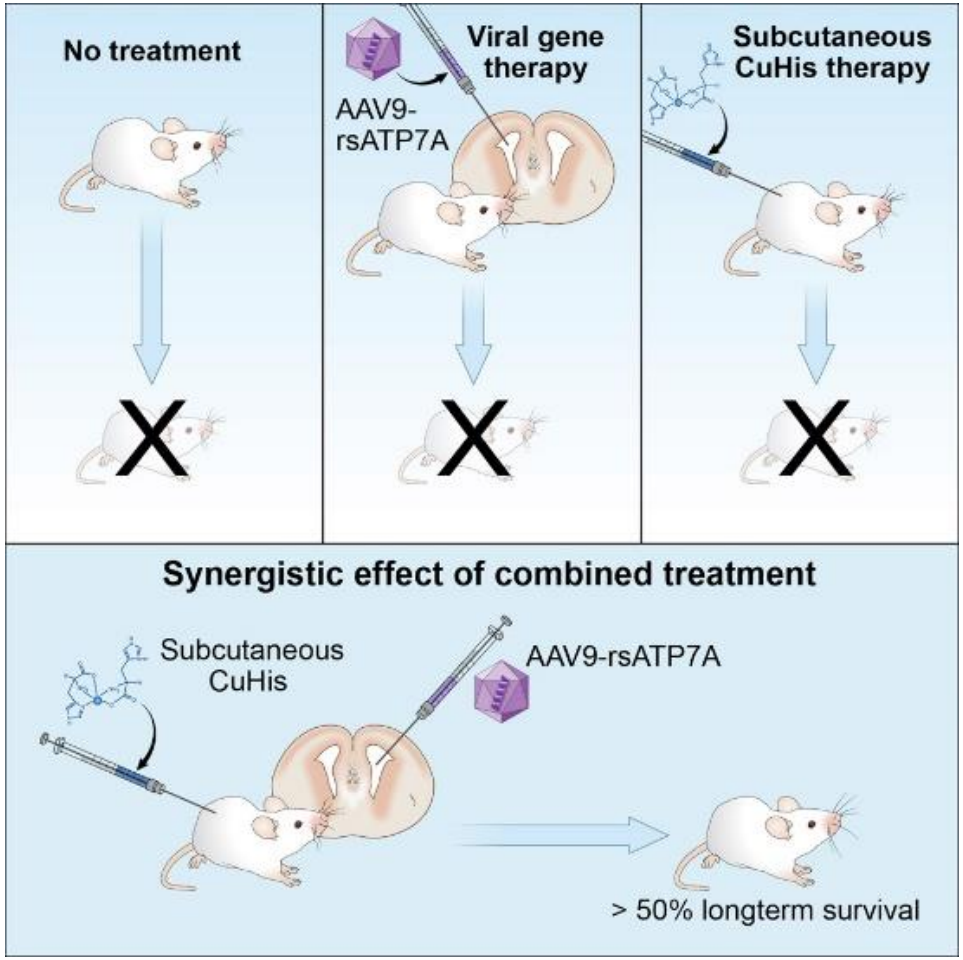
- *Mottled – brindled* mouse model recapitulates the disease phenotype
  - $Atp7a^{mo\text{-}br}$ phenotype
  - A 6 bp in-frame deletion in exon 11 of Atp7a
  - Depigmented coat color and curly whiskers
  - Premature death (~13 days of age)
  - Poor growth; Neurological symptoms
  - Low brain copper; Abnormal catecholamine levels



Source: Stephen G. Kaler, MD;

AAV-ATP7A Gene Therapy for Menkes Disease

- NICHD has developed several constructs for reduced size, codon-optimized AAV-ATP7A gene therapy
- AAV-ATP7A + SC CuHis administration led to:
  - Improvements in muscle strength, balance and coordination in preclinical model
  - Improved biochemical phenotype (Cu and catecholamine)
  - Improved survival



Source: Stephen G. Kaler, MD; Haddad et al, 2018

Projected Milestones

	CUTX-101 (Copper Histidinate)	AAV-ATP7A Gene Therapy
2018	▪ FDA granted Fast Track Designation ✓ ▪ Continue communications with FDA to determine development path towards NDA submission for CUTX-101 ▪ Continue Phase 3 Study of CUTX-101 in Menkes patients (NICHD) ▪ Continue Natural History Study of Untreated Menkes Patients (NICHD) ▪ Planning for PK and nonclinical studies ▪ GMP manufacturing of CUTX-101	▪ Continue *in vitro* and *in vivo* studies to determine the optimal construct for AAV-ATP7A Gene Therapy (NICHD)
2019	▪ Potential NDA submission for CUTX-101 (pending outcomes of FDA meetings)	▪ Nominate candidate for clinical development ▪ Initiate IND enabling studies

Back-up Slides

Selected Drugs Approved for Rare Pediatric Diseases

Year	Company	Drug	Indication	Study Size	No. of patients	Endpoint	Study Design
2014	BioMarin	Vimizim (elosulfase alfa)	MPS IVA (Morquio A syndrome)	176	~800	6MWT	RCT
2015	United Therapeutics	Unituxin (dinutuximab)	High risk neuroblastoma	226	650 new cases of neuroblastoma	RFS?	RCT
2015	Asklepion Pharmaceuticals	Cholbam (cholic acid)	bile acid synthesis disorders due to single enzyme defects	50	1 in 50,000	improvements in baseline liver function tests and weight	Single arm
			peroxisomal disorders (incl. Zellweger spectrum disorders)	29	1 in 50,000 live births	improvements in baseline liver function tests and weight	Single arm
2015	Wellstat Therapeutics	Xuriden (uridine triacetate)	hereditary orotic aciduria	**4**	20 pts worldwide	stability of the hematologic parameters + case reports from literature	Case report
2015	Alexion Pharmaceuticals	Strensiq (asfotase alfa)	perinatal, infantile and juvenile-onset hypophosphatasia (HPP)	99	1 in 100,000 newborns	improvement in low weight or short stature or maintained normal height and weight compared to historical control; improvements in bone mineralization	Historical control
2015	Alexion Pharmaceuticals	Kanuma (sebelipase alfa)	lysosomal acid lipase (LAL) deficiency: Wolman + CESD	**9 infants w Wolman**	Wolman disease: 1-2 infants / million births;	Survival	Historical control
				66 pediatric & adult patients w CESD	CESD affects 25 per million births	improvement in LDL-cholesterol levels and other disease-related parameters	RCT
2016	Sarepta Therapeutics	Exondys 51 (eteplirsen)	Duchenne muscular dystrophy (DMD)	12+13=25	1 in 3,600 male infants worldwide	Dystrophin expression	Single arm
2016	Ionis Pharmaceuticals	Spinraza (nusinersen)	spinal muscular atrophy (SMA)	121 (82 at interim)	1 in 10,000 live births	HINES Motor (Responder)	RCT
2017	Marathon Pharmaceuticals	Emflaza (deflazacort)	Duchenne muscular dystrophy (DMD)	196	1 in 3,600 male infants worldwide	change between Baseline and Week 12 in average strength of 18 muscle groups	Previously published RCT
2017	BioMarin	Brineura (cerliponase alfa)	Batten Disease -- late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)	22 symptomatic pediatric patients with CLN2 disease	2 to 4 of every 100,000 live births	decline in the Motor domain of the CLN2 Clinical Rating Scale at 48, 72 and 96 weeks.	single-arm dose escalation study + natural hx cohort
2017	Novartis	Kymriah (tisagenlecleucel)	pediatric and young adult patients with acute lymphoblastic leukemia (ALL).	63	15-20% of 3,100 patients (465-620)	overall remission rate within three months of treatment	one multicenter clinical trial
2017	UltraGenyx	Mepsevii (vestronidase alfa-vjbk)	mucopolysaccharidosis type VII (MPS VII)/ Sly syndrome	23 patients (12 randomized)	1 in 250,000 births	6MWT	RCT (pbo then cross-over to active tx)
2017	Spark Therapeutics	Luxturna (voretigene neparvovec-rzyl)	biallelic RPE65 mutation-associated retinal dystrophy	41 patients; 31 randomized	1,000 to 2,000 patients in the U.S.	ability to navigate an obstacle course at various light levels	RCT
2018	Ultragenyx	Crysvita (burosumab-twza)	x-linked hypophosphatemia (XLH)	52 XLH patients (age 5-12); 13 XLH pts (age 1-4)	3,000 children and 12,000 adults in U.S.	normal phosphorus levels	RCT

Source: www.raps.org; NORD; FDA.gov; FDA Prescribing Information

Thank you!

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