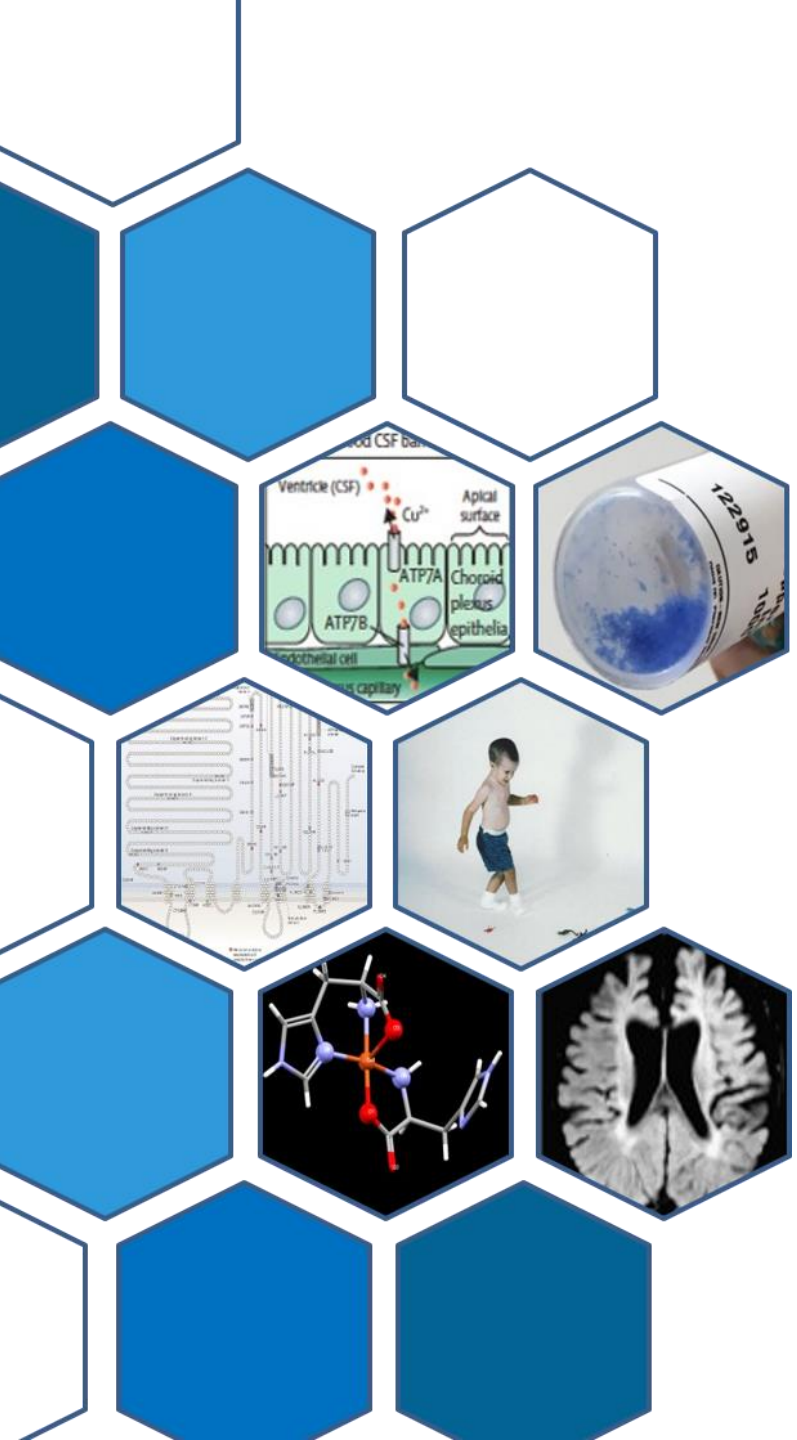


CYPRIUM THERAPEUTICS

Corporate Presentation

September 2020

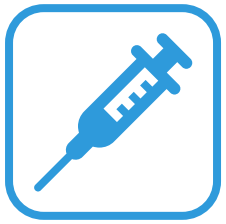
Forward Looking Statements

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 the SEC filings of Fortress Biotech, Inc. 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.

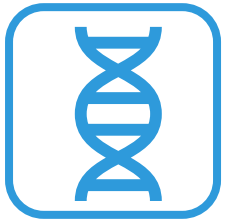
Cover Page Image Sources: Kaler SG, NIH

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 disease program at NIH/NICHD through CRADA and licensing agreements with NICHD.

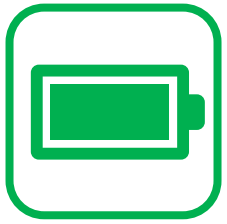


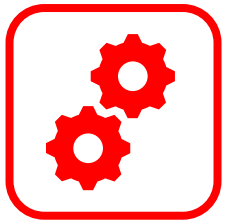
- **CUTX-101 (Copper Histidinate Injections):** ODD FT RPD OMP
  - **Reported positive topline clinical efficacy data, showing a nearly 80% reduction in the risk of death (Hazard Ratio = 0.21, p<0.0001)**
  - Intermediate-size Expanded Access protocol and Natural History Study ongoing
  - FDA granted Orphan Drug, Fast Track, and Rare Pediatric Disease Designation → Eligible for the Rare Pediatric Disease Priority Review Voucher
  - EMA COMP issued positive opinion on Orphan Medicinal Product Designation in July 2020
  - **Rolling NDA submission in 2020 – would be the first FDA-approved treatment for Menkes Disease**



- **AAV-ATP7A Gene Therapy:** ODD
  - Preclinical and already has Orphan Drug Designation from FDA
  - **Expects to nominate candidate for clinical development in 2021**

Copper is Required 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 is a Rare Pediatric Disease

Menkes Disease

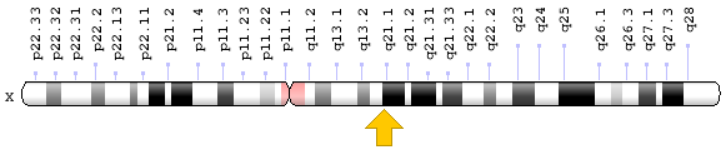
- First described by Dr. John Menkes in 1962
- X-linked recessive disease: affecting mostly boys
- Minimum birth prevalence for Menkes disease believed to be 1 in 34,810 live male births, but could potentially be as high as 1 in 8,664 live male births, higher than previously recognized
- Disorder of copper metabolism caused by mutations in the Copper transporter ATP7A
- **If untreated, premature death ~ 3 years**

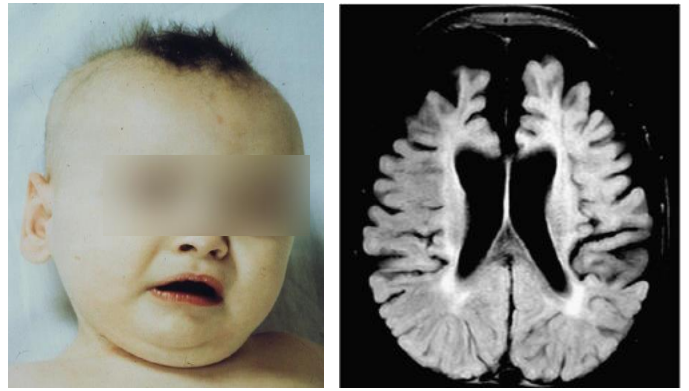
Distinctive clinical phenotypes

- Sparse, depigmented hair ("kinky hair")
- Onset of neurologic symptoms: seizures, hypotonia, and developmental delays
- Failure to thrive
- Connective tissue problems

Diagnosis

- Low serum copper and ceruloplasmin levels
- Abnormal catecholamine levels
- ATP7A gene sequencing confirmation





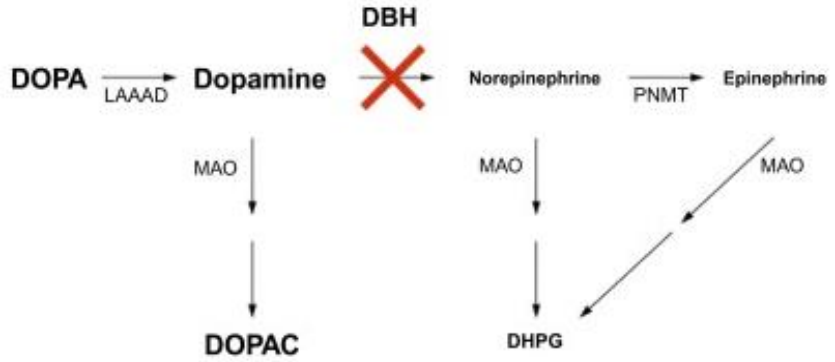
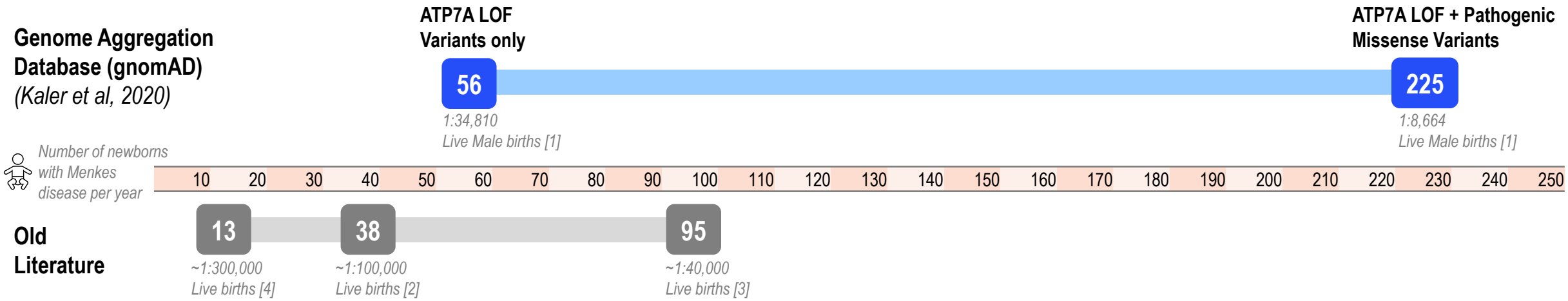


Image Source: Stephen G. Kaler, MD; NCBI;

Menkes Disease is Under-estimated and Under-diagnosed

New study estimated birth prevalence of Menkes disease based on the Genome Aggregation Database

- Accessed Genome Aggregation Database (gnomAD) at MIT/Broad Institute → over 200,000 ATP7A alleles
- Identified 1,106 ATP7A variants
  - 4 Loss-of-Function (LOF) variants → 4 alleles → 1:34,810 live male births → 56 patients per year
  - 28 potentially pathogenic missense variants (PolyPhen-2) → 12 alleles with high confidence (REVEL >0.85)
  - Including both LOF and pathogenic missense variants → 1:8,664 live male births → 225 patients per year
- Newborn screening (NBS) will likely increase the number of Menkes disease patients identified and allow early diagnosis and treatment with CUTX-101



References: [1] Kaler, et al, 2020; [2] Kaler, SG, 1998; [3] Danks DM, 1971; [4] Tonnesen et al 1991

Potentials of gnomAD and Newborn Screening to Discover More Patients in Rare Pediatric Diseases

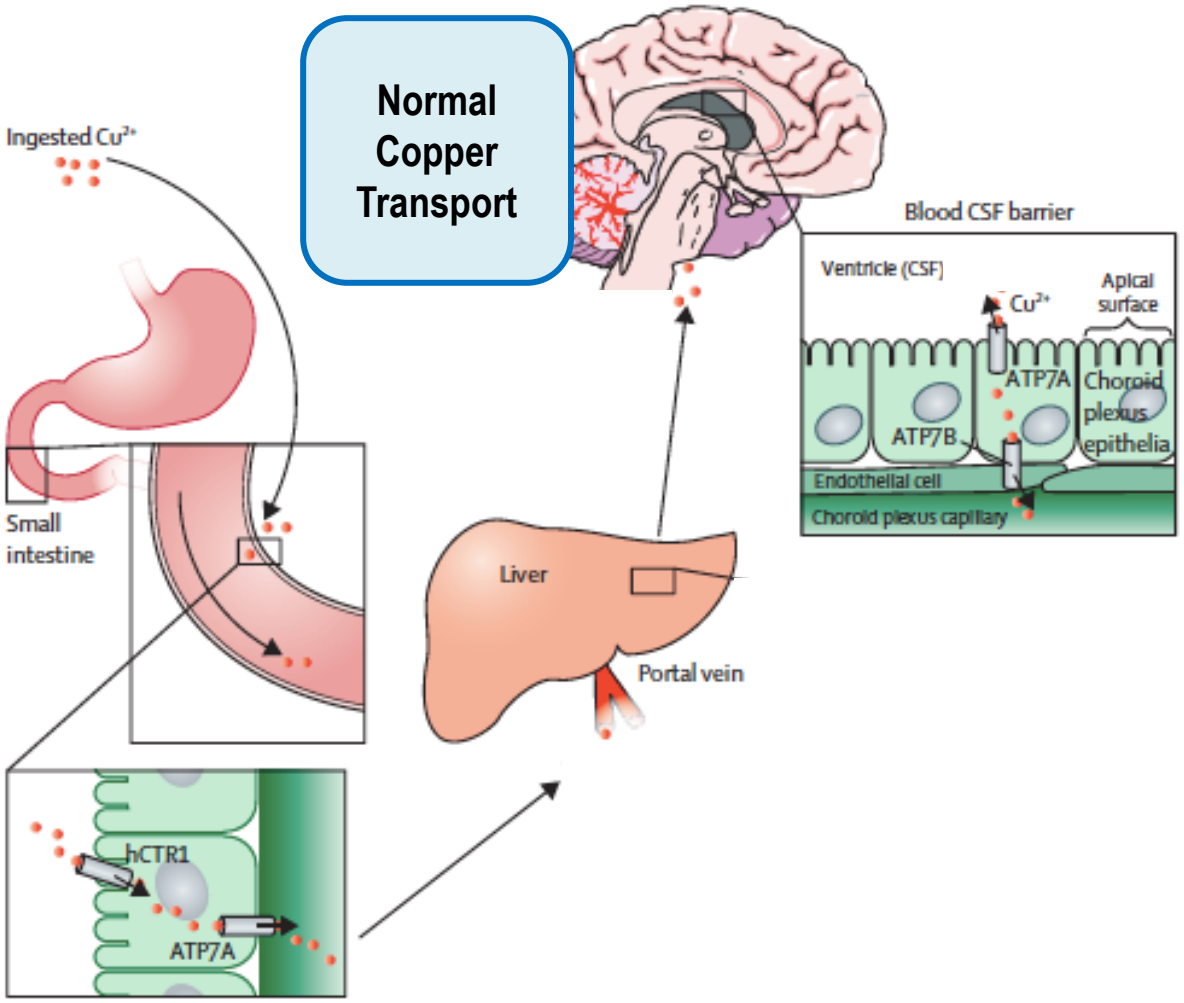
- Kaler 2020 study applied the same approach to a different X-linked recessive disorder, Duchenne Muscular Dystrophy (DMD), for which incidence data are better established due to longer lifespan.

- Analysis of gnomAD database entries for the DMD locus indicated 19 unequivocally loss-of-function alleles out of a total of 204,738 sequenced → predicted birth prevalence of DMD equals 1 in 7,246 live male births, in reasonable agreement with population-based estimates (1 in 5,000 newborn males) [1]

- Newborn screening detected a higher than previously estimated prevalence:
  - **Fabry Disease:** 1 in 8,454 in NBS [2] vs 1 in 40,000 to 60,000 males [3]
  - **Pompe Disease:** 1 in 21,979 in NBS [2] vs 1 in 40,000 births [4]

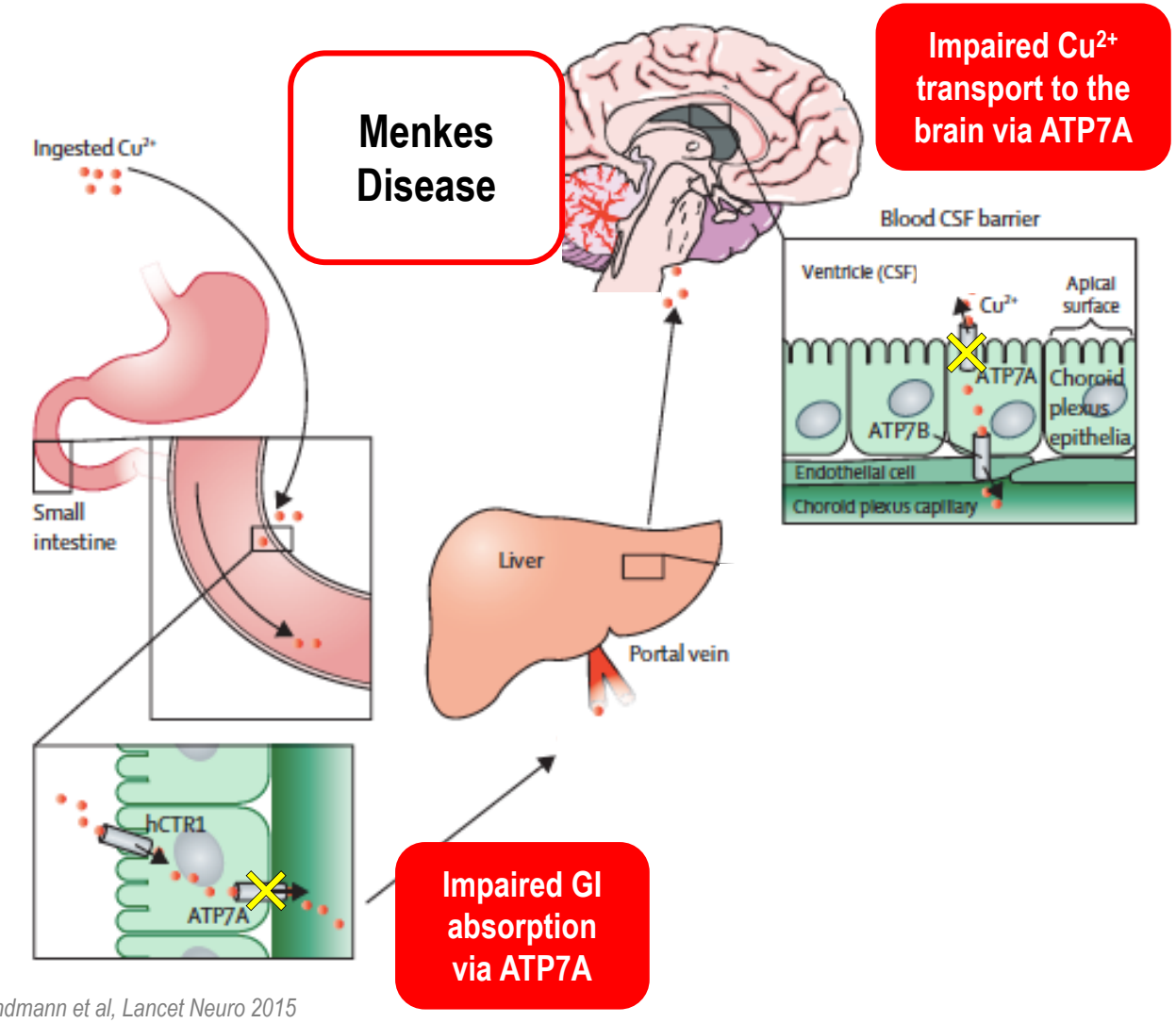
References:
[1] Kaler, et al, 2020
[2] Burton et al, 2017
[3] https://rarediseases.org/rare-diseases/fabry-disease/
[4] https://rarediseases.org/rare-diseases/pompe-disease/

ATP7A is Critical for Copper Transport to the Brain & GI



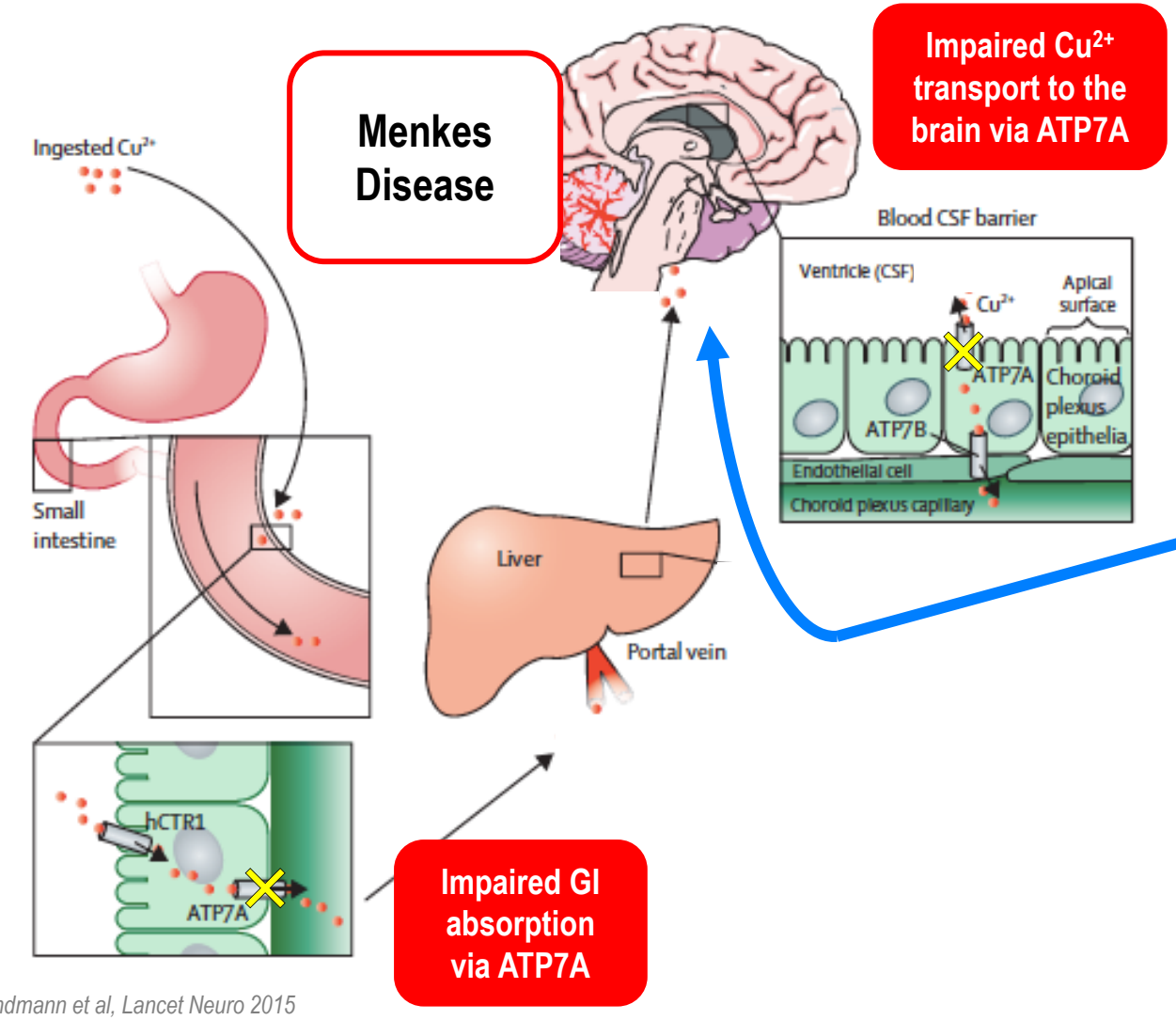
Adapted from: Bandmann et al, Lancet Neuro 2015

Copper Transport is impaired in Menkes Disease



Adapted from: Bandmann et al, Lancet Neuro 2015

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



1

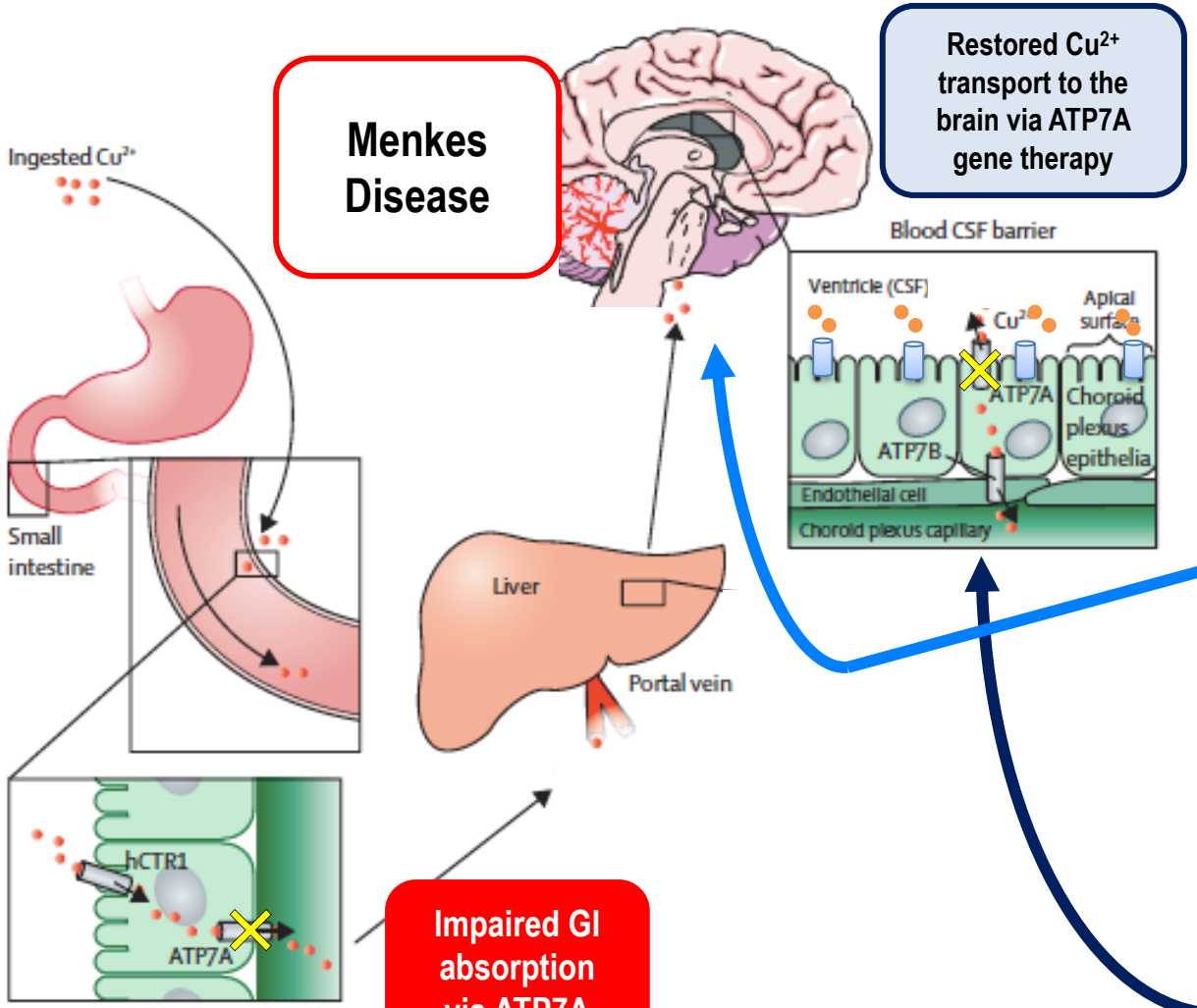
CUTX-101 Copper Histidinate

- SC injection to replenish CuHis
- 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 completed enrollment;
- Expanded Access protocol & 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



Adapted from: Bandmann et al, Lancet Neuro 2015

1

CUTX-101 Copper Histidinate

- SC injection to replenish CuHis
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- Phase 3 Study completed enrollment;
- Expanded Access protocol & 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 need CUTX-101 injections

Preclinical

CUTX-101 is Optimized for Menkes Disease 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; 130+ patients treated	Minimal	Minimal

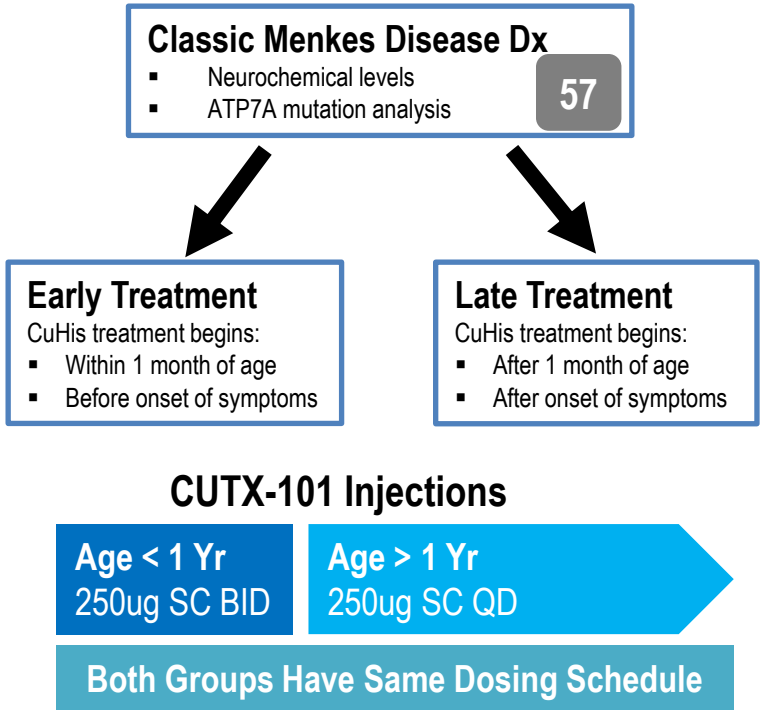
Product label; Deschamps et al 2005

Partnership with NICHD/NIH

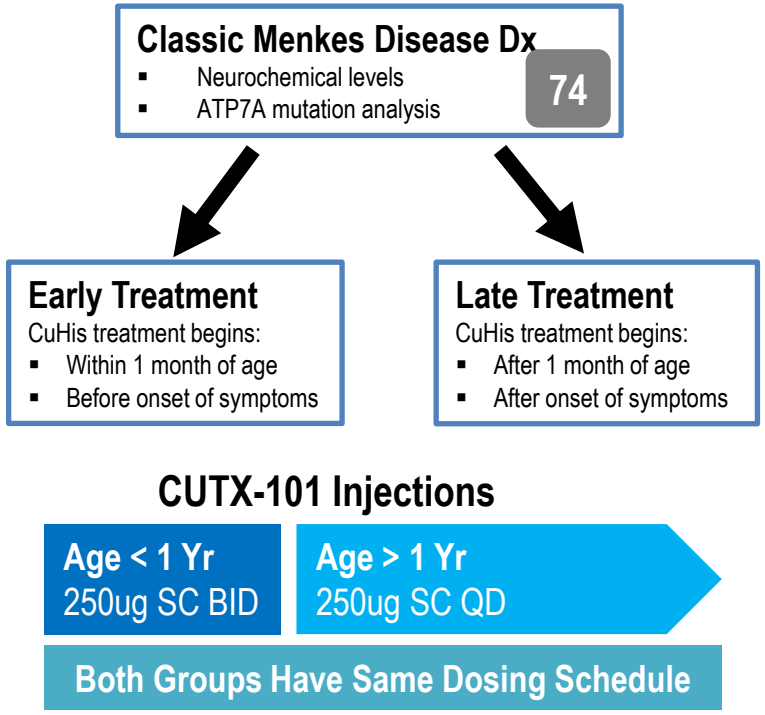
- **Menkes disease program originated at *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD):**
  - Led by Stephen G. Kaler, MD, Senior Investigator and Head, Section on Translational Neuroscience, Molecular Medicine Branch, NICHD
    - Recently relocated to Center for Gene Therapy at Nationwide Children's Hospital (Columbus, OH)
- **Cooperative Research And Development Agreement (CRADA) with NICHD**
  - Executed and announced in March 2017
  - Cyprium continues GMP manufacturing of CUTX-101
  - IND transferred to Cyprium in Jan 2019
  - NICHD leadership supportive of NDA and will complete data transfer to Cyprium for NDA submission
- **Licensing Agreement for AAV-ATP7A Gene Therapy with NICHD**
  - 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

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

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



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



Both studies are included in efficacy and safety analyses in CUTX-101 NDA*

*Additional analyses and criteria are specified in Statistical Analysis Plan (SAP) for NDA

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

Clinical Summary for CUTX-101

- In the published Phase 1/2 NIH study, Menkes disease 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 disease patients treated with CUTX-101 was significantly lower than untreated historical control (preliminary data not yet reported).
- In addition, in the Phase 1/2 study, early treatment with CUTX-101 significantly improved Denver Developmental Screening Test in all 4 scales (gross motor, fine motor/adaptive, personal-social, and language).
- CUTX-101 appears to be safe and well tolerated. Low incidence of renal tubular dysfunction was observed, which was reversible upon drug discontinuation.
- Dr. Kaler/Cyprium are conducting a Natural History Study of Menkes disease patients who have not been treated with copper supplements. Data from this Natural History Study will serve as a historical control to demonstrate the efficacy of CUTX-101.
- Cyprium reached consensus with FDA on Statistical Analysis Plan (SAP) for NDA with additional pre-specified criteria for analyses.

Positive Topline Clinical Efficacy Data for CUTX-101

Summary	
Statistical Analysis Plan (SAP)	Agreed upon with the FDA for Integrated Summary of Effectiveness (ISE) section of the NDA
Primary Efficacy Endpoint	Overall survival (OS) measured from birth
Treatment Cohorts (as defined in SAP)	**Early Treatment (ET):** received CUTX-101 beginning within 4 weeks of age (adjusted for prematurity) (n=31) **Historical Control (HC):** did not receive copper therapy (n=18)
Overall Survival (OS) Results	Statistically significant improvement in overall survival for Menkes disease subjects who received early treatment (ET) with CUTX-101, compared to an untreated historical control (HC) cohort, with a nearly 80% reduction in the risk of death (Hazard Ratio = 0.21, $p<0.0001$).
Median survival	**Early Treatment (ET):** 14.8 years (177.1 months) **Historical Control (HC):** 1.3 years (15.9 months)

- The topline primary efficacy data and other relevant briefing materials will be presented to the FDA at a pre-NDA meeting scheduled for late 3Q2020. Other pre-specified secondary and sensitivity analyses will be included in the NDA submission. Additional data and analyses will be disclosed in peer-reviewed publications and at future medical or scientific conferences.

SAP Pre-specified Criteria Ensured the Two Cohorts are Comparable

- Inclusion criteria pre-specified in the Statistical Analysis Plan (SAP) agreed upon with the FDA*

Early Treatment (ET) Cohort	Historical Control (HC) Cohort	*Rationales*
▪ Enrolled in protocols 90-CH-0149 (Phase 1/2) or 09-CH-0059 (Phase 3)	▪ Enrolled in a pre-specified HC cohort	*Well defined, pre-specified patient populations*
▪ Carried a severe pathogenic mutation of the ATP7A gene (deletion/duplication, nonsense, or canonical splice junction)	▪ Carried a severe pathogenic mutation of the ATP7A gene (deletion/duplication, nonsense, or canonical splice junction)	*Most stringent and severe ATP7A genotypes*
▪ Born within the past 20 years (i.e., born after December 31, 1999)	▪ Born within the past 20 years (i.e., born after December 31, 1999)	*Similar standards of medical care*
▪ Survived at least 4 weeks after birth and were asymptomatic for significant neurological signs and symptoms during the first 4 weeks.	▪ Survived at least 4 weeks after birth and were asymptomatic for significant neurological signs and symptoms during the first 4 weeks.	*Similar course of disease in neonatal period*
▪ **Initiated treatment with CUTX-101 within four weeks of age (adjusted for prematurity)**	▪ **Did not receive CUTX-101 therapy**	***CUTX-101 treatment is the key difference between the 2 cohorts***

*Updated survival data and long-term follow-up data were collected under Cyprium-sponsored protocols CYP-001 and CYP-002 for both cohorts.

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 to continue frequent communications (Fast Track Designation).
- Cyprium will submit NDA based on data from NIH studies and historical control, using overall survival as the primary endpoint.
- **FDA granted Rare Pediatric Disease Designation in January 2020**
- **EMA COMP issued positive opinion on Orphan Medicinal Product Designation in July 2020**
- **Pre-NDA meeting with FDA scheduled for late 3Q2020**
- Additional regulatory activities in US and other territories

Clinical:

- Cyprium's Intermediate-Size Expanded Access Protocol CYP-001 (NCT04074512)
  - Provides CUTX-101 for newly diagnosed Menkes disease patients and patients from NIH study
- Continues Natural History Study of untreated Menkes disease patients

CMC:

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

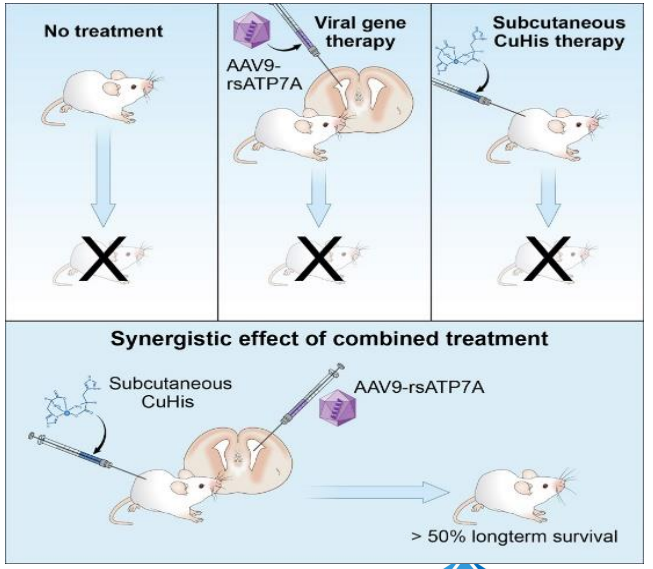
Others:

- 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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