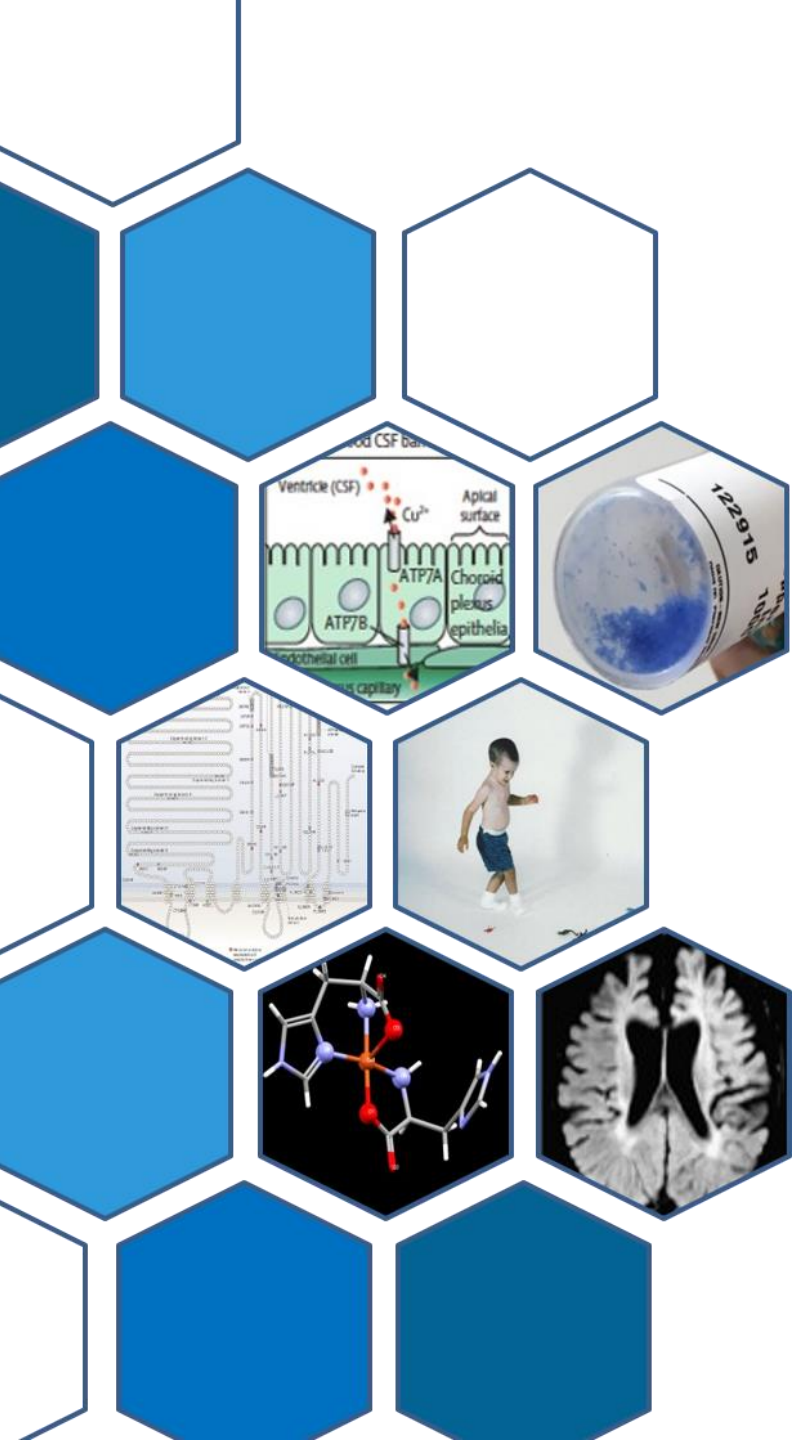


CYPRIUM THERAPEUTICS

Corporate Presentation

September 2019

Forward Looking Statements

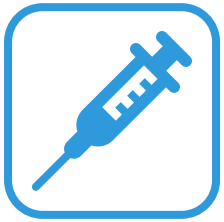
This presentation may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, as amended. Such statements include, but are not limited to, any statements relating to our growth strategy and product development 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 Sources: Kaler SG; NIH

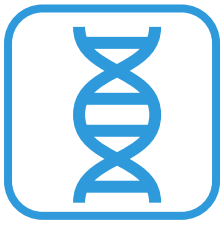
Company Highlights

- **Cyprium Therapeutics** is an orphan disease company 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):**
  - Reported compelling Phase 1/2 data; Phase 3 study completed enrollment
  - Orphan Drug and Fast Track Designations granted by FDA
  - Natural History Study of untreated Menkes patients ongoing
  - Meetings with FDA to discuss regulatory pathway
  - Eligible for the Rare Pediatric Disease Priority Review Voucher
  - **NDA filing in 1H20 – 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 1H20**

Copper in Human Development and Health

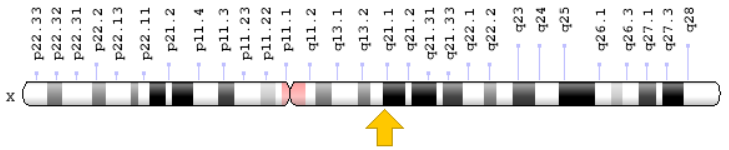
Biological Functions	Copper Containing Proteins
Brain Development	
Catecholamine production	Dopamine β-hydroxylase
Mitochondrial respiration	Cytochrome C oxidase
Iron and copper transport	Ceruloplasmin
Peptide amidation	Peptidylglycine α-amidating monooxygenase
Antioxidant defense	Superoxide dismutase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

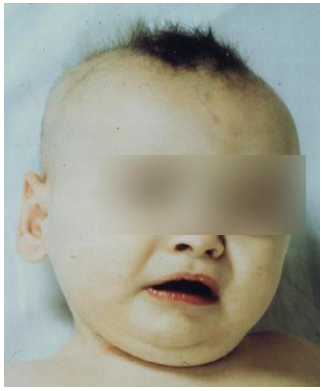
Source: de Bie, et al, 2007; Image source: freepik.com

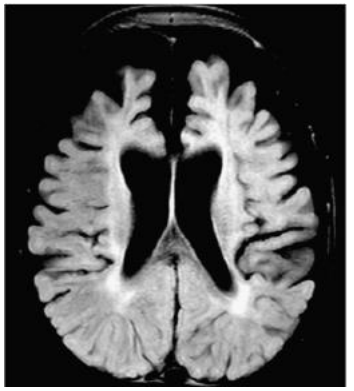
Menkes Disease

Menkes Disease

- First described by Dr. John Menkes in 1962
- X-linked recessive disease: affecting mostly boys
- 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")
- Neuro symptoms: Seizures, Hypotonia, and Developmental delays
- Failure to thrive
- Connective tissue problems

Distinctive biochemical phenotypes

- Low copper in blood and brain
- Abnormal catecholamine levels

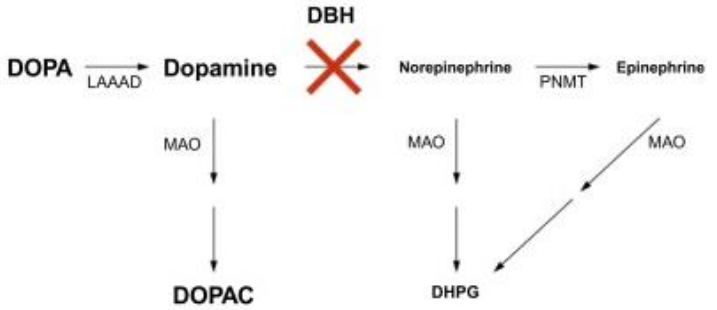
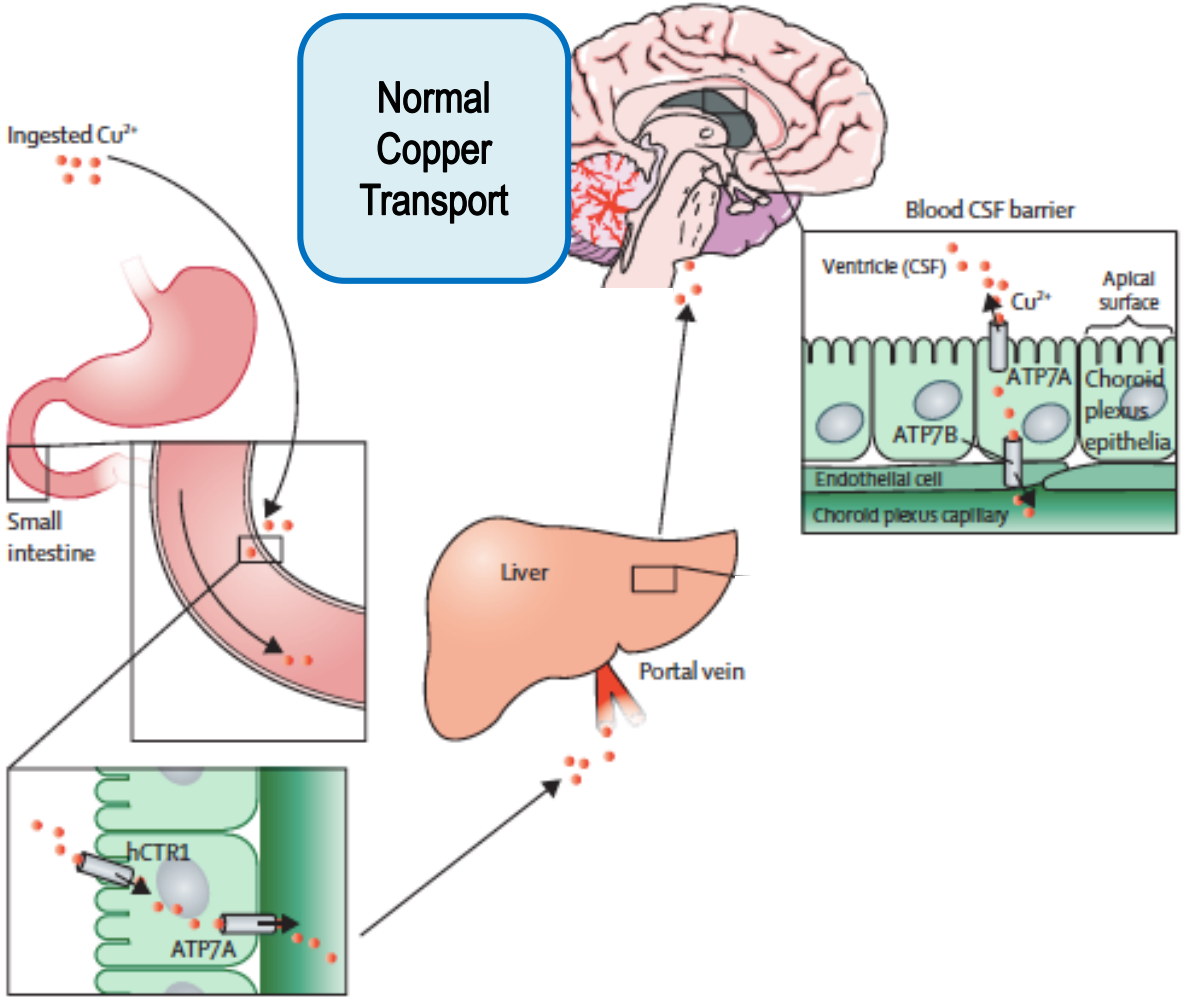


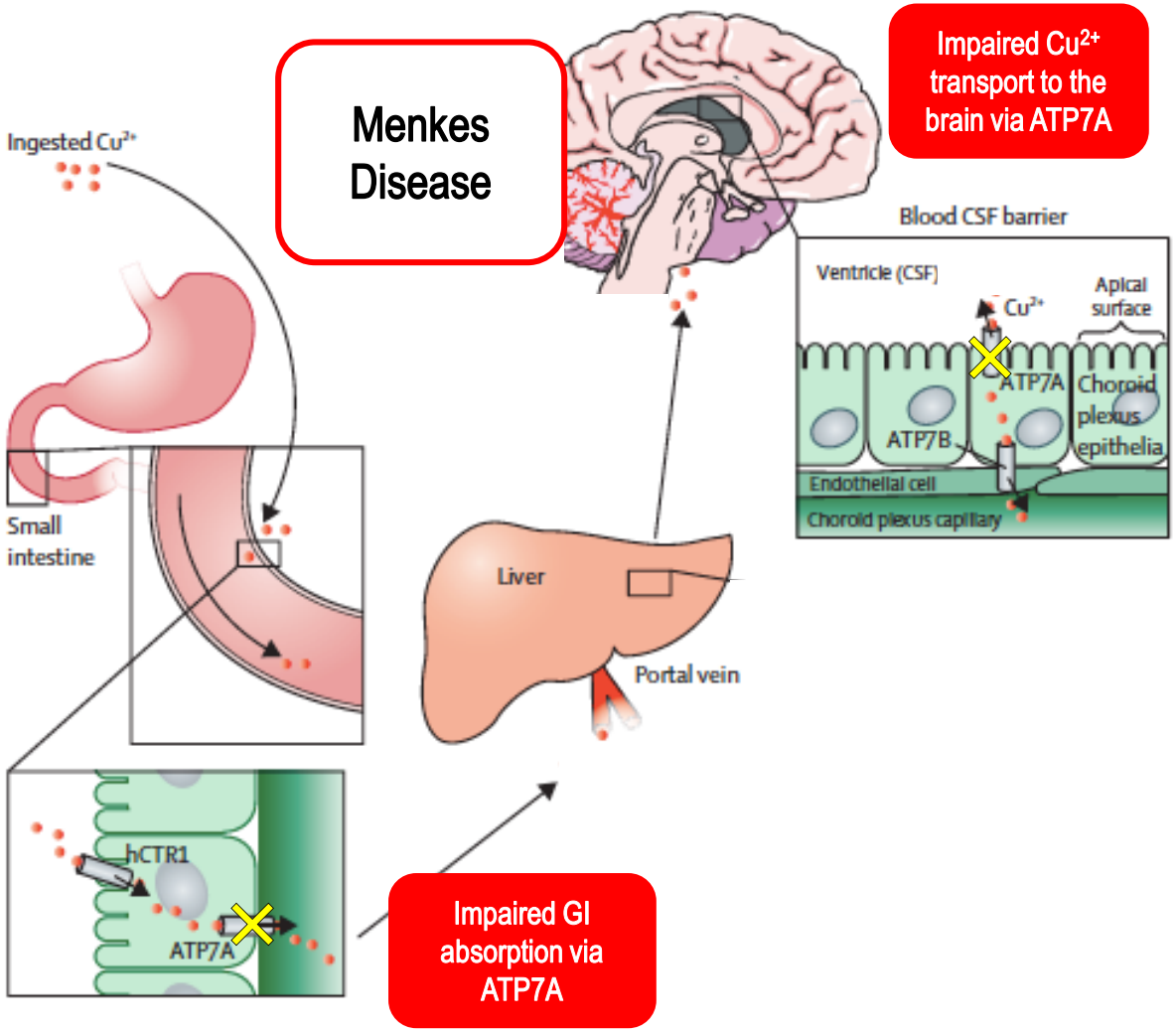
Image Source: Stephen G. Kaler, MD; NCBI;

ATP7A Critical for Copper Transport to the Brain & GI



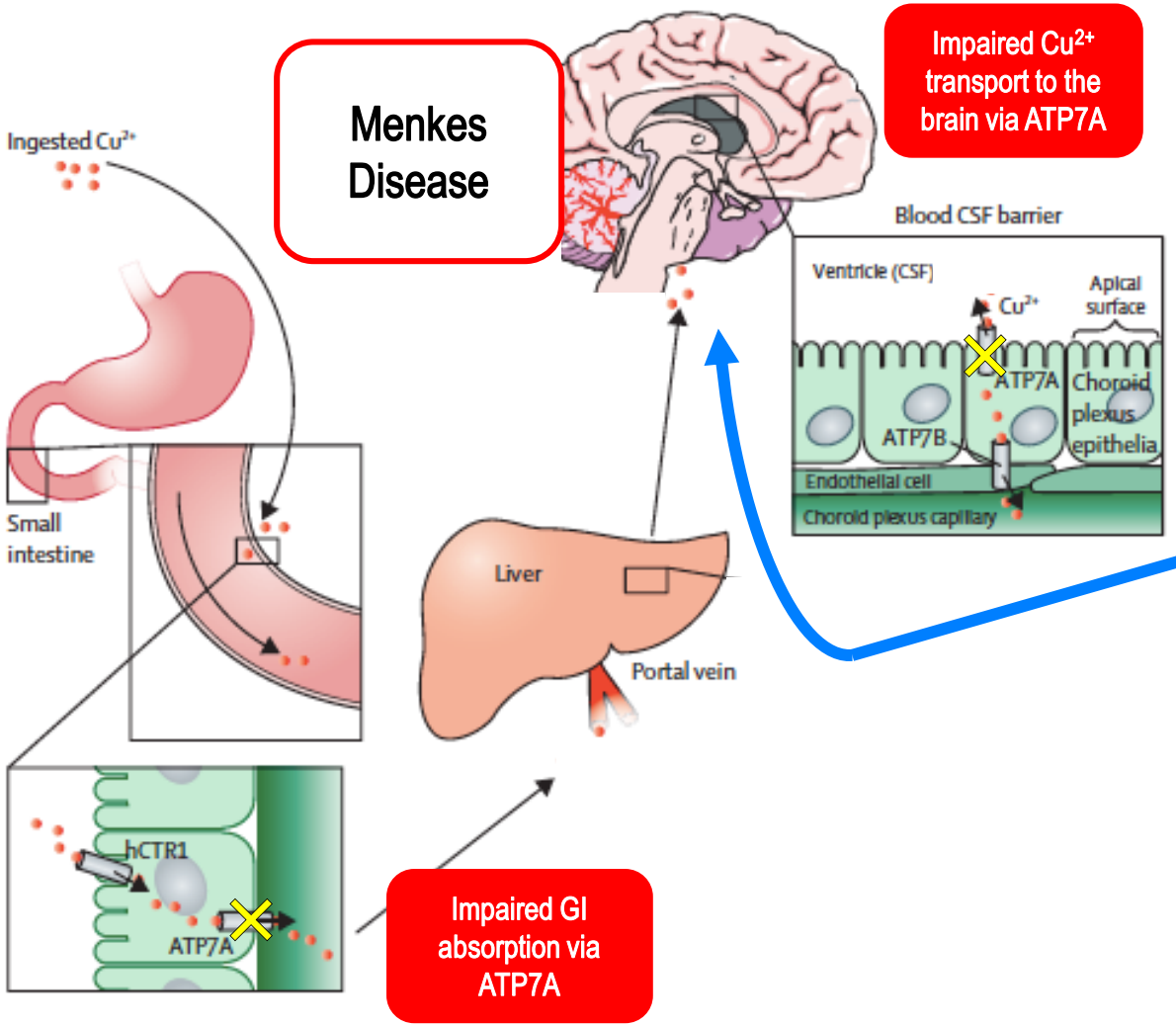
Adapted from: Bandmann et al, Lancet Neuro 2015

Copper Transport is impaired in Menkes Disease



Adapted from: Bandmann et al, Lancet Neuro 2015

Therapeutic Strategy for Menkes Disease: CUTX-101 (Copper Histidinate)



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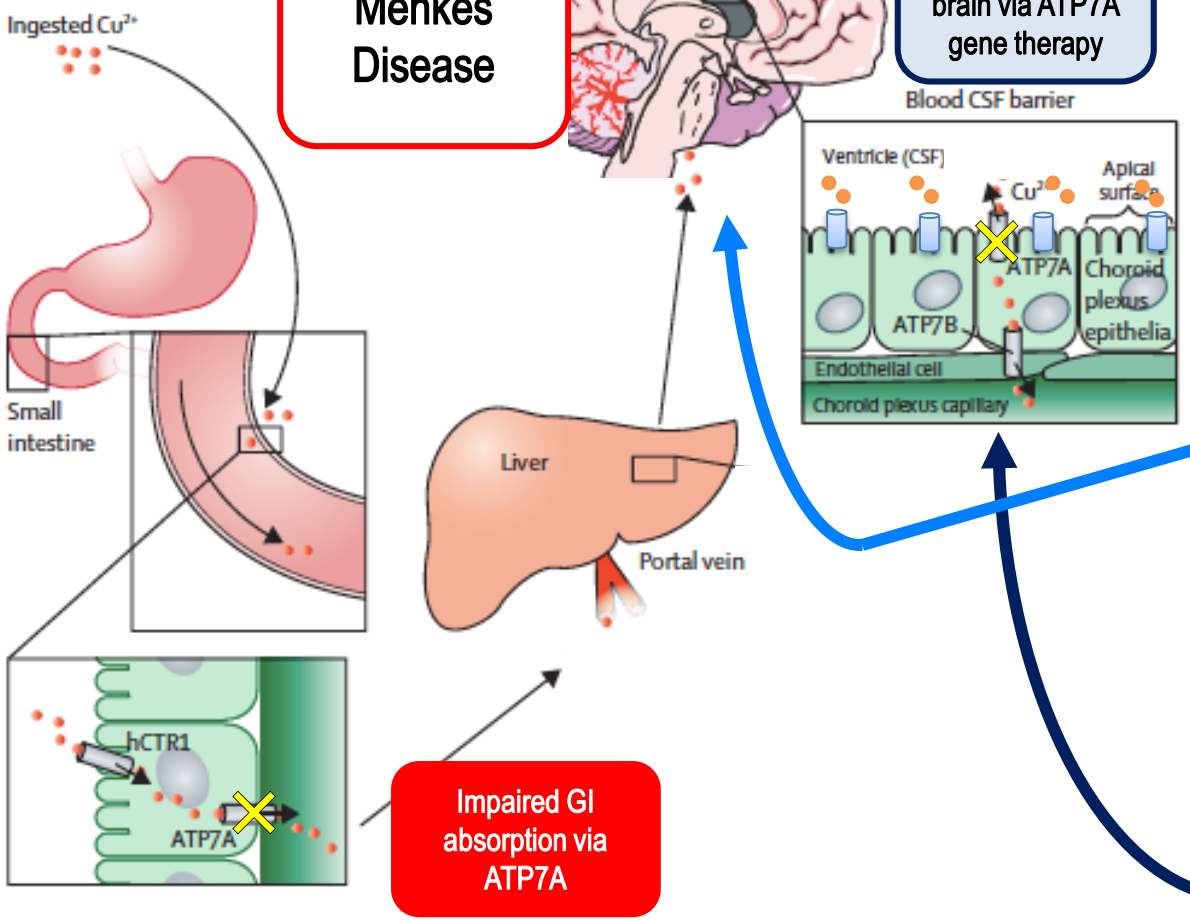
CUTX-101 Copper Histidinate

- 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

Adapted from: Bandmann et al, Lancet Neuro 2015

Therapeutic Strategy for Menkes Disease: CUTX-101 (Copper Histidinate) + AAV-ATP7A Gene Therapy



1 CUTX-101 Copper Histidinate

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- 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

Adapted from: Bandmann et al, Lancet Neuro 2015

CUTX-101 is Optimized for Menkes Patients

	CUTX-101 (Copper Histidinate)	Cupric Chloride ($CuCl_2$)	Oral Cu supplements
Route of Administration	Subcutaneous (SC)	IV (additive to TPN)	Oral
pH	7.4 (physiologic)	2.0 (highly acidic)	N/A
Tolerability	Good	Poor (if injected SC)	N/A
GI absorption in Menkes patients	Bypassed	Bypassed	Very low
Bioavailability to cells	High	Low (Cu^{2+} ions bound to albumin)	N/A
Chemistry	Coordination complex (not free Cu^{2+} ions)	Inorganic salt (reactive free Cu^{2+} ions)	Inorganic salts
Clinical experience in Menkes patients	20+ years experience at NIH; 100+ patients treated	Minimal	Minimal

Product label; Deschamps et al 2005

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
  - 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 Worldwide exclusive rights to develop and commercialize codon-optimized AAV-ATP7A Gene Therapy program for the treatment of Menkes disease and related disorders

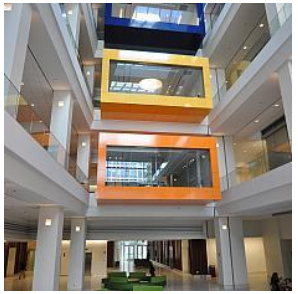
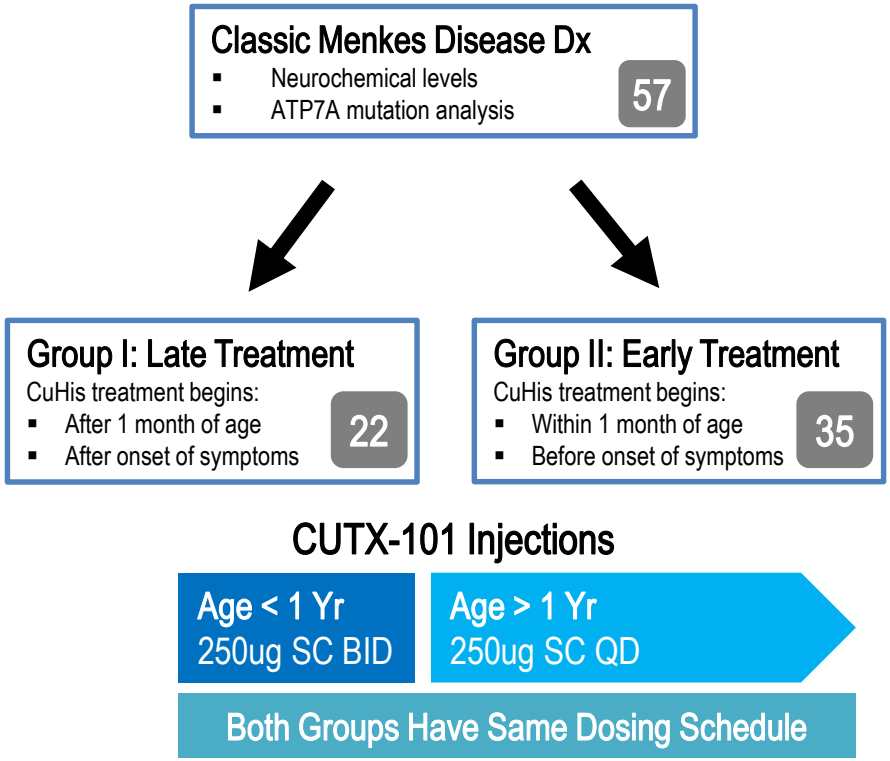


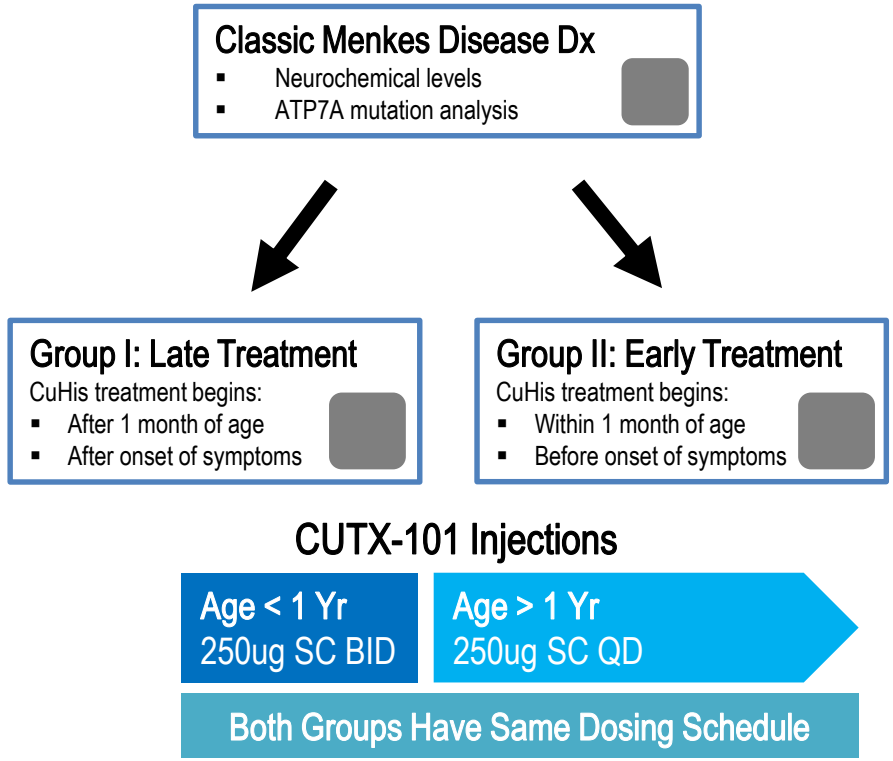
Image Source: NIH.gov

Clinical Studies of CUTX-101 in Menkes Patients (Dosing up to 3 Years)

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



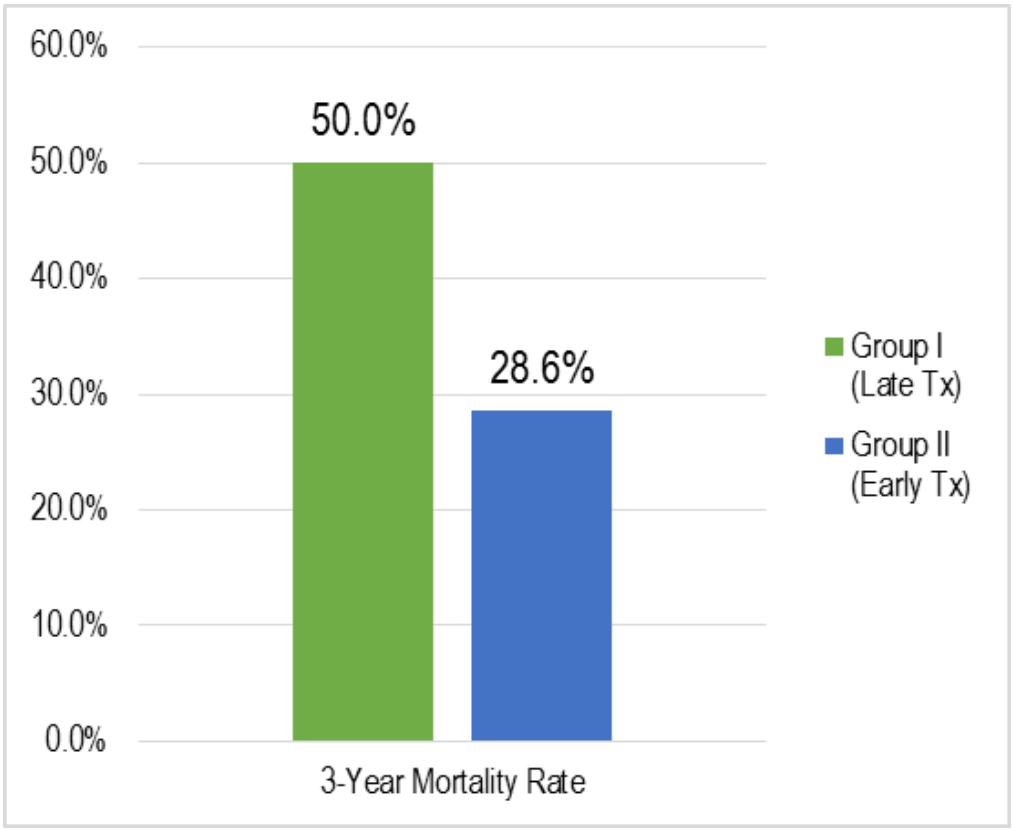
- Phase 3 Study (NCT00811785)
- Status: Completed enrollment (Parallel with NDA filing)



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
- IND transferred to Cyprium in January 2019
- Additional regulatory activities in US and other territories

Clinical:

- In parallel with filing, continue Phase 3 Study of CUTX-101 in Menkes patients (NICHD) (NCT00811785)
- Continue Natural History Study of Untreated Menkes Patients (NICHD)

CMC:

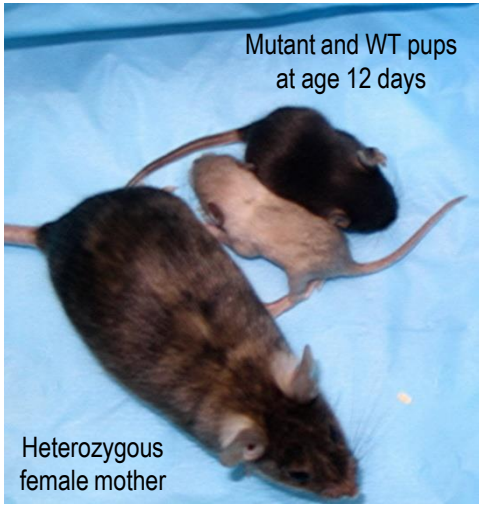
- Continue GMP manufacturing of CUTX-101
- Additional CMC and product development activities

Others:

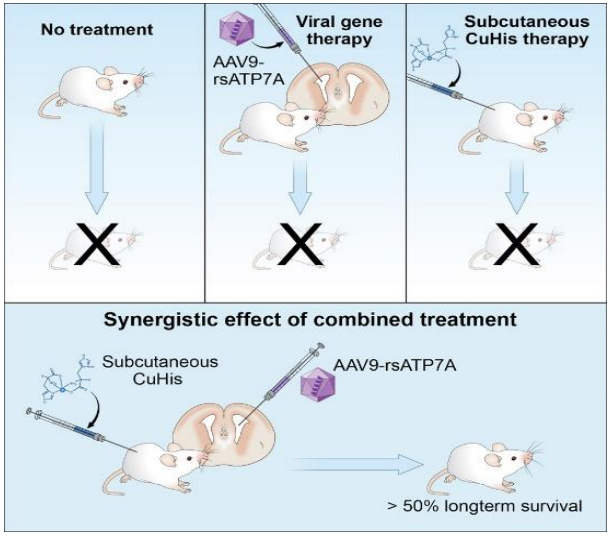
- Additional PK and nonclinical studies to be completed based on FDA communications

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



- 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

Thank you!

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