



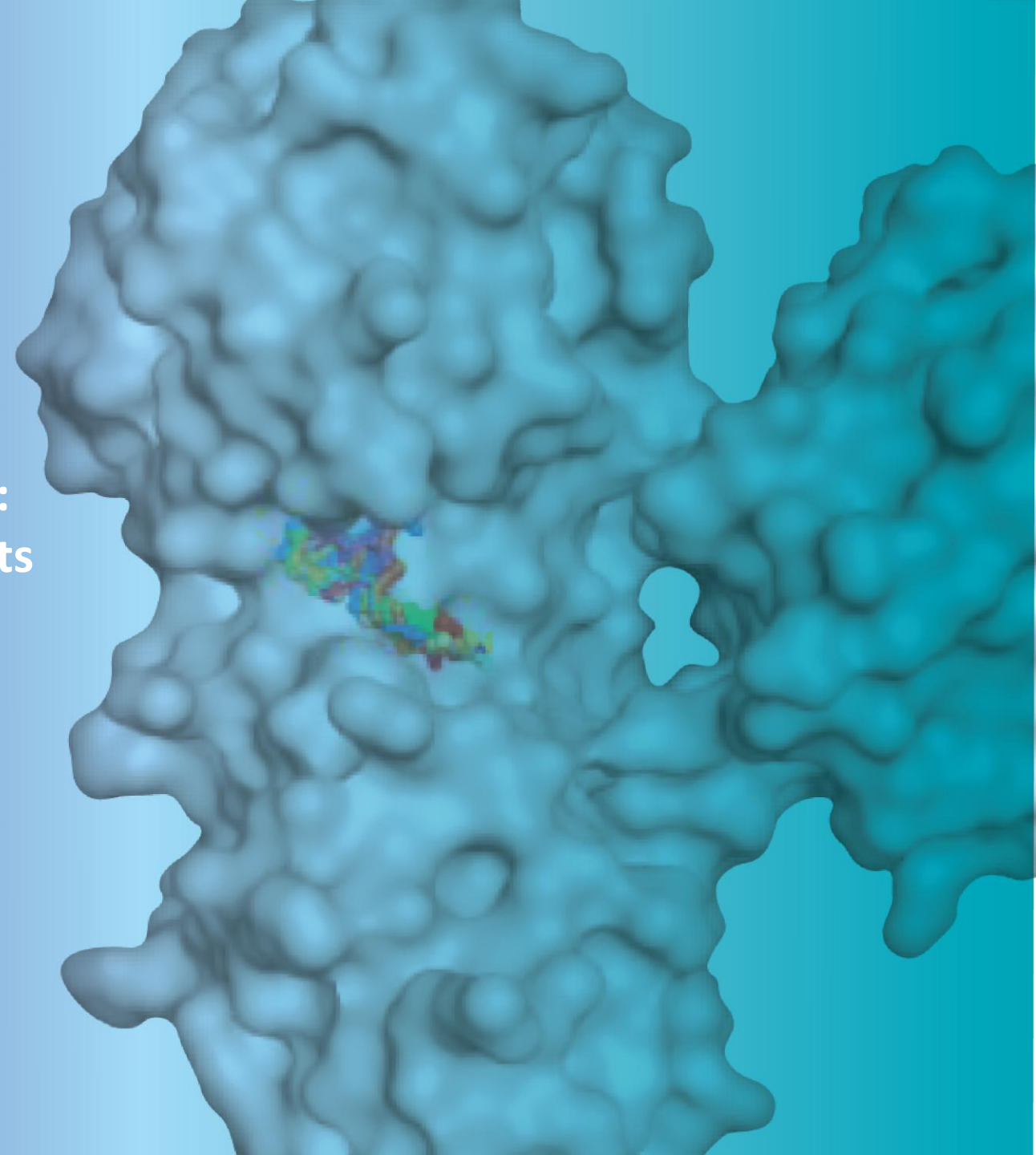
First Oral Direct-Acting Antiviral CDI-988 for Norovirus Infection Prevention and Treatment: Mechanism of Action and Phase 1 Study Results

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Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including our development pipeline; our technology platform's ability to produce viable drug candidates at reduced development timelines and costs; development efforts in our clinical programs, including our ongoing Phase 2a study for oral influenza PB2 inhibitor; our Phase 1 study with 3CL protease inhibitor for coronavirus and norovirus; and the expected sufficiency of our cash balance to fund our planned operations.

Forward-looking statements are prefaced by words such as “anticipate,” “expect,” “plan,” “could,” “may,” “will,” “should,” “would,” “intend,” “seem,” “potential,” “appear,” “continue,” “future,” “believe,” “estimate,” “forecast,” “project,” and similar words. Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. We caution you, therefore, against relying on any of these forward-looking statements. Our actual results may differ materially from those contemplated by the forward-looking statements for a variety of reasons, including, without limitation, the risks arising from any future interest rate increases in response to inflation, uncertainty in the financial markets, the possibility of a recession and the geopolitical conflicts in Israel and Ukraine on our Company, our collaboration partners, and on the U.S., UK, Australia and global economies, our ability to proceed with studies including recruiting volunteers for and procuring or manufacturing materials for such studies by our clinical research organizations and vendors, the results of our CRO's studies referred to above, our and our collaboration partners' technology and software performing as expected and maintenance and protection of related intellectual property rights, financial difficulties experienced by certain partners and our ability to secure and maintain new collaboration partners, general risks arising from clinical trials, receipt of regulatory approvals, regulatory changes, development of effective treatments and/or vaccines by competitors, including as part of the programs financed by the U.S. government, and potential mutations in the viruses we are targeting which may result in variants that are resistant to a product candidate we develop. Further information on our risk factors is contained in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2024. Any forward-looking statement made by us in this presentation speaks only as of the date on which it is made. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law.

The Hidden \$60 Billion Norovirus Burden

Significant unmet need of Norovirus as a leading cause of acute gastroenteritis across all age groups and regions.

700M

Infections
Worldwide
Annually

200K

Deaths
Worldwide
Annually

7

GII.4
Pandemic
Outbreaks

No Approved Norovirus Vaccines or Treatments Available

1968-2025

1

Multiple vaccine clinical studies initiated since 2010

Challenge

2

**High norovirus genetic variation and drift:
10 genogroups & 49 genotypes**

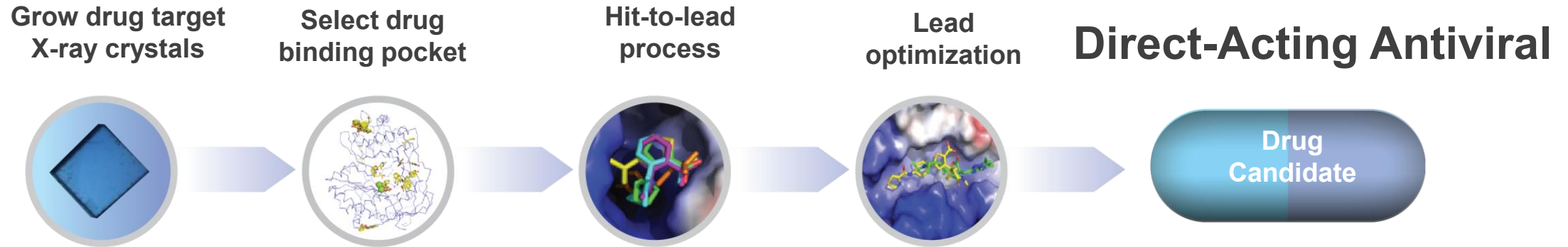
Solution

3

Pan-viral protease inhibitor CDI-988

- Convenient oral regimen for both prevention and treatment
- Stockpile readiness for norovirus outbreak

Proprietary Drug Discovery Platform Technology for Direct-Acting Antivirals

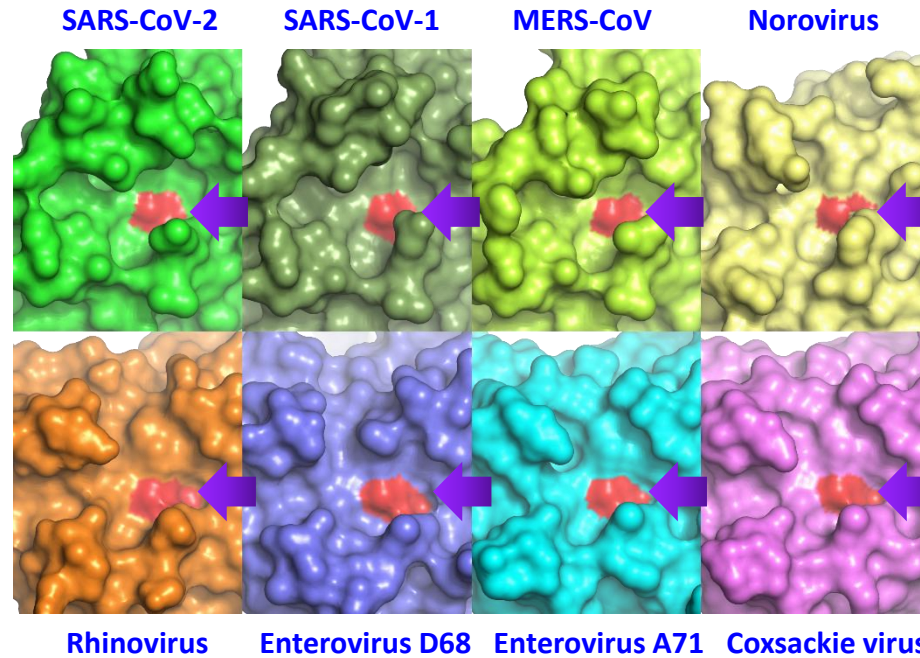


(A) In-house screening: Protease crystals and assays (>150)

- Viral proteases
- SARS-CoV-1 & 2
- MERS-CoV
- Norovirus
- Rhinovirus A/B/C
- Enterovirus D68 & A71
- Coxsackie
- HCV
- Dengue
- Zika
- Chikungunya

- Norovirus
- GI.1
- GI.2
- GII.1
- GII.2
- GII.3
- GII.4
- GII.6
- GII.17

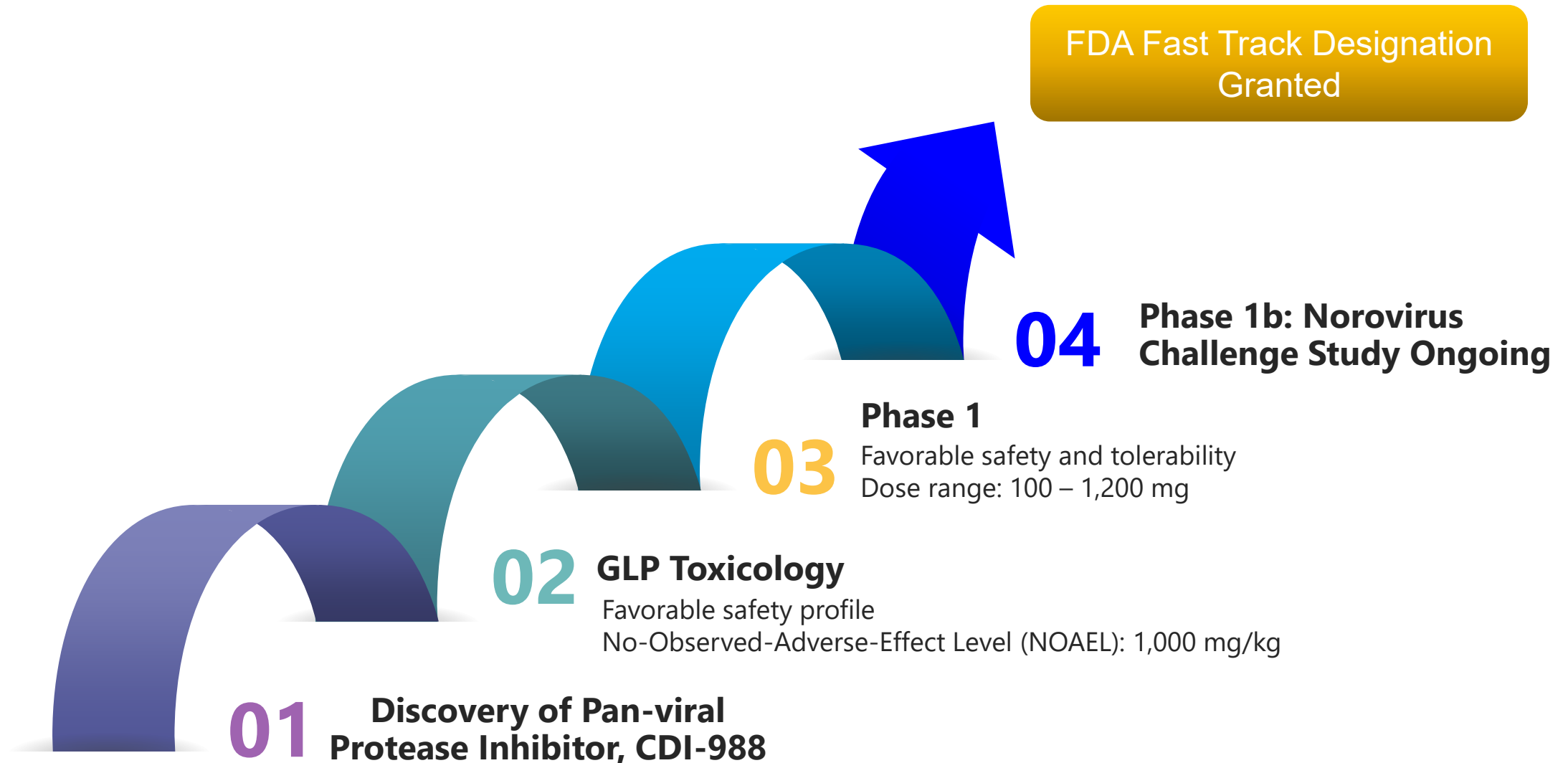
(B) Focus on highly conserved region



(C) Develop pan-viral antiviral

Viral 3CL protease	Nirmatrelvir, (Pfizer) IC50 μM	Ensitrelvir (Shionogi) IC50 μM	CDI-988 (Cocrystal) IC50 μM
SARS-CoV-2	0.06	0.015	0.002
GI.1 Norwalk	>20	>20	0.06
GII.4 Norovirus (MD-145)	>20	>20	0.06
GII.17 Norovirus	>20	>20	0.02
Enterovirus D68	>20	>20	0.056
Rhinovirus	>20	>20	0.94

Roadmap For First Antiviral, CDI-988, For Acute and Chronic Norovirus Infection

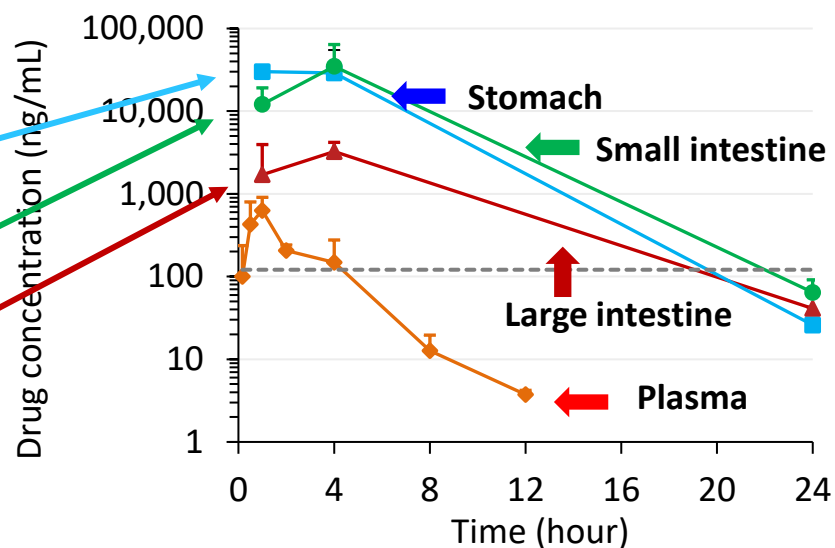
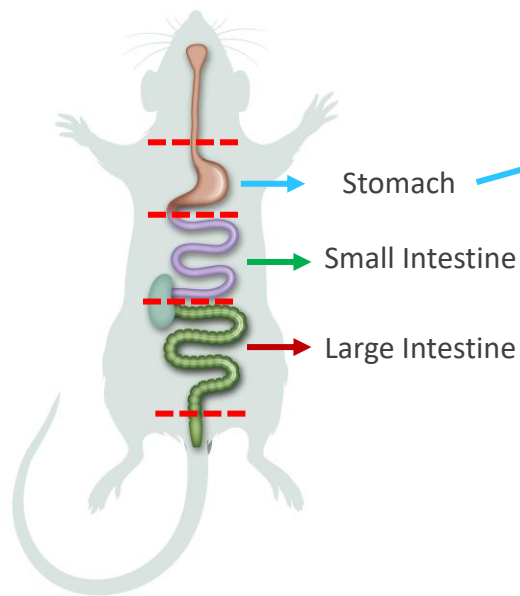
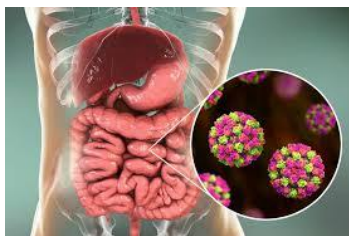


High Resolution X-ray Cocrystal Structures Confirm Broad-Spectrum Coverage

Structures of Norovirus Genogroups I and II, including GII.1, GII.2, GII.3 GII.4, GII.6 and GII.17 (1.1 – 2.3 Å)



Promising PK/PD Property of CDI-988: Significantly Higher Exposure and Longer Half-Life of Oral CDI-988 in Intestine and Stomach

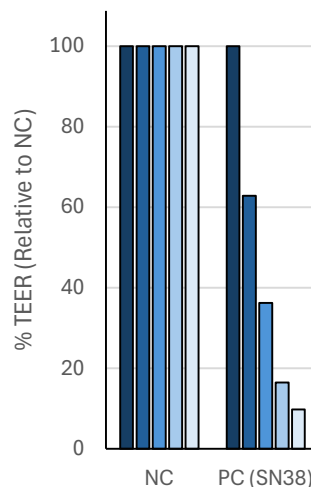
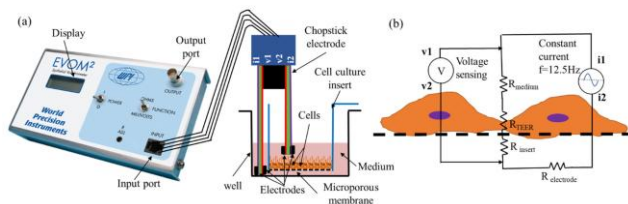


Pharmacokinetic evaluation of CDI-988:
Mean CDI-988 concentration-time profiles
after a single dose of CDI-988 after oral dosing in rats

- GI-targeted activity was one of the norovirus lead selection criteria
- Demonstrated higher drug concentrations in GI (>100-fold higher at 4 hr time point)
- Showed a longer drug-target tissue residence time; potentially increases *in vivo* antiviral efficacy in norovirus-infected small intestine

Safety Assessment Using Human 3-D Small Intestinal Tissue System (EpiIntestinalFT Model System)

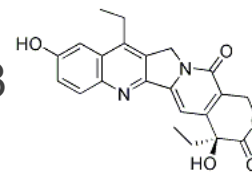
(A) TEER (Transepithelial Electrical Resistance) Assay



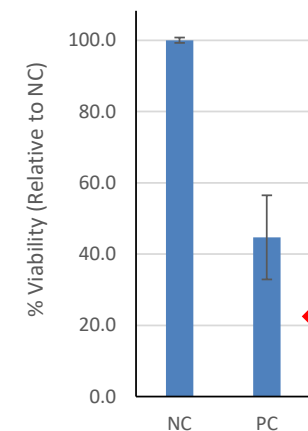
■ Day 0 ■ Day 1 ■ Day 2 ■ Day 3 ■ Day 4

Reference compound, SN-38, causes GI toxicity, causing diarrhea, nausea, and vomiting

SN-38
20 μ M

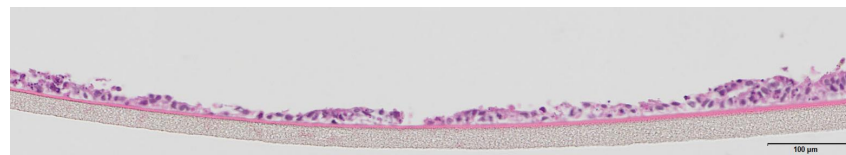
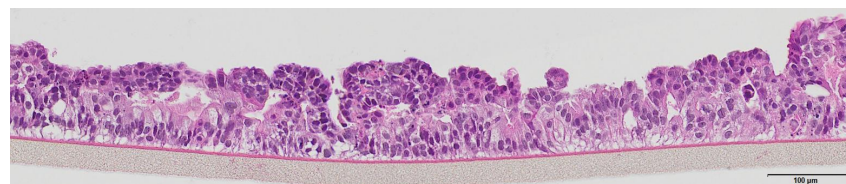


(B) MTT cell viability assay



SN-38
20 μ M

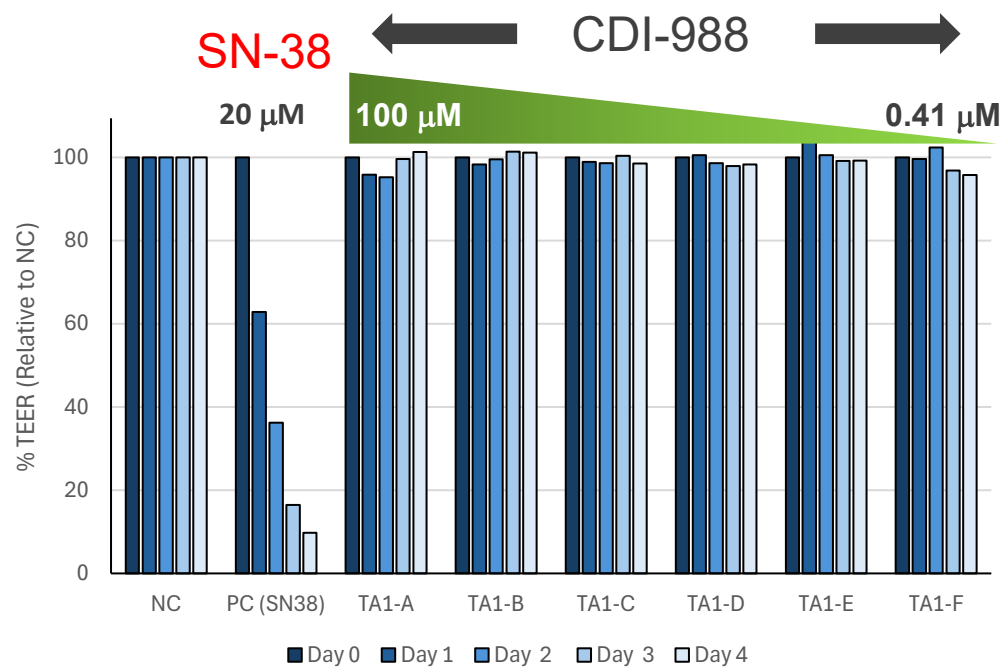
(C) Histological assessment of human small intestine gastrointestinal toxicity



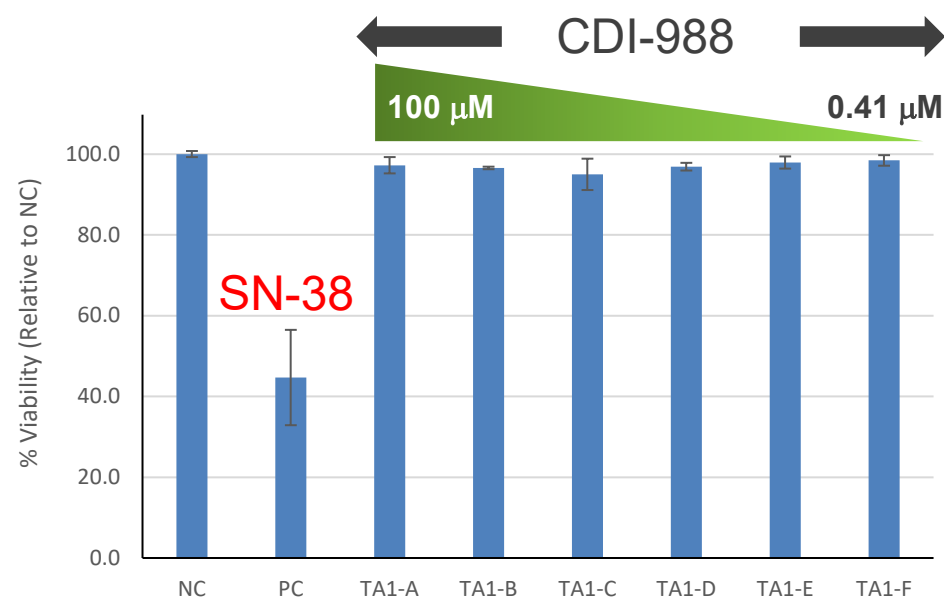
SN-38
20 μ M

CDI-988 Shows Favorable Safety and Functional Profiles in Human Small Intestinal Tissue

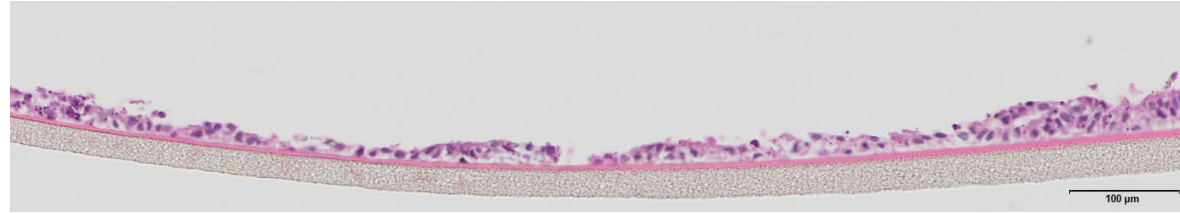
(A) TEER (Transepithelial Electrical Resistance) Assay



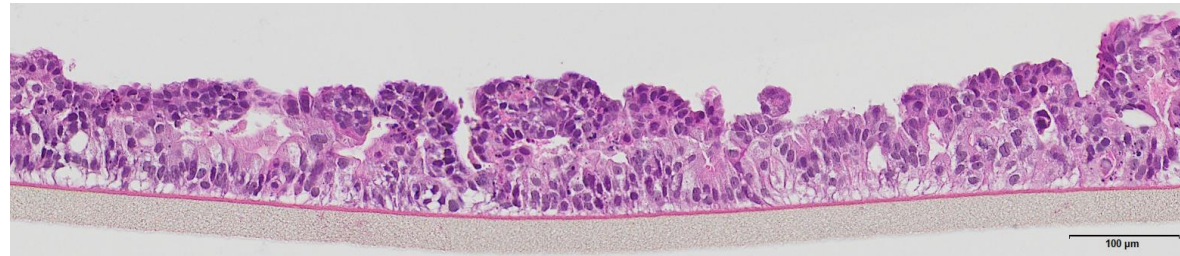
(B) MTT cell viability assay



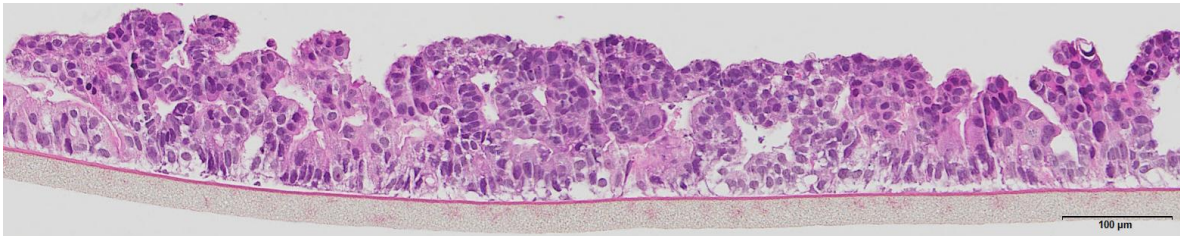
CDI-988 Shows No Gastrointestinal Toxicity in Human Small Intestine Organoid System



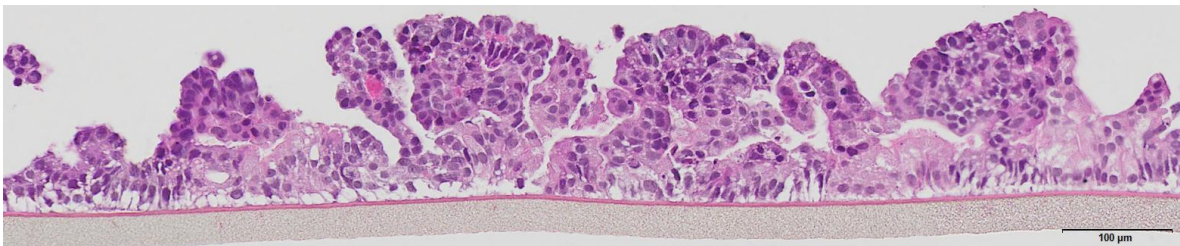
20 μ M SN-38



No CDI-988



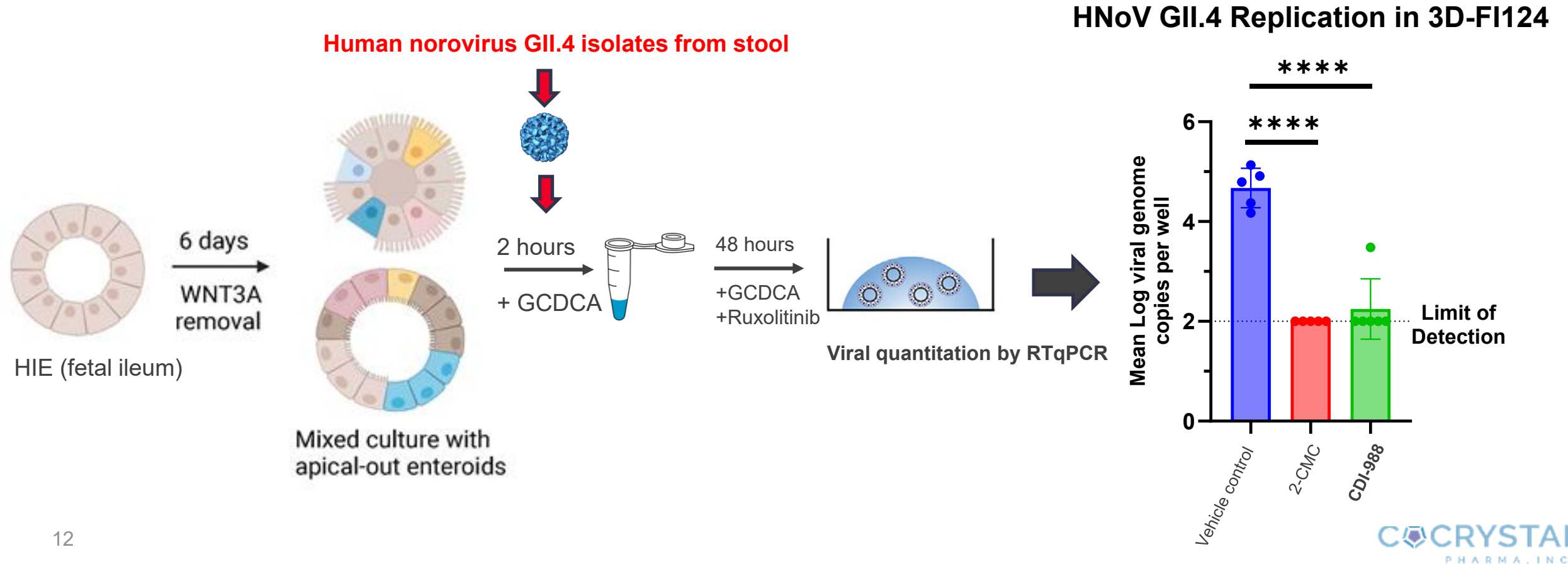
1 μ M CDI-988



100 μ M CDI-988

In Vitro Efficacy of CDI-988 in Norovirus GII.4 Infected 3-D Differentiated Human Intestinal Enteroids (HIEs)

- 2-log reduction in CDI-988-treated 3-D human intestinal enteroids



Phase 1 Study: Oral Pan-viral Protease Inhibitor CDI-988 Showed Favorable Safety and Tolerability

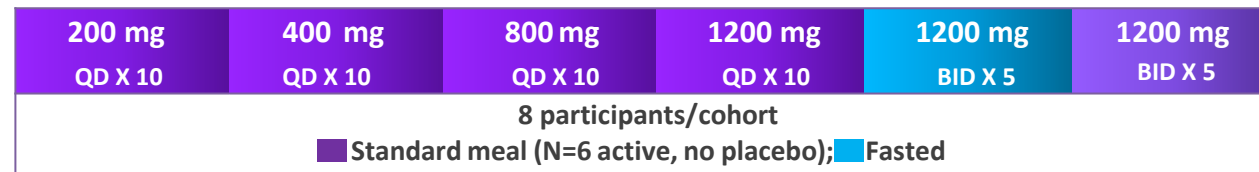
- Single-center, randomized, double-blind, placebo-controlled
- Single-ascending dose (SAD) and Multiple-ascending dose (MAD) cohorts
- Healthy adult volunteers (18 – 55 years old)
- Each cohort comprised 8 participants (6 on CDI-988; 2 on placebo)

Study design

Single-ascending dose
(SAD)



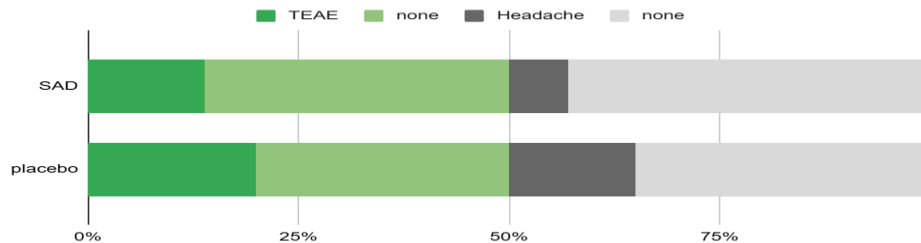
Multiple-ascending dose
(MAD)



Phase 1 Topline Safety Data Summary

- Demonstrated favorable safety profile
- Well tolerated
- Major adverse effect: headache

Single Ascending Dose Cohorts



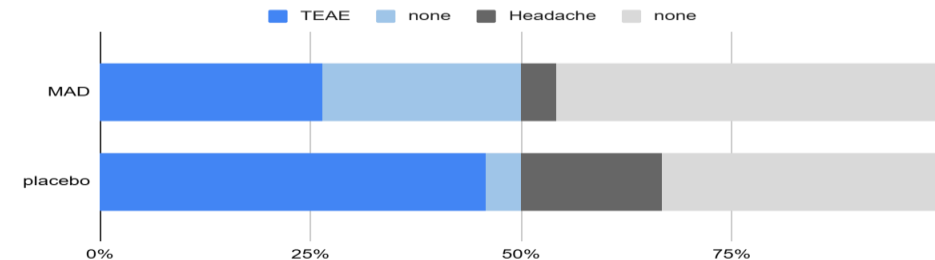
Overall treatment-emergent AE (TEAE) rate

- 28% (10/36) in CDI-988 cohorts
- 40% (4/10) in placebo subjects

Headache was the most frequently reported TEAE

- 14% (5/36) in CDI-988 cohorts
- 30% (3/10) in placebo subjects

Multiple Ascending Dose Cohorts



Overall treatment-emergent (TEAE) rate

- 53% (19/36) in CDI-988 cohorts
- 92% (11/12) in placebo subjects

Headache was the most frequently reported TEAE

- 8% (3/36) in CDI-988 cohorts
- 33% (4/12) in placebo subjects

CDI-988 Phase 1b Norovirus Challenge Study Is Enrolling Participants

- Norovirus GII.2 challenge study developed by our collaborators Emory and the University of North Carolina (UNC)
- Phase 1b study protocol (Sponsor: Cocystal Pharma) has been approved by the FDA
- Current status: First dose with the norovirus GII.2 inoculum completed

The Journal of Infectious Diseases

MAJOR ARTICLE



Dose-Response of a Norovirus GII.2 Controlled Human Challenge Model Inoculum

Nadine Rouphael,^{1,3} Allison Beck,^{1,4} Amy E. Kirby,² Pengbo Liu,² Muktha S. Natrajan,¹ Lilin Lai,¹ Varun Phadke,¹ Juton Winston,¹ Vanessa Raabe,^{1,5} Matthew H. Collins,¹ Tigisty Girmay,¹ Alicarmen Alvarez,¹ Nour Beydoun,^{1,6} Vinit Karmali,¹ Joanne Altieri-Rivera,¹ Lisa C. Lindesmith,⁴ Evan J. Anderson,^{5,6} Yuke Wang,² Jill El-Khorazaty,⁶ Carey Petrie,⁶ Ralph S. Baric,⁴ Shahida Baqar,⁷ Christine L. Moe,^{2,8} and Mark J. Mulligan^{3,8}

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OH NOROVIRUS!

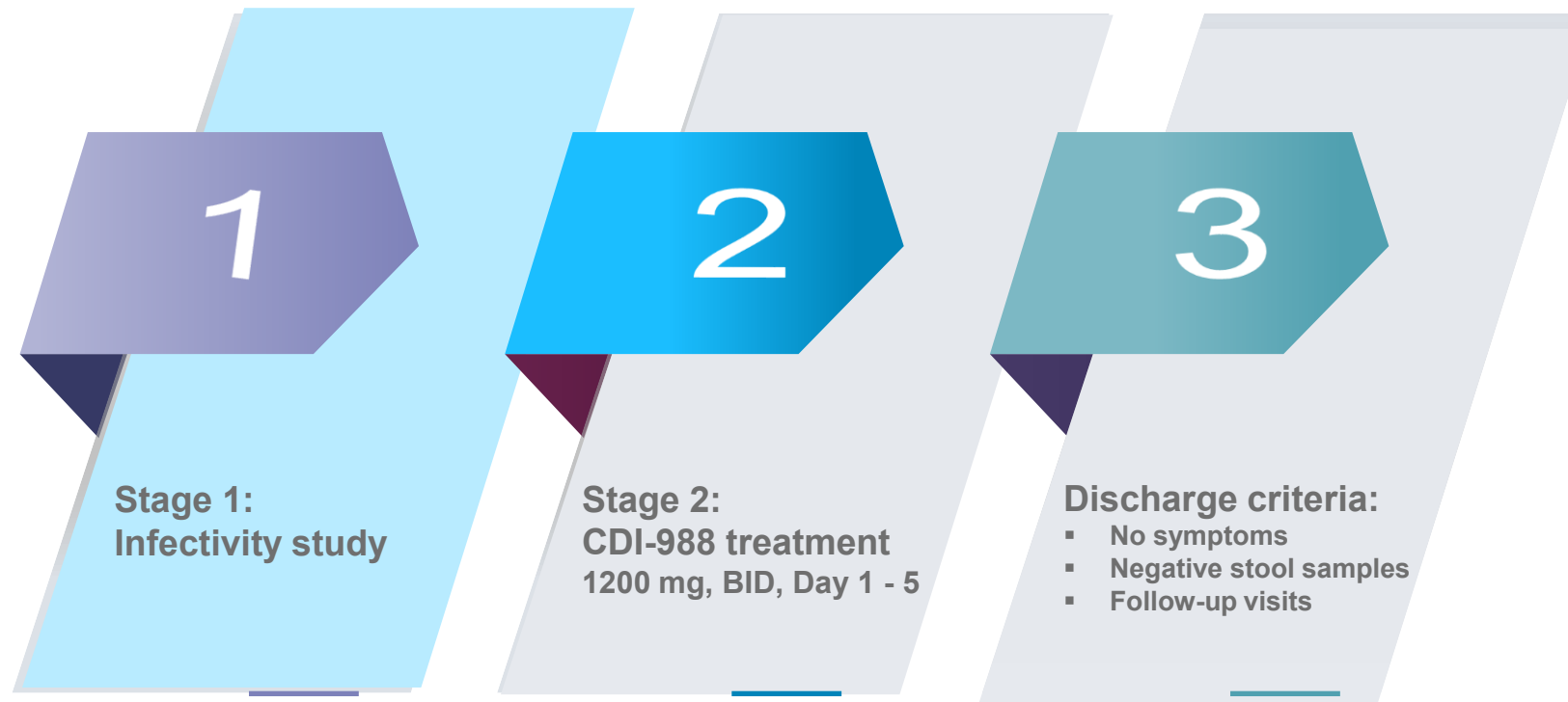
EMORY UNIVERSITY

VOLUNTEERS NEEDED FOR INPATIENT NOROVIRUS STUDY

The Emory Hope Clinic is evaluating how effectively an experimental drug can protect people from Norovirus infection.

Norovirus Challenge Phase 1b Study Design

- **Design:** Randomized, double-blind, placebo-controlled
- **Number of participants:** Up to 40, healthy adult volunteers (18-49 years old)
- **Norovirus inoculum:** GII.2 SMV
- **Treatment:** 1200 mg BID Day 1 – 5
- **Primary efficacy endpoint:** Reduction in incidence of clinical symptoms
- **Secondary efficacy endpoints:** Reduction in viral shedding and disease severity





Many thanks to our collaborators, norovirus experts, scientists, clinical investigators, adult volunteers, the staff at the study centers, the research organizations, and my colleagues at Cocrystal Pharma

