Glycomine Update
4th World Conference on CDG
Lisbon, 2019

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Chief Medical Officer

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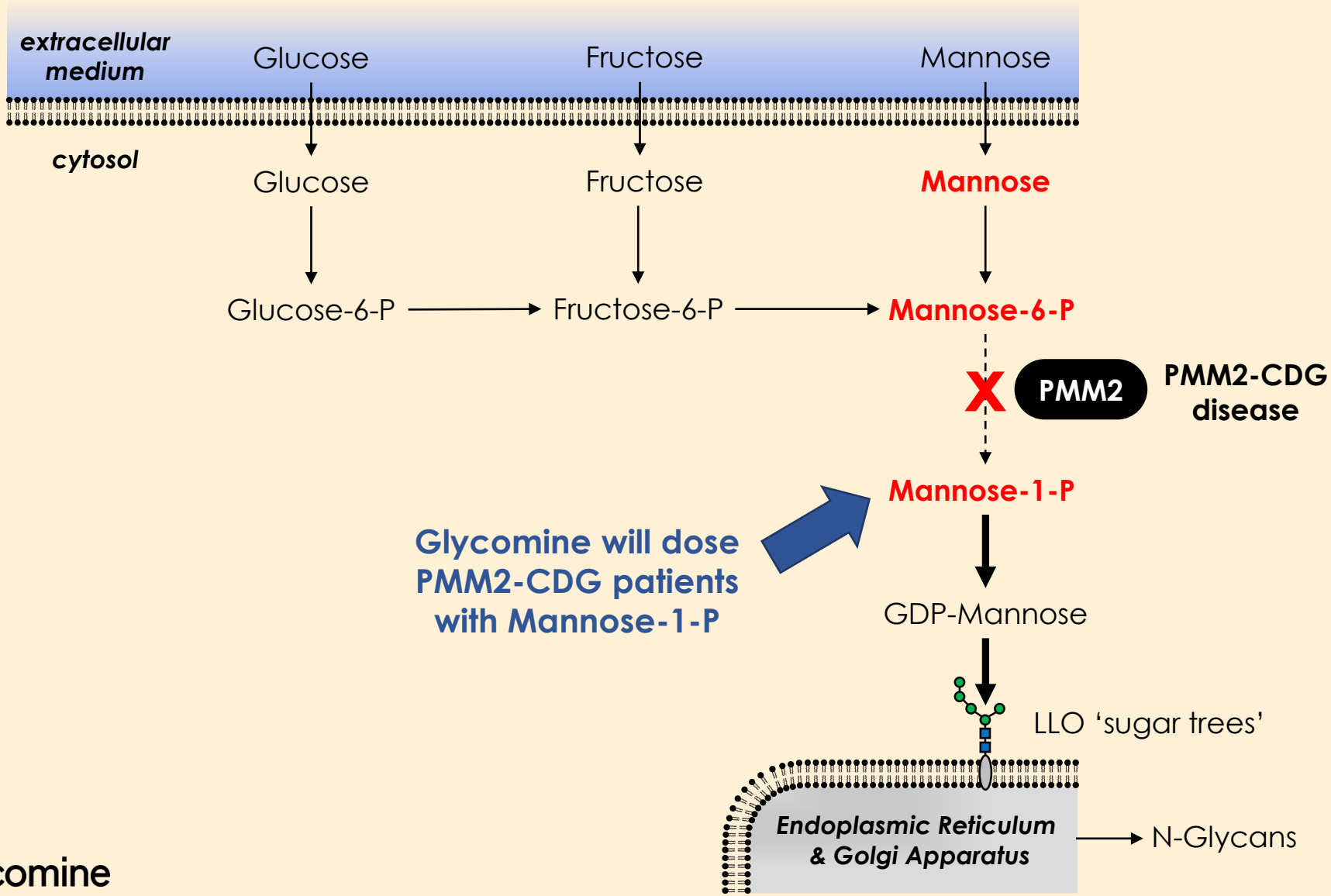
Glycomine, Inc. Overview

- Based in San Francisco, venture capital-funded biotech company
- Focused on developing a new therapy for PMM2-CDG
- Natural history study GLY-000 is currently underway
- Planning to initiate investigational clinical studies in 2020 using Lipo-M1P
  - Healthy volunteers in first half of 2020
  - PMM2-CDG patients immediately thereafter, second half of 2020

PMM2-CDG disease is caused by a loss of function in the PMM2 enzyme that converts Mannose-6-P → Mannose-1-P



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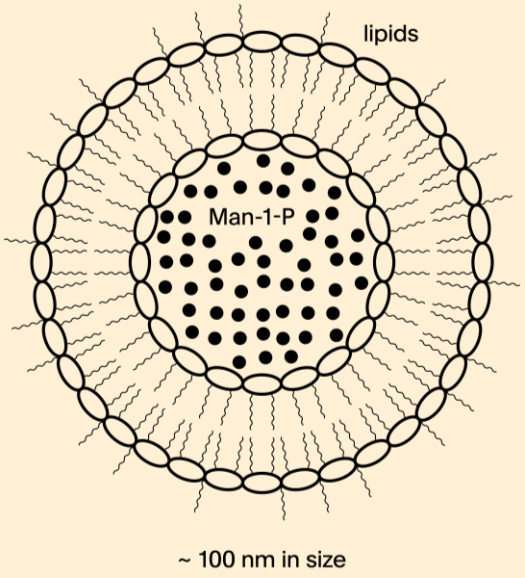
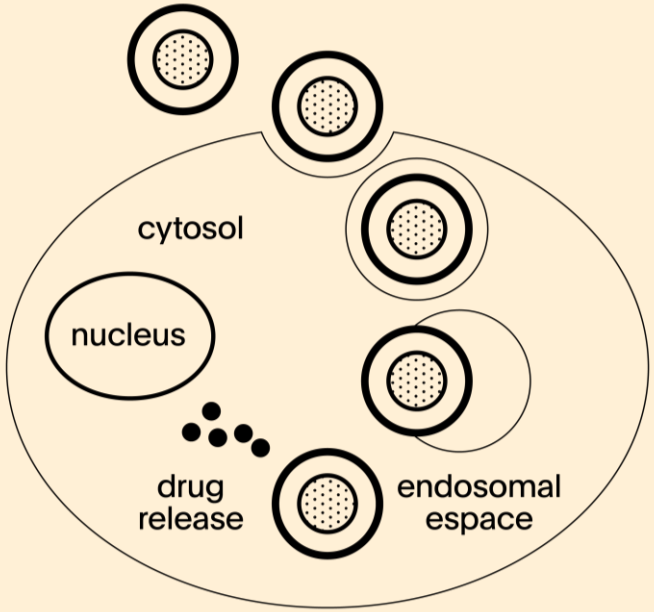
Glycomine's therapy replaces the substrate Mannose-1-P; the liposomal formulation ensures intra-cellular penetration

- Mannose-1-P, the missing substrate, is hydrophilic and therefore not cell permeable
- Liposomes enable M1P to reach the cytosol
  - Safe, non-immunogenic, stable, biodegradable
  - 12 FDA approved therapies and 22 in clinical trials

Lipo-M1P



Cell



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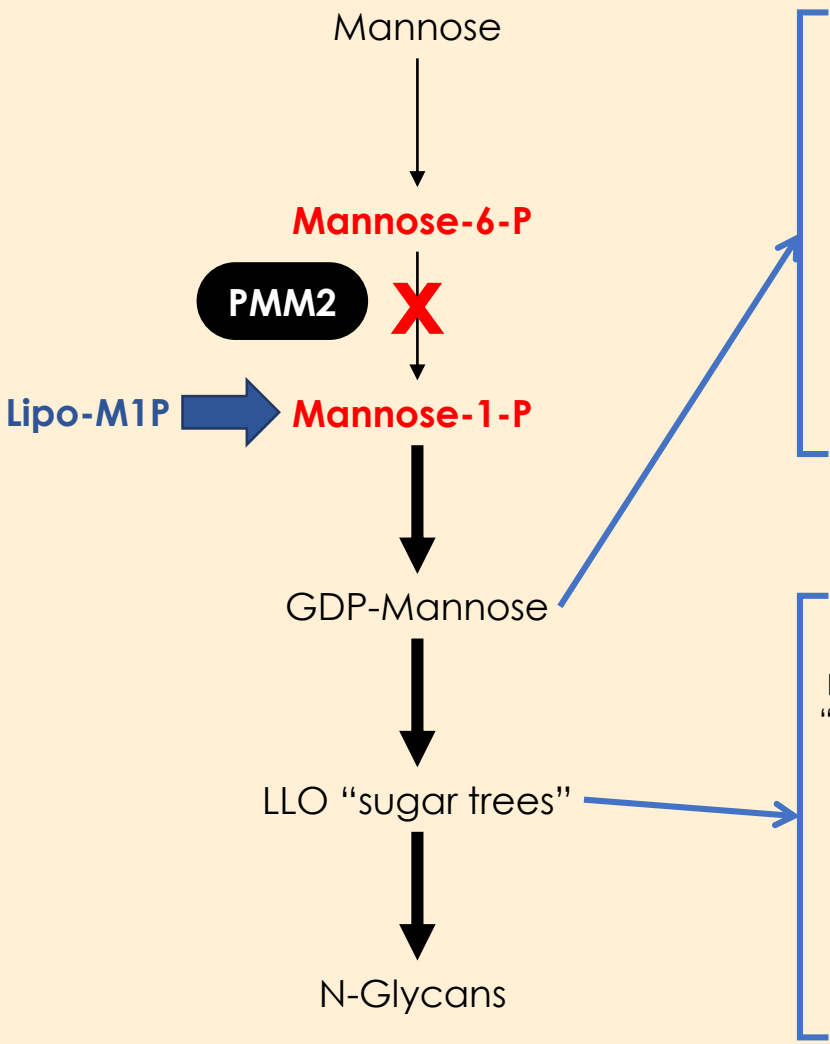
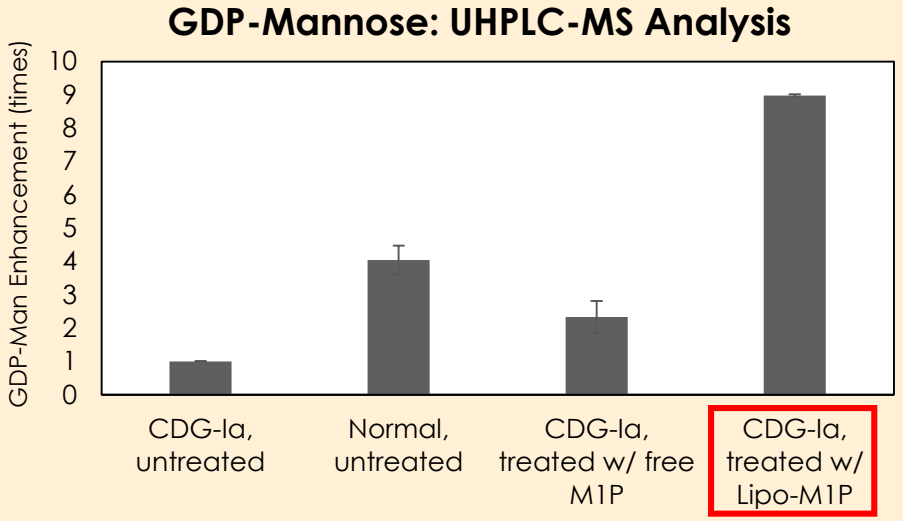
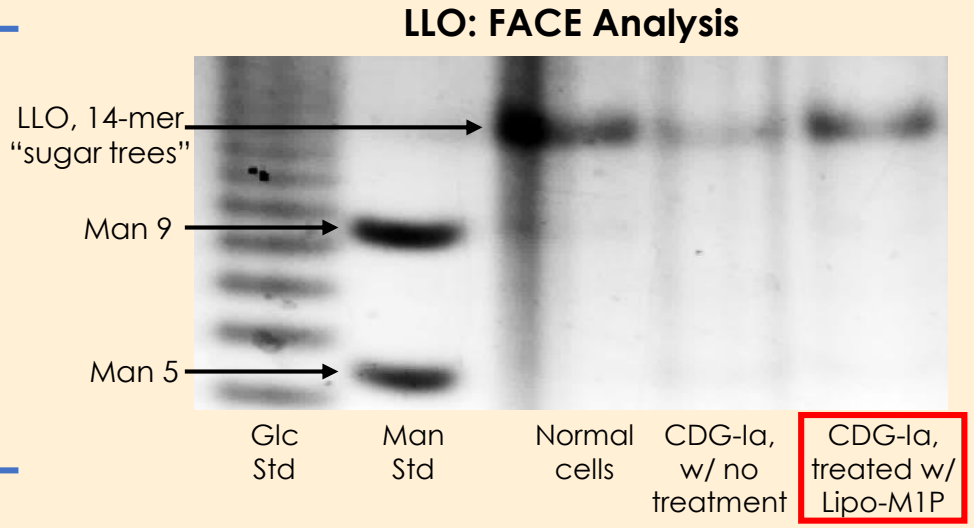
Treatment with Lipo-M1P restores both GDP-Mannose and LLOs ('sugar trees') in PMM2-CDG fibroblasts







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CDG-Ia cells have R141H/F119L mutation

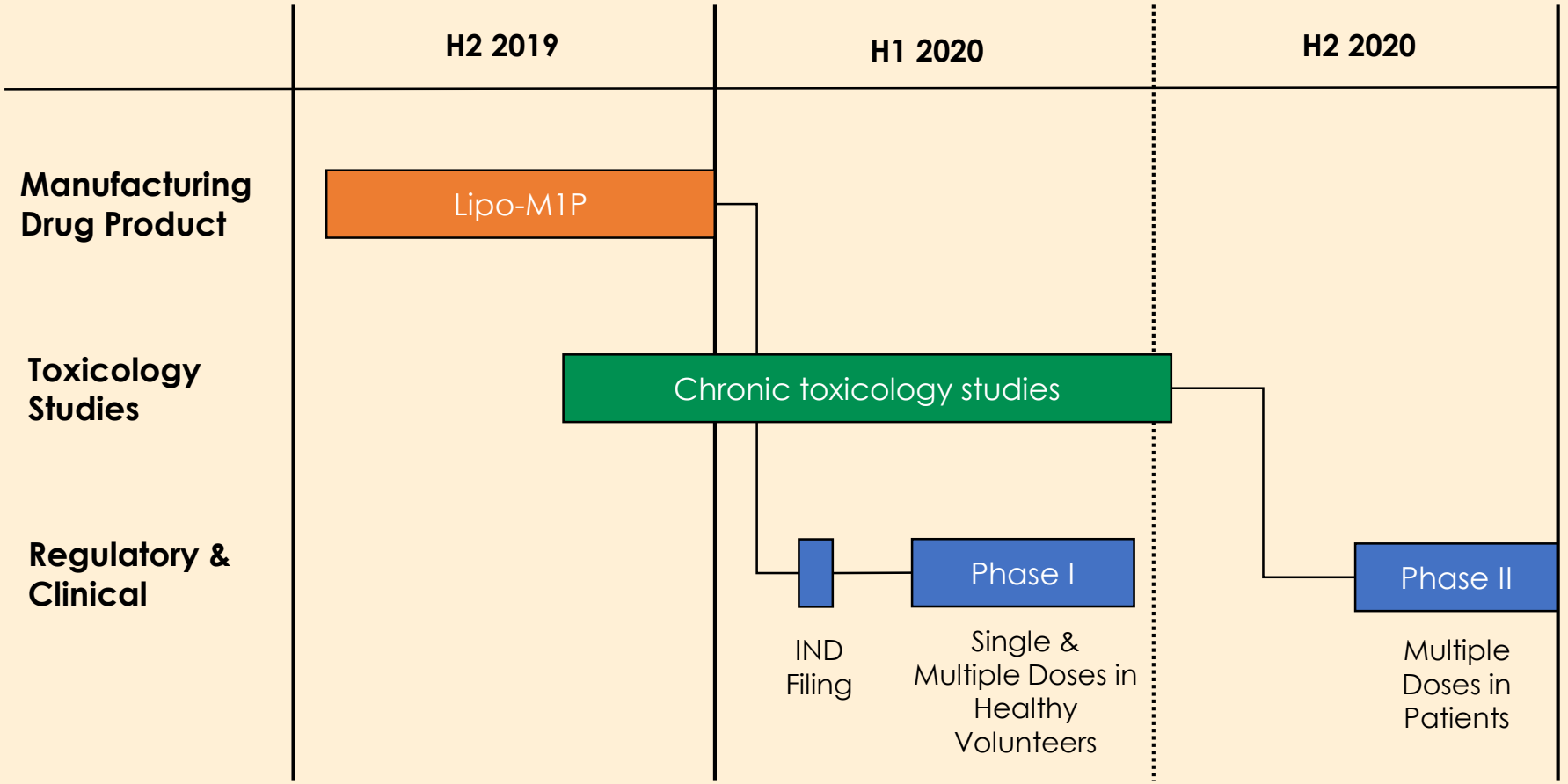
Company is poised to achieve significant milestones

- Significant achievements completed
  - ✓ 28-day GLP toxicology
  - ✓ GMP drug substance (Mannose-1-Phosphate) manufacturing
  - ✓ Met with European Medicines Authority (EMA) and US FDA
  - ✓ Natural history study underway

- Tasks in progress and on track for completion
  - Manufacturing investigational drug product (Lipo-M1P) on a large scale for use in upcoming clinical trials
  - Chronic (long-term) toxicology studies

- Significant milestones over next 12 – 24 months
  - IND filing with FDA in first half of 2020
  - Phase I trial in first half of 2020
  - Phase II first-in-patient trial in H2 2020

Significant milestones in the next 12-24 months



- ✓ 28-day GLP toxicology
- ✓ cGMP drug substance (M1P)
- ✓ Met with EMA and US FDA
- ✓ Observational study GLY-000 underway

UPCOMING:

- File IND with FDA in H1, 2020
- Phase I HV trial in H1, 2020
- Phase II patient trial in H2, 2020

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Upcoming clinical trials with Lipo-M1P

- Healthy Volunteers
  - Phase: I (first in humans)
  - Single dose in several patients, then
  - Multiple doses in several patients
  - Number of patients and frequency of dosing not yet agreed with regulators

- PMM2-CDG (CDG-1a) Patients
  - Phase: II
  - Multiple doses
  - Duration: likely 6 months
  - Planned frequency and route of administration: weekly dose, administered by intravenous infusion over 1-2 hours
  - Number of patients and ages not yet agreed with regulators

PMM2-CDG

GLY-000 Observational Study

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GLY-000 Observational Study – Overview

- **Phase:** IV (no intervention)
- **Primary Objective**: collect clinical and biological information in patients with PMM2-CDG (CDG-1a)
- **Secondary Objectives:** determine parameters and endpoints to be used in clinical trials, and to select sites with significant number of PMM2-CDG patients and adequate resources to conduct the trial
- **Study Duration:** patients will participate a minimum of 6 months before being considered for the planned clinical trial (to begin once Lipo-M1P investigational drug is available and healthy volunteers data verifies its safety); maximum participation is 3 years if not entered into a clinical trial
- **Participants:** 48 patients of all ages
- **Sites:** up to 12 sites, in the US and EU

GLY-000 Observational Study – Current status

- **Planned Enrollment:** 48 patients
- **Actual Enrollment:** 41 patients
  - 1 early termination
  - 40 active
- **Planned Sites:** up to 12 (6 US + 6 EU)
- **Actual Sites Active:** 8 (5 US + 3 EU)
- **Expected Enrollment Completion/Closure:** end of 2019

GLY-000 Observational Study – Investigators/sites

USA	EUROPE
Hans Andersson Sub-Inv: Eva Morava-Kozicz Tulane University, New Orleans LA	Peter Witters University Hospital Leuven
Can Ficicioglu / Andrew Edmonson Children's Hospital of Philadelphia (CHOP)	Pascale de Lonlay Necker Enfants-Malades Hospital, Paris
Christina Lam UW & Seattle Children's Hospital	Tomas Honzik University Hospital of Prague
Gerard Vockley Children's Hospital of Pittsburgh of UPMC	
Eva Morava-Kozicz/ Marc Patterson Mayo Clinic of Medicine, Rochester MN	

- Additional sites will be opened in 2019

Thank You

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