EDP-323, a First-in-Class, Once-Daily, Oral Non-Nucleoside L-Protein, Replication Inhibitor Antiviral for the Treatment of RSV: Results From a Phase 2a Human Viral Challenge Study

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Presenter

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13th International RSV Symposium. Iguazu Falls, Brazil. March 12-15, 2025

Disclosure of Relevant Financial Relationships and Acknowledgments

Disclosures

- **JPD, AA**, **SC**, and **STR** are employees of Enanta Pharmaceuticals and hold Enanta Pharmaceuticals stock
- **BL**, **AM**, **JM**, and **AC** are employees of hVivo and hold hVivo stock

Acknowledgments

- Authors thank those who chose to volunteer for this study, and for the dedicated work of the Enanta and hVivo teams

Under the direction of authors, medical writing assistance was provided by Syneos Health Medical Communications, LLC, and supported by Enanta Pharmaceuticals.

EDP-323: First-in-Class, Oral, Once Daily, L-Protein Inhibitor for the Treatment of RSV Infection

- Significant unmet need for RSV antiviral therapies despite availability of prophylaxis[1]
  - Complementary to effective preventive vaccines and monoclonal antibodies
  - See late breaker poster #253, Huang et al – First in Pediatrics Phase 2 Trial of N-Targeting Antiviral, Zelicapavir
- **EDP-323**: first-in-class, non-nucleoside, direct-acting L-protein inhibitor in clinical development as an oral, once-daily therapy[2]
  - Blocks viral replication and transcription[2]
- Strong preclinical profile[2-4]
  - Picomolar in vitro potency against RSV-A and RSV-B[2]
  - Reduced viral load and disease dose dependently (prophylactically and therapeutically)[2,3]
- Phase 1 study evaluated 7 daily oral doses up to 800 mg/dose[5,6]
  - Once daily oral dosing supported by PK profile[5,6]
  - Side effects and safety lab profile similar to placebo at all dose ranges[5,6]
  - C_{24} (trough concentrations) of 200 mg and 600 mg dosing: 11- and 44-fold above in vitro protein-adjusted EC_{90}[5,6]

C_{24}, observed concentration at 24 hours after dose administration; EC_{90}, EC90, 90% effective concentration; PK, pharmacokinetic; RSV, respiratory syncytial virus.

1. Walsh E. N Engl J Med 2024;391:1155-1156. **2.** Rhodin MHJ, et al. Presented at: Discovery at Target: New Antivirals Conference. October 17-20, 2022. Boston, MA, US. **3.** Levene RE, et al. Presented at: 12th International RSV Symposium. September 29-October 2, 2022. Belfast, Northern Ireland, UK. **4.** Levene RE, et al. Presentation at: 13th International RSV Symposium. Poster #161. March 12-15, 2025. Iguazu Falls, Brazil. **5.** Mills K, et al. Presented at: European Scientific Working Group on Influenza (ESWI). 9th Influenza Conference 2023. September 17-20, 2023. Valencia, Spain. **6.** Mills K, et al. Manuscript submitted for publication to *Clin Trans Sci*. 2025.

Unique Properties of EDP-323 Mechanism of Action

Detailed in Poster #161: In Vitro Characterization of Respiratory Syncytial Virus Inhibitors

- EDP-323 maintained antiviral effect even when dosed up through 3 days post-infection in a 3D primary human airway epithelial cell system[1,4]
  - Antiviral effect of Fusion Inhibitors ablated if dosed shortly after infection[4]
- Development of antiviral resistance
  - Fusion inhibitors: low barrier to resistance; little impact to viral fitness[4]
  - EDP-323: higher barrier to resistance[4]
  - N inhibitor zelicapavir: highest barrier to resistance; viral fitness defects[4]
- Will these Mechanism of Action properties translate into outcome improvements in clinical trials?

*NCT05587478.
3-D, 3 dimensional; EC_{90}, 90% effective concentration; L, large; N, nucleoprotein; RNA, ribonucleic acid; RSV, respiratory syncytial virus.
1. Rhodin MHJ, et al. Presented at: Discovery at Target: New Antivirals Conference. October 17-20, 2022. Boston, MA, US. **2.** Mills K, et al. Presented at: European Scientific Working Group on Influenza (ESWI). 9th Influenza Conference 2023. September 17-20, 2023. Valencia, Spain. **3.** Mills K, et al. Manuscript submitted for publication to *Clin Trans Sci*. 2025. **4.** Levene RE, et al. Presentation at: 13th International RSV Symposium. March 12-15. Iguazu Falls, Brazil. **5.** Data on file, Enanta Pharmaceuticals.

Study Overview

Objective

- Evaluate the PK profile, safety, and antiviral activity of multiple doses of EDP-323 in a human RSV challenge study* among healthy adults[1]

Description

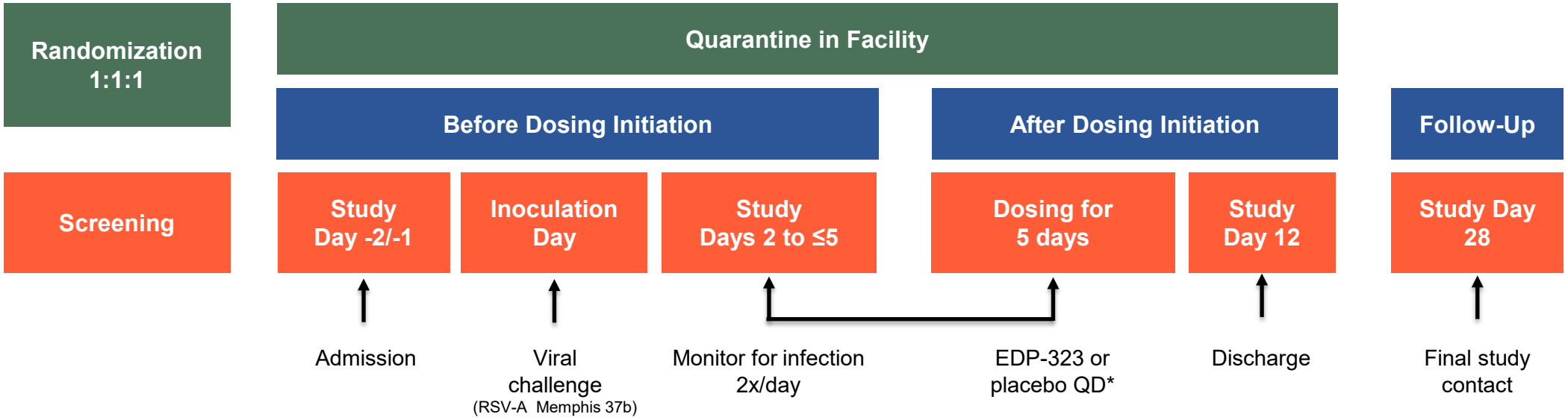
- Randomized, double-blind, placebo-controlled human viral challenge (RSV-A Memphis 37b strain) Phase 2a study†

Population

- Healthy, 18-55 years old, low serum RSV neutralizing antibody titer, weight ≥50 kg, BMI 18-35 kg/m^2

*RSV human challenge model mimics natural infection, allowing to evaluate safety/efficacy/immunogenicity of RSV therapeutics; utilized in the development of successful RSV vaccines.
†NCT06170242.
BMI, body mass index; PK, pharmacokinetic; RSV, respiratory syncytial virus.
1. DeVincenzo JP, et al. *Am J Respir Crit Care Med.* 2010;182(10):1305-1314.

Study Design and Endpoints



Dosing QD for 5 days (N=141), followed for 28 days

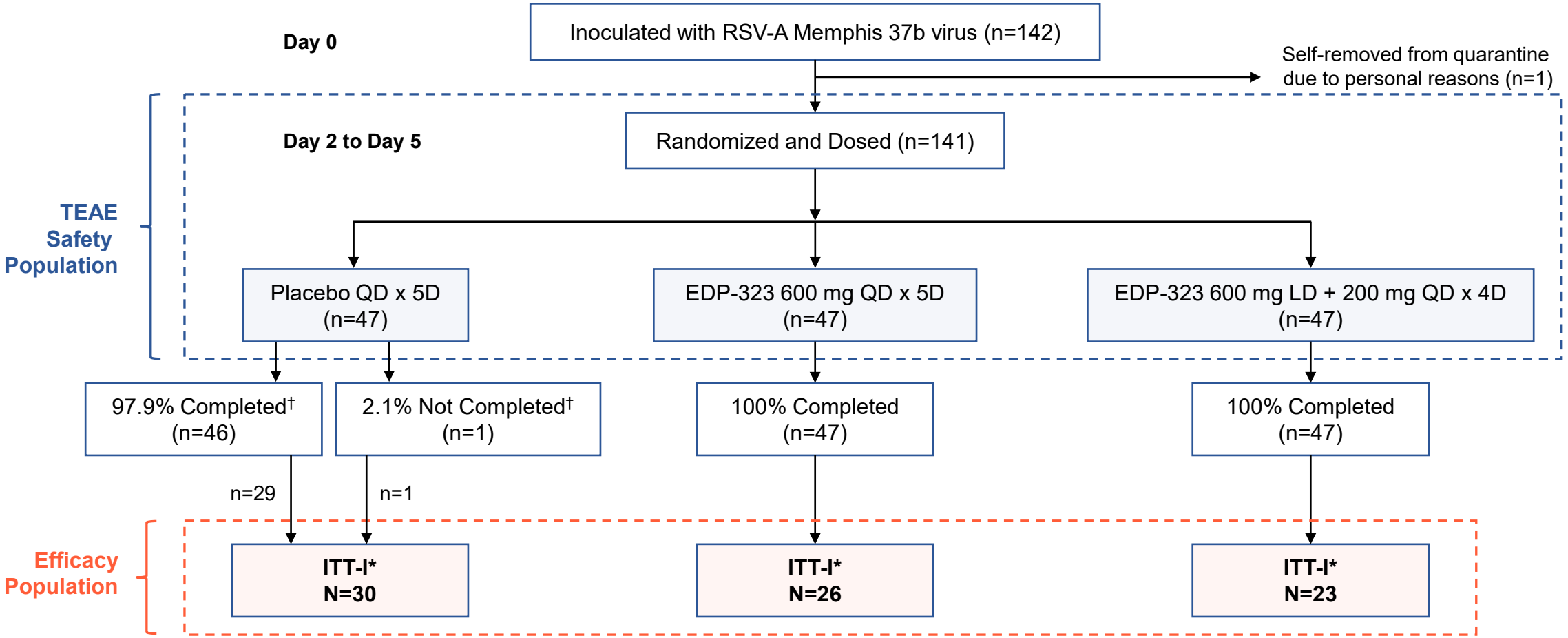
- **EDP-323 high dose: 600 mg (n=47)**
- **EDP-323 low dose: 200 mg (600 mg loading dose on Day 1 followed by 200 mg for 4 days) (n=47)**
- **Placebo (n=47)**

Please see Poster #153, Mills (Elmore) et al
PK and PK/PD Evaluation in RSV Human Challenge Study

- **Primary endpoint**
  - **Viral load AUC measured by qRT-PCR in nasal samples**
- **Selected secondary endpoints**
  - **PK profile**
  - **Safety profile**
  - **Reduction in viral load AUC measured by viral culture**
  - **Reduction in total symptom score AUC**

*Dosing initiated 12 hours after + RSV test (qualitative RT-PCR) or Day 5, whichever was first.
AUC, area under the curve; PK, pharmacokinetic; QD, once daily; qRT-PCR, quantitative reverse transcription-polymerase chain reaction; RT-PCR, reverse transcription-polymerase chain reaction; RSV, respiratory syncytial virus.

Participant Disposition



†1 participant discontinued the study due to personal reasons on Day 9 after completing the full 5-day dosing period; data from this participant were used in analyses

***Primary efficacy analysis, intent-to-treat infected (ITT-I):** all randomized participants who received challenge virus and ≥1 dose of study drug, and with RSV infection confirmed by central lab RT-PCR (>1 sample time-points positive by RT-PCR or a single sample time-point positive by culture)

D, day; LD, loading dose; QD, once daily; RT-PCR, reverse transcription-polymerase chain reaction; RSV, respiratory syncytial virus; TEAE, treatment-emergent adverse event.

Summary of Demographics

- Demographics were balanced across study arms

	EDP-323 High Dose (n=47)	EDP-323 Low Dose (n=47)	Placebo (n=47)
Age, years, median (Q1, Q3)	28 (24, 33)	26 (24, 30)	27 (23, 30)
Sex, male, n (%)	32 (68.1)	30 (63.8)	28 (59.6)
Race, White, n (%)	39 (83.0)	35 (74.5)	38 (80.9)

Q, quartile.

Summary of PK and Safety Outcomes

PK - EDP-323 mean trough plasma concentrations were maintained at 16- to 35-fold above protein-adjusted EC_{90} against both RSV-A and RSV-B subtypes

- See Poster #153, Elmore et al – PK and PK/PD Evaluations of Human Viral Challenge Study

Safety - The frequency of TEAEs was similar across EDP-323 and placebo arms

- There were no serious TEAEs, severe AEs, or AEs leading to treatment discontinuation/ study withdrawal
- TEAEs reflected usual RSV and quarantine-related patterns

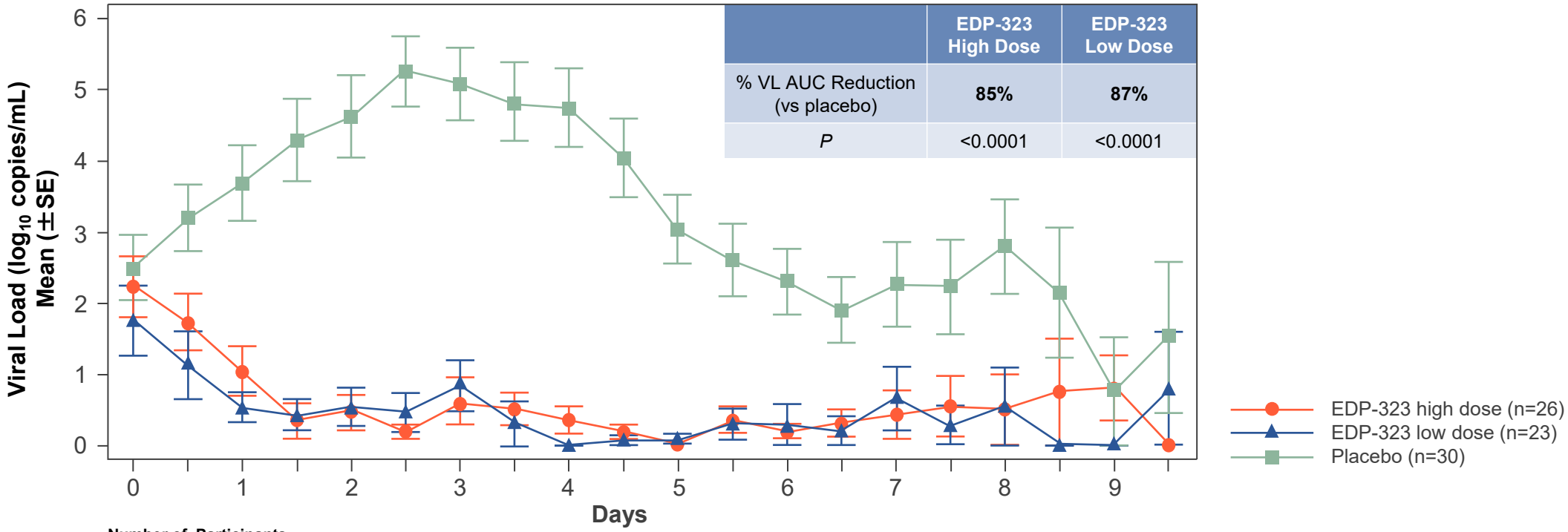
	EDP-323 High Dose (n=47)	EDP-323 Low Dose (n=47)	Pooled EDP-323 (N=94)	Placebo (n=47)
Participants with any TEAEs, n (%)	11 (23.4)	14 (29.8)	25 (26.6)	13 (27.7)
Any TEAEs considered related to study drug, n (%)	1 (2.1)*	1 (2.1)*	2 (2.1)*	0 (0)
Participants with TEAEs graded at least moderate in severity	1 (2.1)	1 (2.1)	2 (2.1)	2 (4.3)

*Grade 1/mild diarrhea.
AE, adverse event; EC_{90}, 90% effective concentration; PK, pharmacokinetic; TEAE, treatment-emergent adverse event.

Mean Viral Load Over Time and AUC by qRT-PCR

Primary Efficacy Endpoint: AUC (ITT-I Population)

- EDP-323 showed 85% (high dose) and 87% (low dose) greater mean reductions in viral load AUC vs placebo (*P* <0.0001)
  - No statistically significant differences between the 2 EDP-323 dosing regimens



	EDP-323 High Dose	EDP-323 Low Dose
% VL AUC Reduction (vs placebo)	**85%**	**87%**
P	<0.0001	<0.0001

Number of Participants

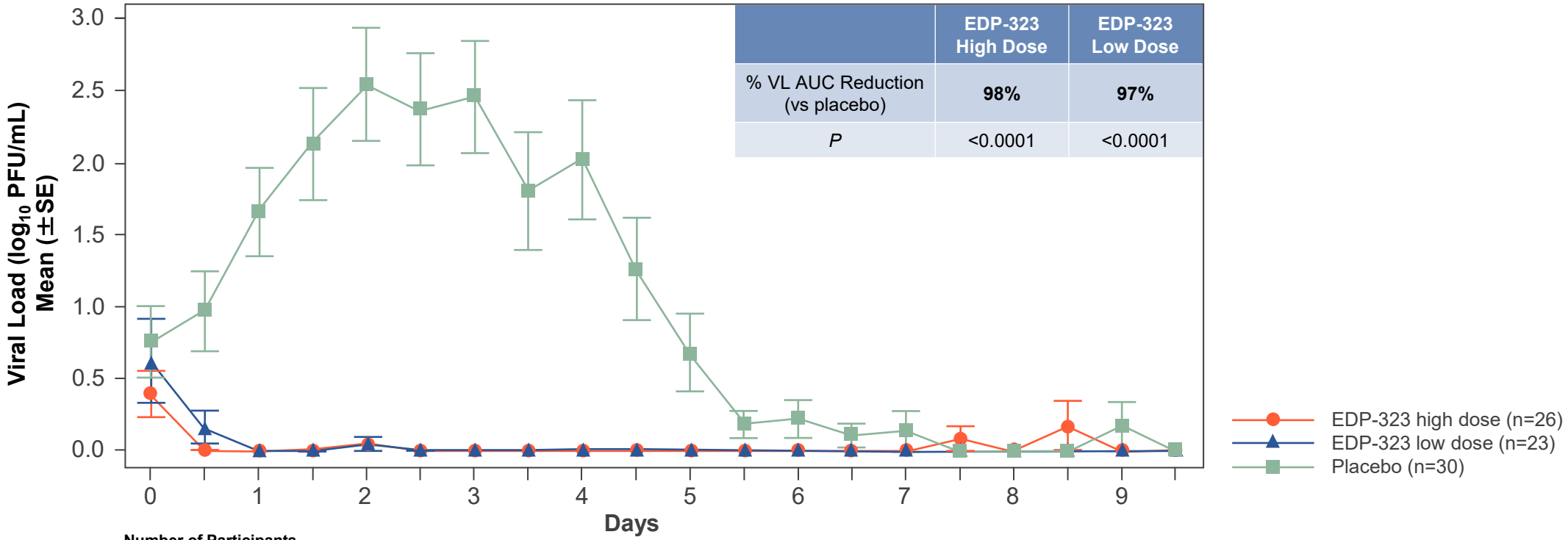
EDP-323 high dose	26	26	26	26	26	26	26	26	26	26	26	26	26	26	15	12	10	6	4	1
EDP-323 low dose	23	23	23	23	23	23	23	23	23	23	23	23	23	23	17	16	10	5	4	2
Placebo	30	30	30	30	30	30	30	30	30	30	30	30	30	30	19	18	11	8	6	4

AUC, area under the curve; ITT-I, intent-to-treat infected; qRT-PCR: quantitative reverse transcription-polymerase chain reaction; VL, viral load.

Mean Viral Load Over Time and AUC by Viral Culture

Secondary Efficacy Endpoint: AUC (ITT-I Population)

- EDP-323 showed 98% (high dose) and 97% (low dose) greater mean reductions in viral load AUC vs placebo (*P* <0.0001)
  - No statistically significant differences between the 2 EDP-323 dosing regimens



	EDP-323 High Dose	EDP-323 Low Dose
% VL AUC Reduction (vs placebo)	**98%**	**97%**
P	<0.0001	<0.0001

Number of Participants

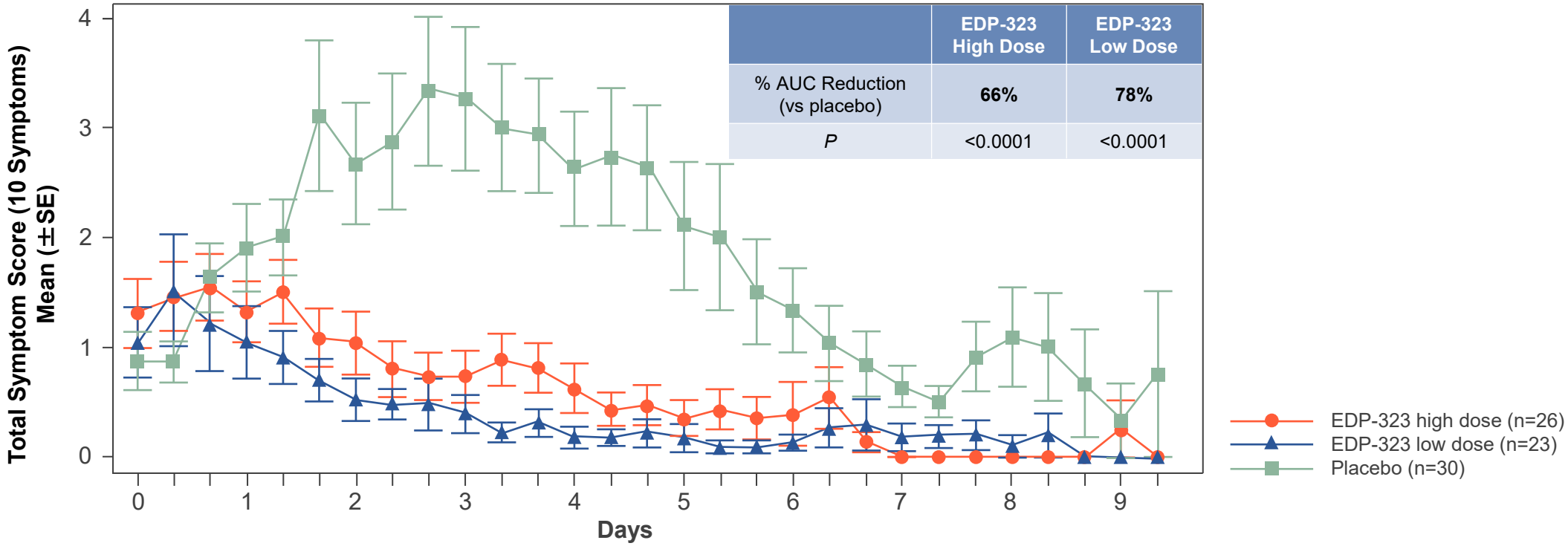
EDP-323 high dose	26	26	26	26	26	26	26	26	26	26	26	26	26	26	15	12	10	6	4	1
EDP-323 low dose	23	23	23	23	23	23	23	23	23	23	23	23	23	23	17	16	10	5	4	2
Placebo	30	30	30	30	30	30	30	30	30	30	30	30	30	30	19	18	11	8	6	4

AUC, area under the curve; ITT-I, intent-to-treat infected; VL, viral load.

Mean Total Symptom Score and AUC

Secondary Efficacy Endpoint: AUC (ITT-I Population)

- EDP-323 showed 66% (high dose) and 78% (low dose) greater mean reductions in total symptom score AUC vs placebo (*P* <0.0001)
  - No statistically significant differences between the 2 EDP-323 dosing regimens



	EDP-323 High Dose	EDP-323 Low Dose
% AUC Reduction (vs placebo)	**66%**	**78%**
P	<0.0001	<0.0001

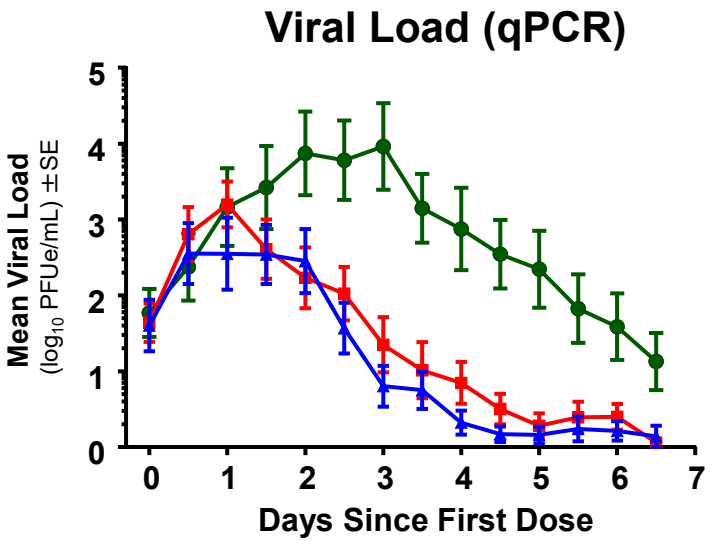
Number of Participants

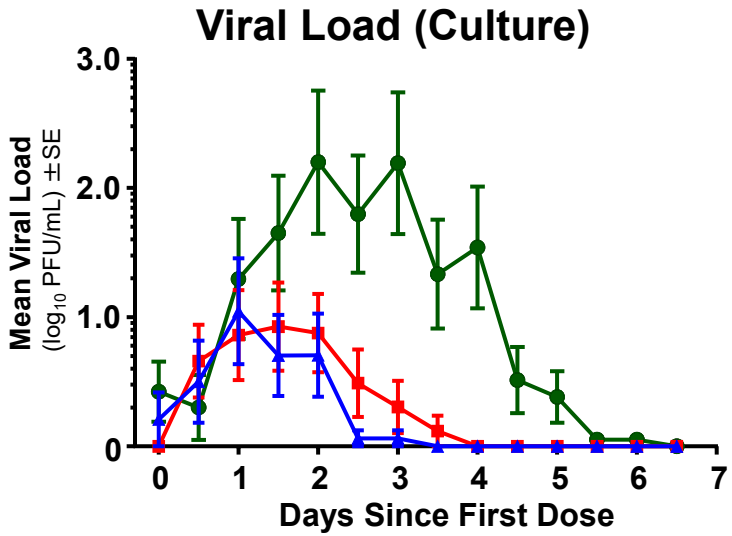
EDP-323 high dose	26	26	26	25	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	15	15	12	10	10	6	4	4	1
EDP-323 low dose	23	23	23	23	22	23	23	23	23	23	23	23	23	23	23	23	23	23	23	23	17	17	16	10	10	5	4	4	2
Placebo	30	30	30	30	30	29	30	30	30	30	30	30	30	30	30	30	30	30	30	30	19	19	18	11	11	8	6	6	4

AUC, area under the curve; ITT-I, intent-to-treat infected; VL, viral load.

Viral Dynamics in Human RSV Challenge Studies (Memphis-37b)

Fusion Inhibitor vs Polymerase Inhibitor

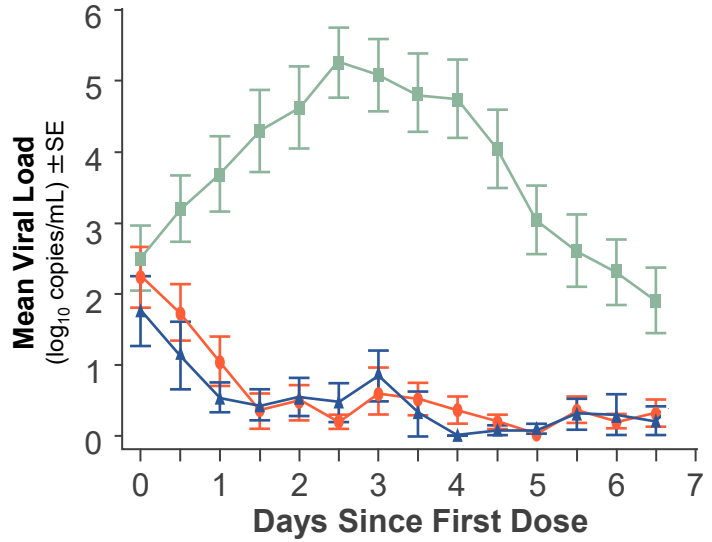


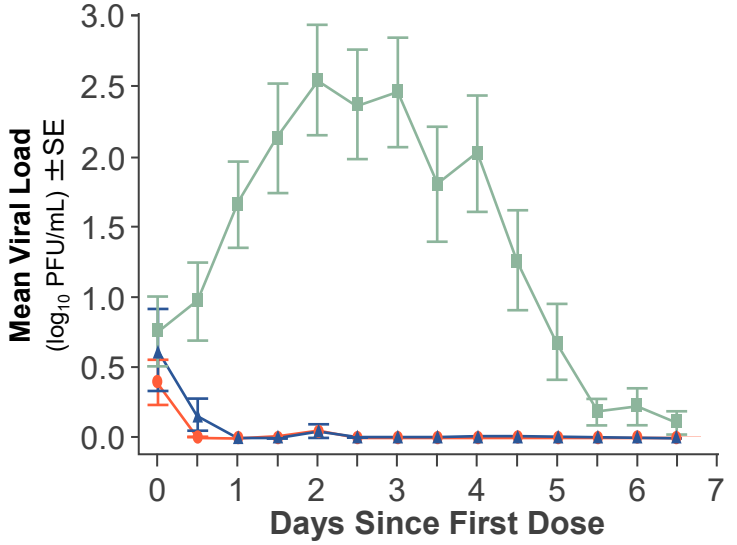


Fusion Inhibitor (RV521)

- RV521 350mg PO BID x 5 days (n=16)
- RV521 200mg PO BID x 5 days (n=18)
- Placebo (n=19)

DeVincenzo et al. Antimicrobial Agents and Chemotherapy. 2020;64(2):e01884-19; and DeVincenzo et al. ATS 2018.





Polymerase Inhibitor (EDP-323)

- EDP-323 high dose PO QD x 5 days (n=26)
- EDP-323 low dose PO QD x 5 days (n=23)
- Placebo (n=30)

DeVincenzo et al. RSV-2025 (ISIRV) Iguazu Falls, Brazil.

EDP-323 RSV Human Challenge Study

Conclusions

- Well tolerated with safety profile similar to placebo
- Mean trough plasma concentrations maintained at 16- to 35-fold above protein-adjusted EC_{90}
- Primary and key secondary endpoints achieved with statistical significance at both dose levels vs placebo

	EDP-323 Low Dose	EDP-323 High Dose	P*
qRT-PCR	87%	85%	<0.0001
Viral culture	97%	98%	<0.0001
Total symptom score	78%	66%	<0.0001

  - No statistically significant differences between the 2 dosing regimens

- Outcomes confirm the potential of EDP-323 as a once-daily oral treatment for RSV and support further clinical evaluation

P for both comparisons.
EC_{90}, 90% effective concentration; qRT-PCR, quantitative reverse transcription-polymerase chain reaction; RSV, respiratory syncytial virus.

Poster Presentation: Zelicapavir for Treatment of RSV Infection in Young Children

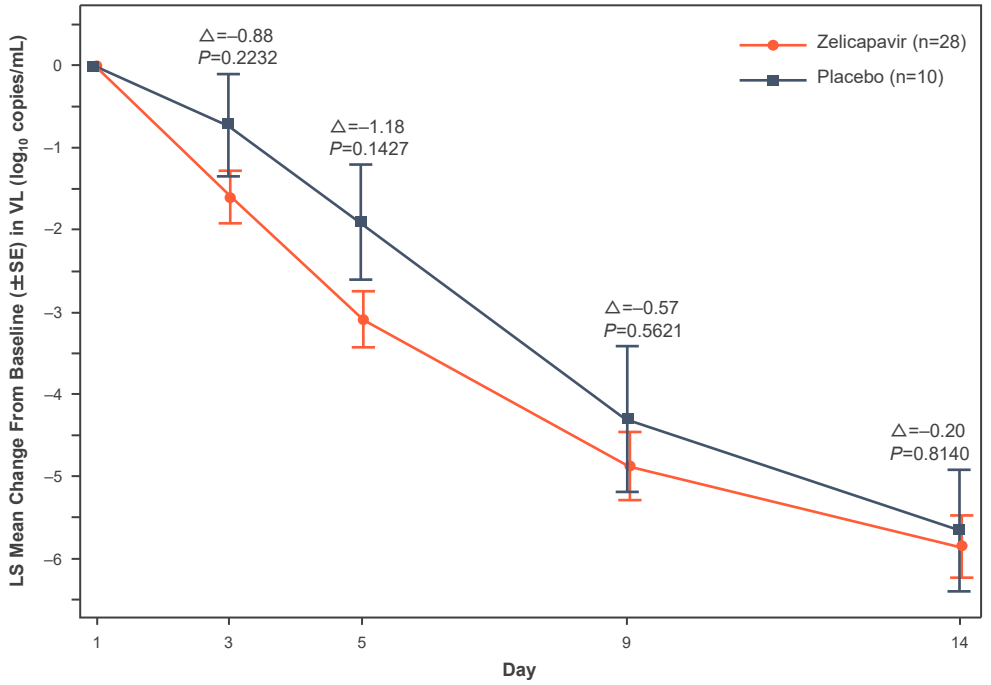
Enanta Pharmaceuticals

A Phase-2, Double-Blind, Placebo-Controlled, International Trial of Zelicapavir for Treatment of RSV Infection in Young Children

Stephen Huang, Christopher Harris, John P DeVincenzo, Alaa Ahmad, Shijie Chen, Taylor Ngo, Scott T Rottinghaus

- Late breaker poster **#253**
- Poster session: **RSV Monoclonal Antibodies and Antivirals**
  - Date: **Friday, March 14**
  - Time: **4:15 – 5:15 PM**
  - Location: **Pavillion C**

LS Mean Change (± SE) From Baseline in Viral Load in Prespecified mITT-3 Population* Measured by qRT-PCR



LS, least-squares; mITT, modified intent-to-treat; RESOLVE-P, Respiratory Observable Reported Outcome-Pediatric; qRT-PCR, quantitative reverse transcription polymerase chain reaction.
*Prespecified mITT-3 population: participants randomized within 3 days of symptom onset.

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Thank you!