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Delivering on the promise
of Prime Editing

Restoring Copper Homeostasis: Prime Medicine's Path to Developing Transformative Therapies for Wilson Disease

November 12, 2025

Forward Looking Statements

This presentation contains forward-looking statements of Prime Medicine, Inc. ("Prime", "we" or "our") within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements contain information about our current and future prospects and our operations, which are based on currently available information. All statements other than statements of historical facts contained in this presentation, including statements regarding our strategy, projects and plans are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “hope,” “intend,” “may,” “might,” “objective,” “opportunity,” “plan,” “predict,” “positioned,” “possible,” “potential,” “project,” “seek,” “should,” “strategy,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, express or implied statements about Prime’s beliefs and expectations regarding: the potential of Prime Editing to correct the causative mutations of diseases, including CGD, Wilson Disease, CF, and AATD; the continued development and advancement of its AATD and Wilson Disease programs, including the timing of the filing of IND and/or CTA applications in mid-2026 and 1H 2026, respectively, and the timing of initial data for both programs in 2027; the initiation, timing, progress and results of our research and development programs, preclinical studies and future clinical trials, including the release of data related thereto; the safety profile of Prime Editing, our modular LNP, and our programs; our ability to launch therapeutics; the timing of, and our ability to achieve, clinical validation and sustained, long-term value creation; the modularity of the Prime Editing platform and the benefits thereof; the collaboration with Bristol Myers Squibb and the intended and potential benefits thereof, including the receipt of potential milestone and royalty payments from commercial product sales, if any; the 2025 agreement with the Cystic Fibrosis Foundation ("CF Foundation"), its expanded funding pursuant thereto, and the intended and potential benefits thereof, including the receipt of payments based on scientific milestones; our expectations regarding the breadth of Prime Editing, including the potential of Prime Editing to address more than 90% of genetic diseases and to address non-genetic diseases; the continued development and optimization of various non-viral and viral delivery systems, including our universal liver-targeted LNP delivery approach; the scope of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology; the implementation of our strategic plans for our business, programs and technology, including our ability to maintain collaborations or strategic relationships and identify and enter into future license agreements and collaborations; regulatory developments in the United States and foreign countries; developments related to our competitors and our industry; our ability to attract and retain key scientific and management personnel; our estimates of our expenses, capital requirements, and needs for additional financing; and our expectations regarding the anticipated timeline of our cash runway and future financial performance. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K, as well as any subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent our views only as of the date of this presentation and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise subject to any obligations under applicable law. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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Today's Agenda

SETTING THE STAGE

- Welcome and Introduction
- Why Prime Editing for Wilson Disease

WILSON DISEASE OVERVIEW

- Global Market Opportunity
- Wilson Disease Treatment Landscape and the Opportunity for Prime Editing

PM577 FOR WILSON DISEASE

- Emerging Preclinical Data from AASLD
- Initial Clinical Plans
- Upcoming Milestones

Q&A

SPEAKERS

Allan Reine, M.D.
Chief Executive Officer

Michael Schilsky, M.D.
Professor of Medicine, Yale University

Mohammed Asmal, M.D., Ph.D.
Chief Medical Officer

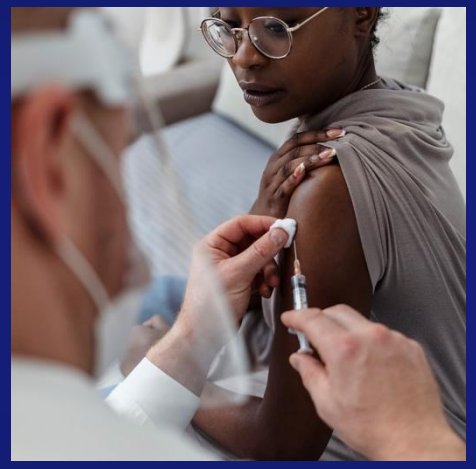
Key Takeaways from Today's Event

1. **Wilson Disease is an area of tremendous unmet need:** no curative therapies available; physicians and patients dissatisfied with current standards of care.

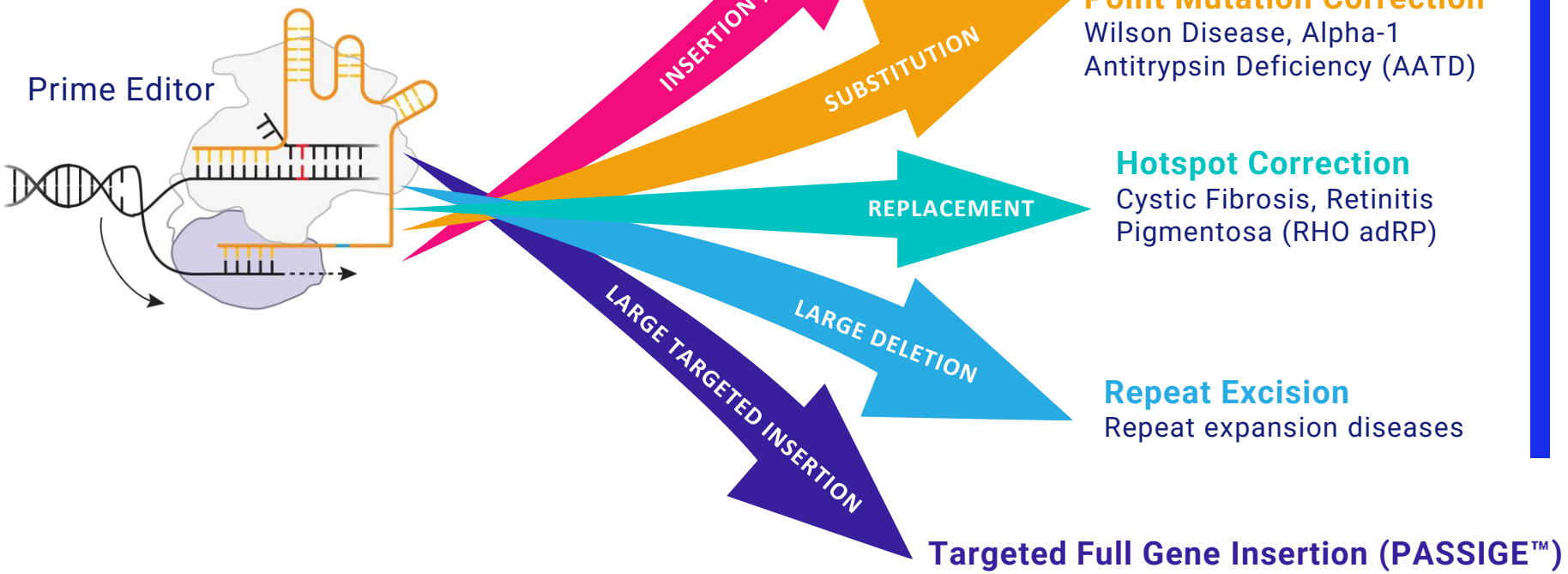
2. **Prime Editing has the potential to provide a durable cure**, by precisely and permanently correcting the causative mutation and restoring wild-type enzyme function, normalizing copper metabolism and halting disease progression.

3. **Prime Medicine intends to leverage platform modularity** to accelerate the development of multiple Prime Editors for Wilson Disease, a multi-billion-dollar global opportunity and other liver diseases

We are advancing Prime Editing to **change the course of how diseases are treated**. We aim to provide **safe, effective and curative treatments,** which offer lifelong benefit to patients.


We Believe Prime Editing is the Only Technology That Can Edit, Correct, Insert and Delete DNA Sequences in Any Target Tissue



Deletion / Insertion Correction
p47 Chronic Granulomatous Disease (CGD)

Point Mutation Correction
Wilson Disease, Alpha-1 Antitrypsin Deficiency (AATD)

Hotspot Correction
Cystic Fibrosis, Retinitis Pigmentosa (RHO adRP)

Repeat Excision
Repeat expansion diseases

Targeted Full Gene Insertion (PASSIGE™)
CAR-T, Cystic Fibrosis

Prime Editing is designed with a **wide range of genome editing capabilities** and the **ability to make edits of any size**, from small base pair swaps to large, multi-kilobase inversions or insertions. This provides tremendous flexibility to select the right approach for each indication and editing need.

We Are Focused on Value Creating Opportunities: Substantial Need, Clear Biology, Potential for Meaningful Commercial Impact

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Modular Platform	Indication	Delivery	Discovery	Lead optimization	IND-enabling	Phase 1/2
LIVER	Wilson Disease	LNP				
LIVER	Alpha-1 Antitrypsin Deficiency (AATD)	LNP				
LUNG	Cystic Fibrosis[1] (including PASSIGE™)	LNP/AAV				
IMMUNOLOGY & ONCOLOGY	*Ex vivo* CAR-T[2] (with PASSIGE™)	*ex vivo*				

CYSTIC FIBROSIS FOUNDATION

Bristol Myers Squibb

Prime Medicine is identifying opportunities to advance its other programs, including CGD, neurological diseases, cell therapy, ocular diseases and hearing loss, in partnership or through internal efforts in the future.

[1] In January 2024 and July 2025, Prime entered into agreements with the CF Foundation for up to $15 million and $24 million, respectively, to support development of Prime Editors for Cystic Fibrosis.
[2] In September 2024, Prime entered into a strategic research collaboration and license agreement with Bristol Myers Squibb to develop and commercialize multiple *ex vivo* T cell products in immunology and oncology.
LNP = lipid nanoparticle; AAV = adeno-associated virus; CGD = chronic granulomatous disease

Our Initial Efforts Are Focused on Two of the Largest Genetic Liver Diseases

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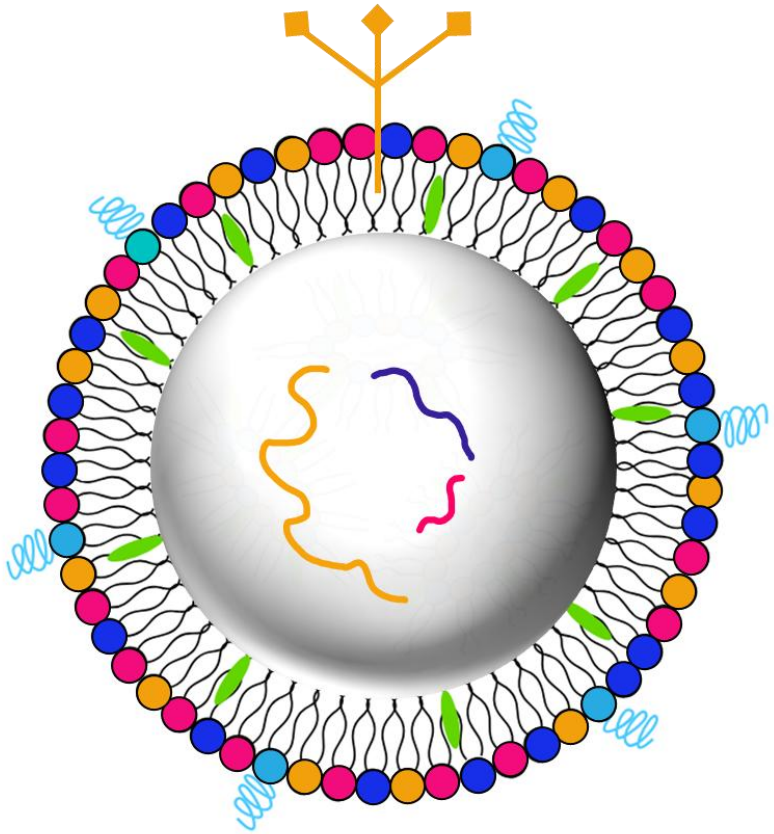
	Wilson Disease	Alpha-1 Antitrypsin Deficiency
CURRENT STATUS	IND-enabling studies ongoing	IND-enabling studies ongoing
UPCOMING MILESTONES	IND and/or CTA on track for 1H 2026 Clinical data in 2027	IND and/or CTA on track for mid-2026 Clinical data in 2027
TARGETED MUTATION	H1069Q (anchor program), R778L (fast follow-on)	E342K (Pi*Z Mutation), D341H (Little Rock*)

WD = Wilson Disease; AATD = Alpha-1 Antitrypsin Deficiency; IND = investigational new drug; CTA = clinical trial application; *Little Rock is a rare mutation in the SERPINA1 gene which leads to destabilization of the A1AT protein; **Based on the estimates of 10-15% of patients diagnosed

We are Advancing a Franchise of Programs for Genetic Liver Diseases, Which Share Our Proprietary, Universal LNP

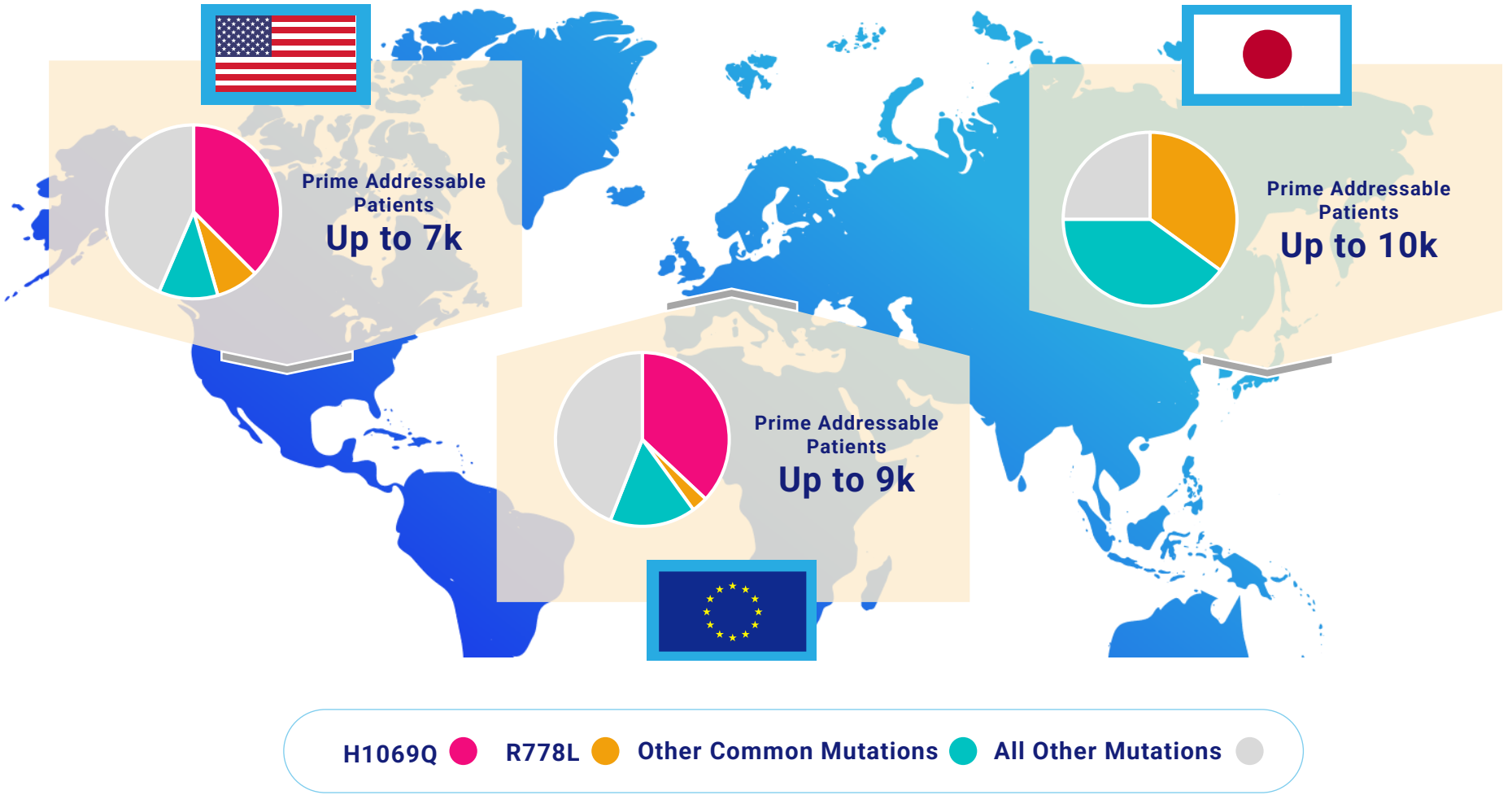


Vast majority of components can be used across liver programs, allowing potential benefit of shared toxicology, manufacturing and regulatory experience

Accelerates, derisks and reduces costs of follow-on efforts

Prime Medicine's Wilson Disease Programs Have Potential to Address Multi-Billion Dollar Market

- **Six most common mutations account for up to 26,000 patients** in addressable markets (US, Europe, Japan) with unique geographic mutational distribution; incidence rate of approximately 300 new patients per year
- **Consistency in disease presentation and management** across mutations and key markets enables Prime Medicine to establish an anchor with PM577 (H1069Q) to provide leverage and read-through to other mutations



We Plan to Leverage Platform Modularity to Rapidly Advance Prime Editors for a Majority of Wilson Disease Patients

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H1069Q (PM577)

ANCHOR MUTATION:

Large commercial opportunity in U.S. and Europe

- 1H 2026 IND/CTA
- Lead in observational study will expedite patient recruitment

Follow-on programs to leverage same liver-targeted LNP; swap out guide sequence

R778L

Large commercial opportunity in Japan

- >90% editing efficiency, minimal preclinical work to formalize DC
- Goal to incorporate into existing regulatory filings; engage PMDA

Other Mutations

Attractive business case to develop follow-on programs

- Fast path to DC (potentially off in vitro data)
- Goal to incorporate into existing regulatory filings

IND = investigational new drug; CTA = clinical trial application; LNP = lipid nanoparticle; DC = development candidate; PMDA = Japan's Pharmaceuticals and Medical Devices Agency

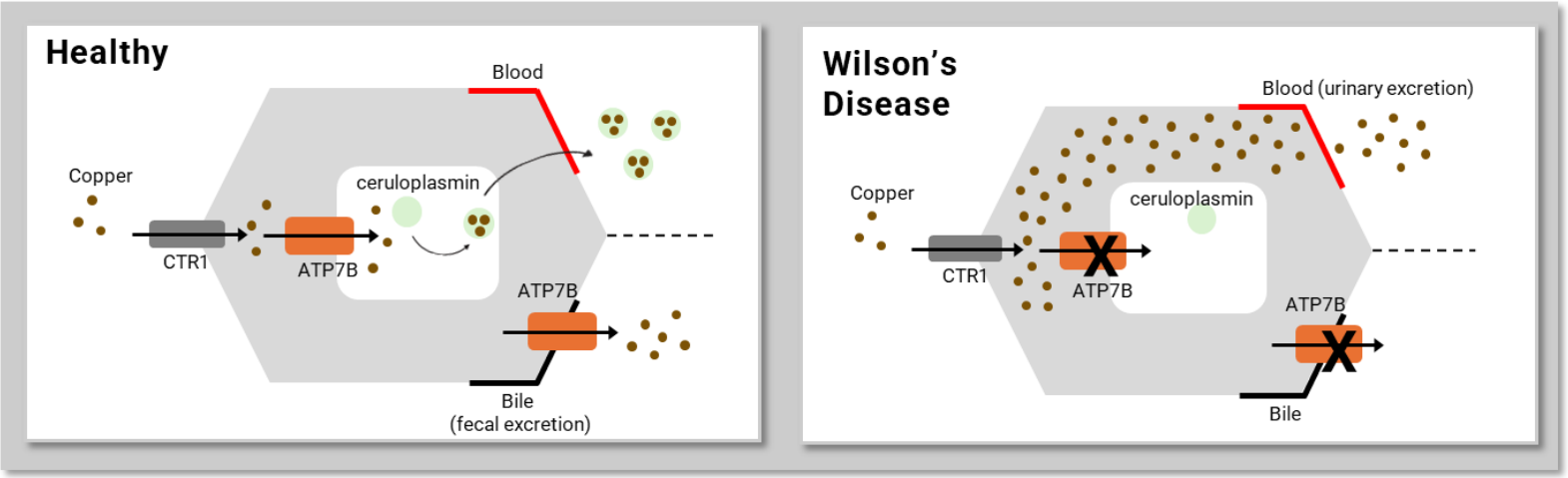
A Clinician’s Perspective on Wilson Disease

Michael Schilsky, M.D.
Professor of Medicine, Yale University

Wilson Disease: A Large, Genetically Defined Disease With No Curative Options

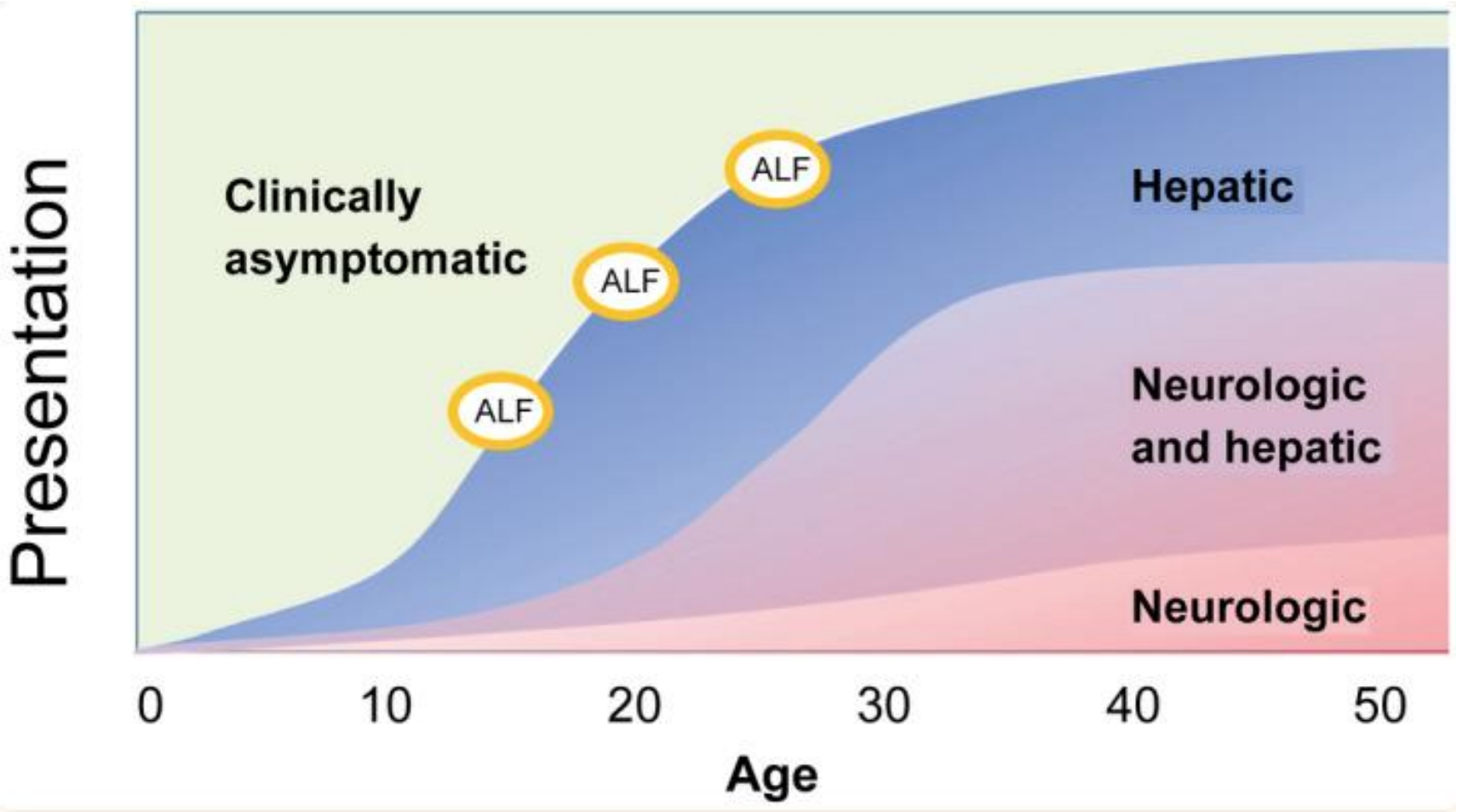
Autosomal-recessive disorder due to mutations in the ATP7B gene, which encodes a copper-transporting ATPase

Mutations in ATP7B impair copper excretion into bile and its incorporation into ceruloplasmin, leading to pathologic copper accumulation in the liver and other organs, including in the CNS



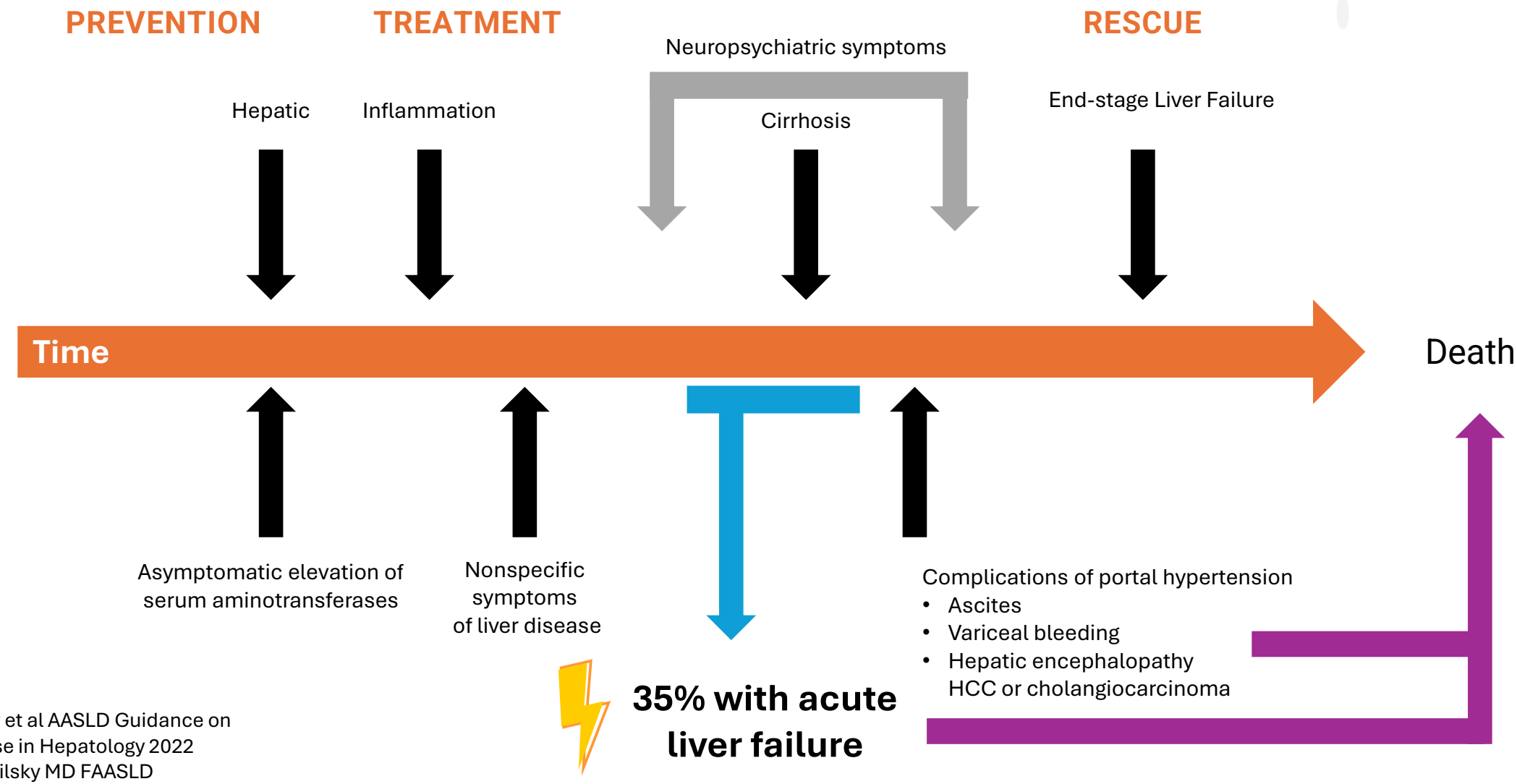
In WD patients, restoring normal copper homeostasis occurs only by targeting the liver for correction of the underlying genetic defect

Phenotype at Presentation of Wilson Disease



From Ott et al Designing clinical trials in Wilson disease.
Hepatology 2021
Michael L Schilsky MD FAASLD

Treatment Goal Depends on Phase of Disease



From Schilsky et al AASLD Guidance on Wilson Disease in Hepatology 2022
Michael L Schilsky MD FAASLD

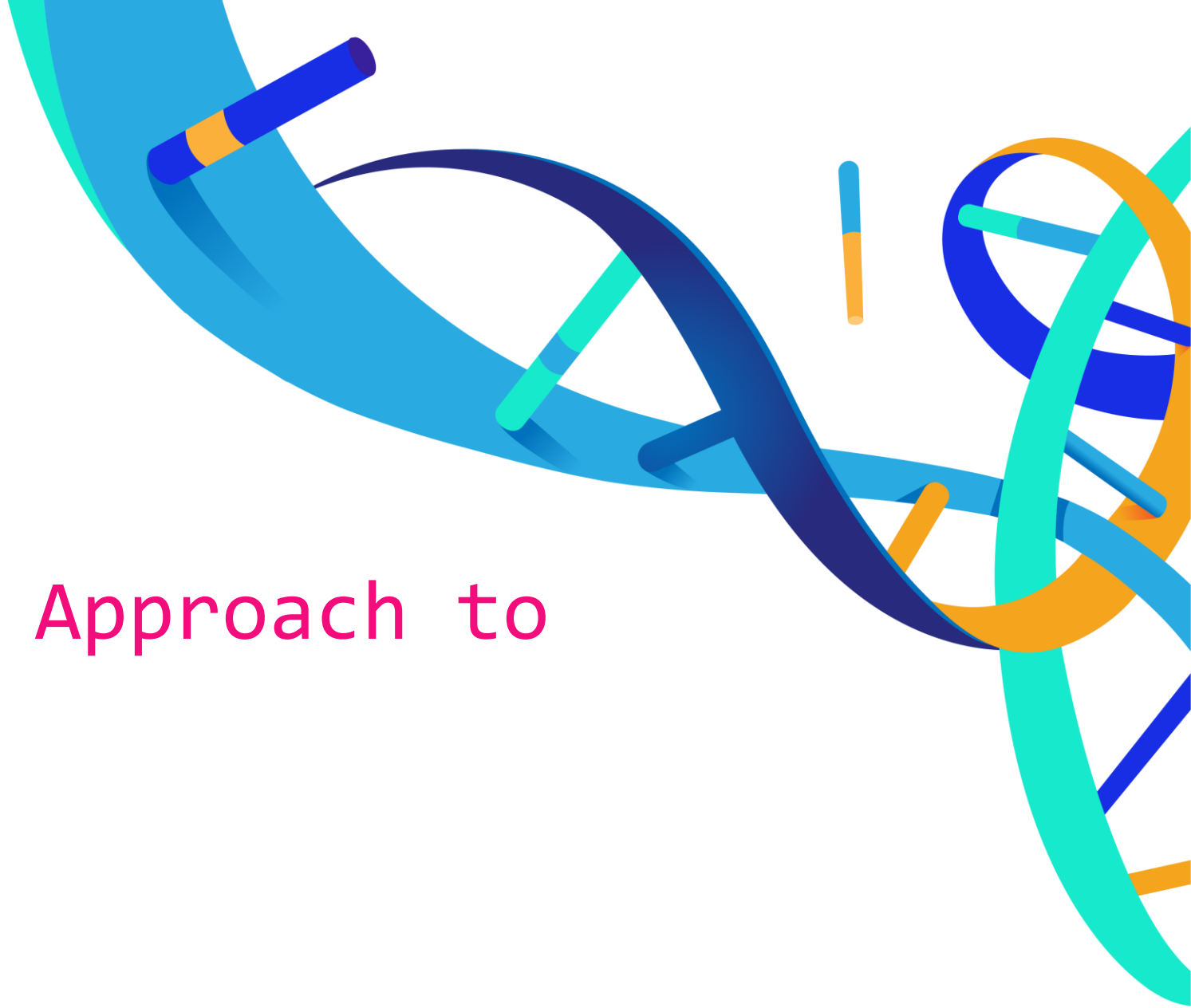
Current Standard-of-Care: High Rates of Non-Adherence, Side Effects

Require multiple daily doses with large pill burden under fasting conditions; therapies bring adverse side effects that can force discontinuation or exacerbate other disease symptoms

Penicillamine (Chelator)	Trientine (Chelator)	Zinc	Liver Transplant
Initial therapy	Penicillamine intolerant patients	Maintenance therapy	Available only to severe patients with significant liver damage with or without neurologic involvement
Chelates copper, causing increased urinary excretion	Chelates copper, causing increased urinary excretion, blocks copper absorption	Induces metallothionein and blocks absorption of copper in intestine	Eliminates disease by removing inherited metabolic defect causing WD
Limitation: Neurological worsening, cutaneous eruptions, lymphadenopathy, neutropenia, thrombocytopenia, proteinuria		**Limitation:** Gastrointestinal intolerance, not all patients respond	**Limitation:** Lifelong immunosuppression

Patients are advised to restrict dietary copper, found in soy, legumes, nuts, chocolate, shellfish, mushrooms, etc.

Prime Medicine’s Approach to Wilson Disease



Prime Editing Has the Potential to Change the Treatment Paradigm in Wilson Disease

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TODAY

Chronic treatment burden: standard-of-care agents and low copper diets are burdensome and often hard to tolerate; long-term compliance is challenging.

Liver transplantation is the only option for patients who progress to liver failure

OUR VISION

One time therapy that precisely and permanently restores wild-type ATP7B function, normalizing copper metabolism, halting disease progression and providing a durable cure

Preclinical Data Strongly Support Potential for PM577 as Transformative Therapy

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DELIVERY	Optimized Prime Editors achieve high levels of hepatocyte editing
SAFETY	Favorable safety profile in mice and NHPs, with no evidence of off-target editing or meaningful LFT elevations at clinically relevant doses
EFFICACY	Efficient correction of the H1069Q and R778L mutations in fully humanized mouse models Evidence of restored copper homeostasis *in vivo* as measured by phenotypic markers and copper PET

Prime Editors Efficiently and Precisely Corrected the Two Most Prevalent Disease-Causing Mutations in Wilson Disease

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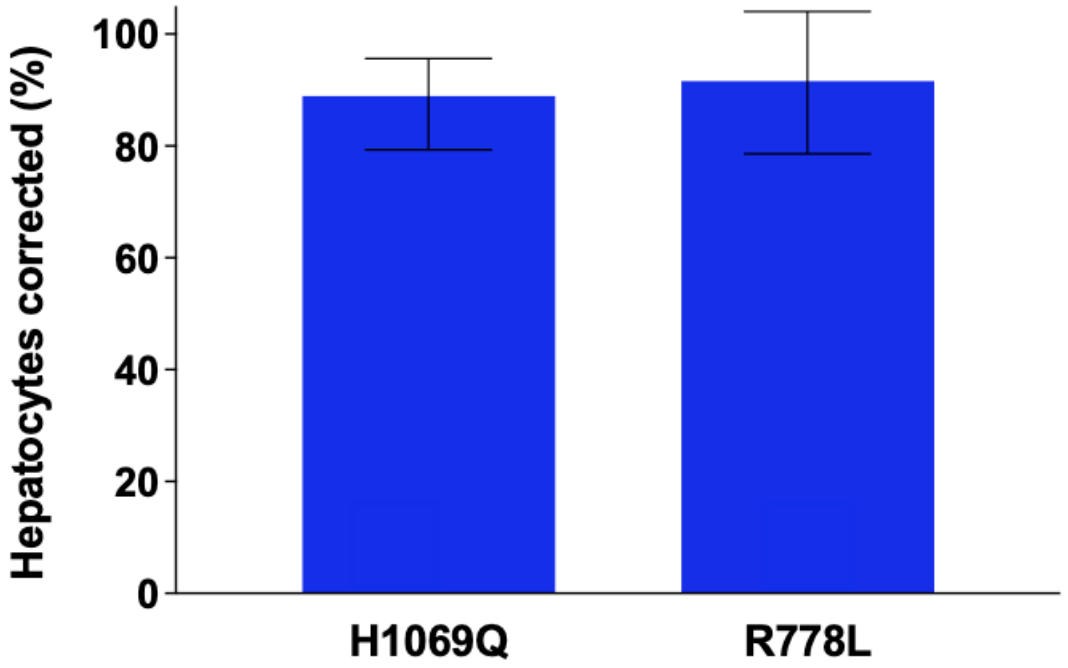
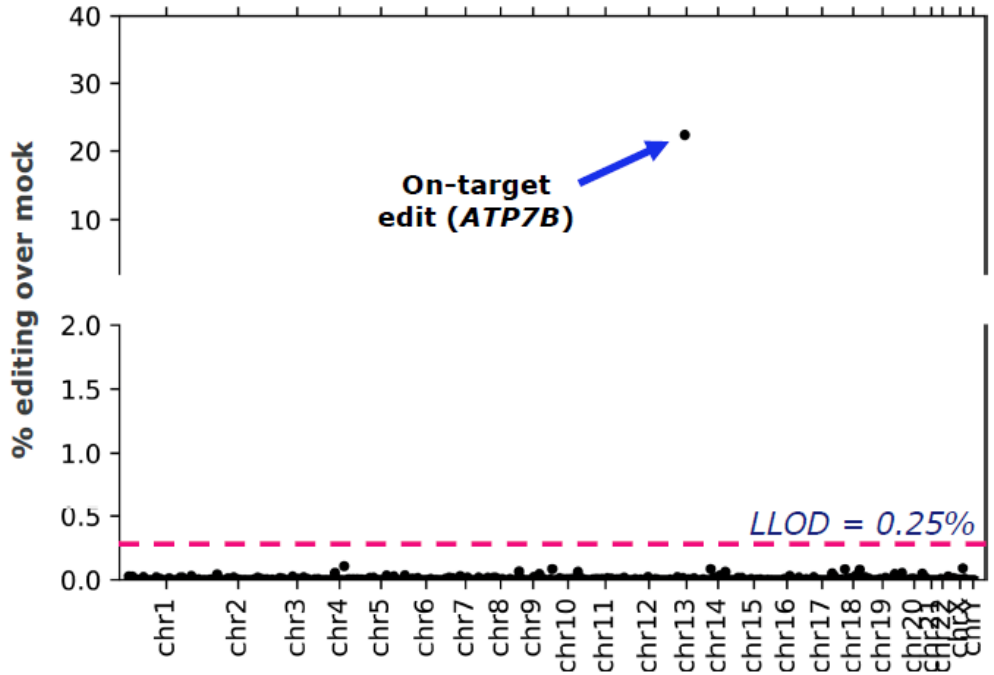
Efficient correction of the H1069Q and R778L mutations in fully humanized mouse models



No detectable off-target editing identified in patient-derived cells



Prime Editors delivered with Prime Medicine's universal liver LNP administered at clinically relevant doses

LNP = lipid nanoparticle

Prime Editors Efficiently Correct the H1069Q Mutation and Completely Restore Wild-Type Copper Concentration *In Vivo*

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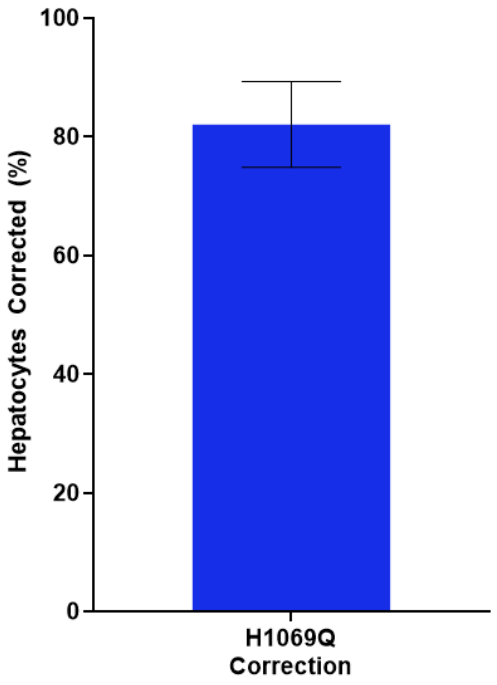
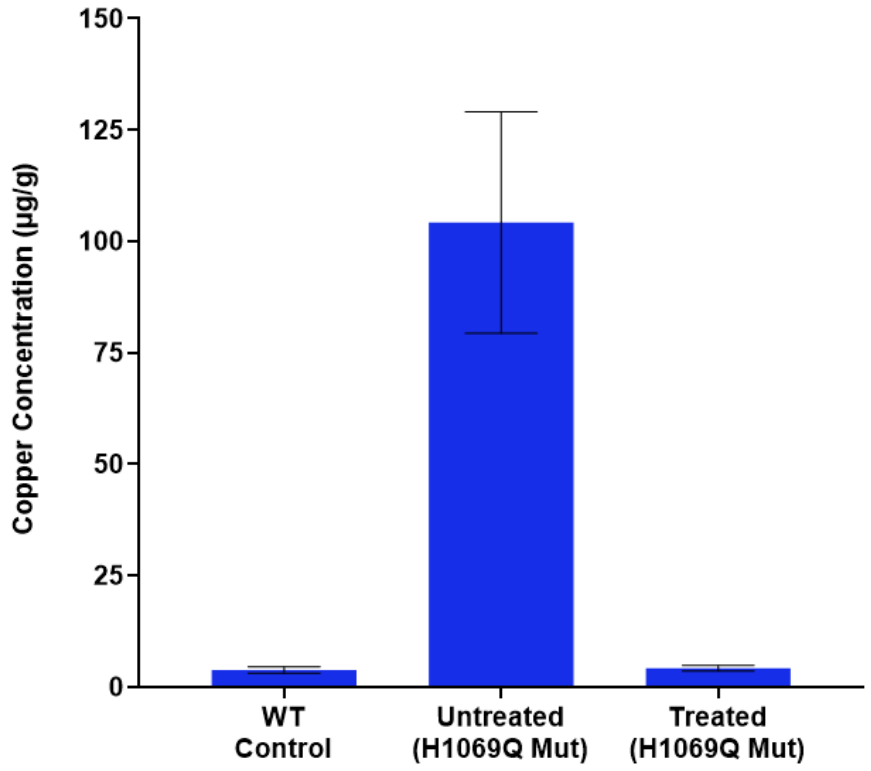
Using optimized Prime Editor in partially humanized homozygous p.H1069Q ATP7B mouse model

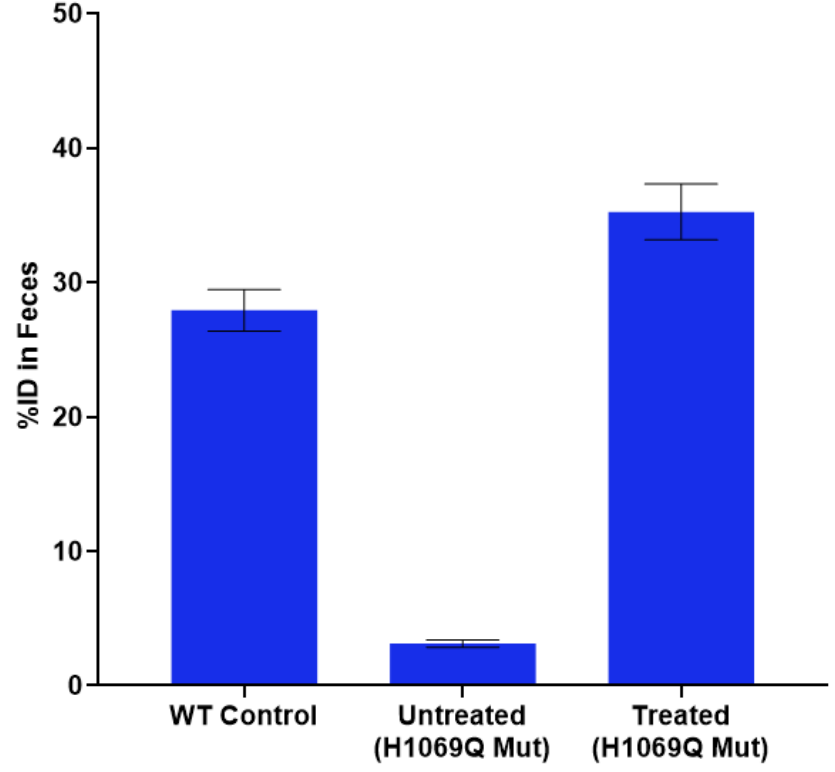
>80% hepatocytes edited



Hepatic copper concentration* returns to wild-type levels at eight weeks



Copper** excreted normally through the feces at four weeks



*Wet tissue weight
**Radiolabeled copper

Prime Edited Mice Challenged with Radiolabeled Copper Demonstrated Normal Copper Clearance 24h Post Injection

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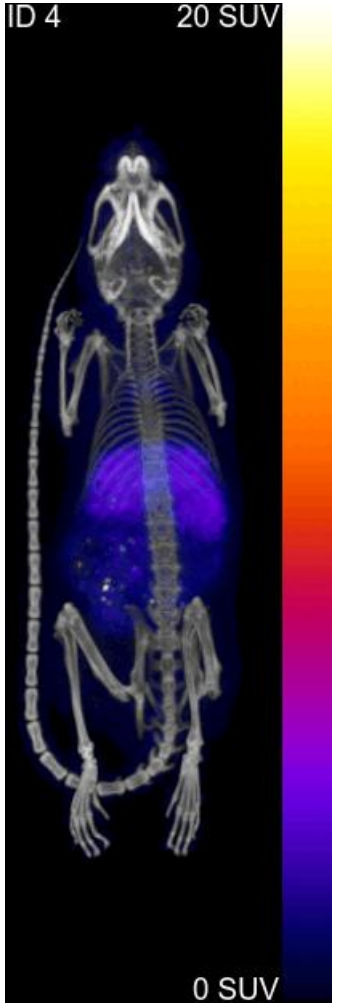
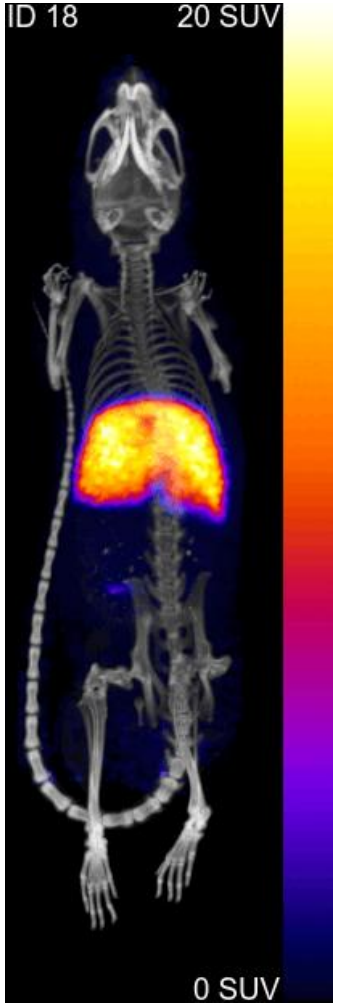
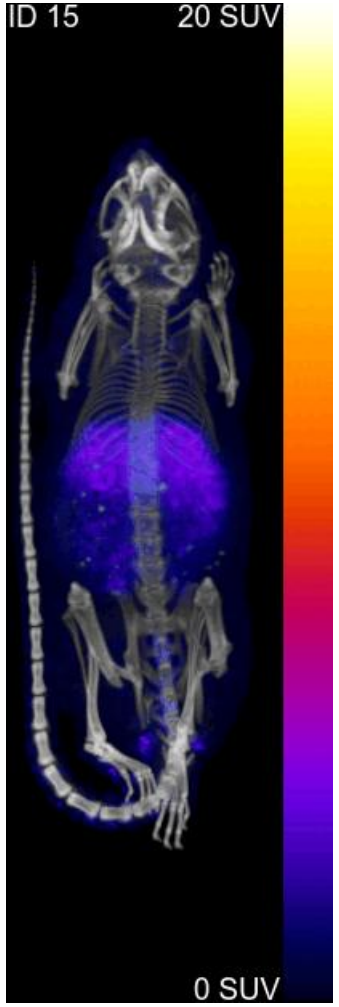
Wild Type Control



Untreated (H1069Q Mut)



Treated (H1069Q Mut)



*Copper challenge and PET imaging performed 4 weeks post PE treatment

PM577 Clinical Development: On Track for H1’26 IND and/or CTA with Proof-of-Concept Data Anticipated in 2027

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ANTICIPATED ENROLLMENT CRITERIA:

- Adult patients who are maintained on standard of care (chelators, zinc salts)

PRIMARY SAFETY ENDPOINTS:

- Safety, tolerability

PRIMARY EFFICACY ENDPOINTS:

- Biomarkers including ceruloplasmin, serum copper, urinary copper
- Copper PET imaging to assess restoration of ATP7B-mediated copper transport

Ultimate goal of the Phase 1/2 study is to demonstrate the ability of PM577 treatment to maintain copper balance post-discontinuation of standard-of-care therapies

IND = investigational new drug; CTA = clinical trial application

Prime Medicine is Entering a New Era of Gene Editing: Generating Clinical Data for Multiple Programs, Leveraging Platform Modularity

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2025

- **PM577 for Wilson Disease:** Prepare for 2026 clinical entry, advance additional mutations pre-clinically
- **PM647 for AATD:** Prepare for 2026 clinical entry
- **Leverage business development** to accelerate pipeline, extend reach
- ☑ **Announced initial positive clinical data** on PM359 in CGD, reinforcing our confidence in the promise of Prime Editing

2026

- **PM577 for Wilson Disease:** File IND and/or CTA in 1H 2026; initiate Phase 1/2 clinical trial
- **PM647 for AATD:** File IND and/or CTA mid-2026; initiate Phase 1/2 clinical trial
- **Advance additional high-value programs:**
  - Share *in vivo* proof-of-concept data in CF and initiate IND-enabling studies
  - Expand pipeline within priority focus areas and beyond

2027+

- **PM577 for Wilson Disease:** Announce initial clinical data in 2027
- **PM647 for AATD:** Announce initial clinical data in 2027
- **Advance additional high-value programs:**
  - File IND and/or CTA for CF and initiate Phase 1 clinical trials
  - Relaunch programs targeting neurological and other large indications

Secure multiple additional strategic partnerships to accelerate our pipeline and bolster our financial resources

AATD = Alpha-1 Antitrypsin Deficiency; CF = cystic fibrosis; IND = investigational new drug; CTA = clinical trial application; CGD = chronic granulomatous disease

Q&A

Prime Medicine is the Leader in Gene Editing Positioned to Create Sustainable Value Through Pipeline Execution and External Partnerships

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The Leader in Prime Editing

- Potential to address approximately 90% of genetic diseases and opportunities in non-genetic diseases
- Breakthrough initial clinical data in CGD demonstrates clinical proof of concept for Prime Editing
- Comprehensive intellectual property position

Platform Modularity Oriented for Growth

- Fully integrated modular platform - pre-clinical, clinical, manufacturing, regulatory
- Proprietary modular delivery systems within target tissues
- Advancing Prime Editing regulatory paradigms - streamlined development

Pipeline Positioned for Value Creation

- PM577 in Wilson Disease IND and/or CTA expected in H1'26; AATD IND and/or CTA expected in mid-2026
- Strategically focused on programs in large genetic diseases, with clear path to value inflection and multi billion-dollar opportunities

Partnerships and BD Potential

- BMS partnership to develop Prime Edited *ex vivo* CAR-T products
- Cystic Fibrosis Foundation relationship and funding to advance Prime Editors for Cystic Fibrosis
- Additional business development to accelerate and expand pipeline

Pro-forma cash, cash equivalents, investments and restricted cash of **$227.0M for 9/30/2025, cash runway into 2027**

AATD = Alpha-1 Antitrypsin Deficiency; IND = investigational new drug; CTA = clinical trial application; CGD = chronic granulomatous disease

Thank You!