Poster #3

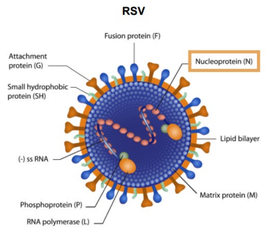
Zelicapavir Decreases Time to Complete RSV Symptom Resolution, Hospitalization and Viral Load in a Global, Randomized, Double-Blinded, Placebo (PBO)-Controlled Phase 2 Trial of High-Risk Adults

C. Harris, J. DeVincenzo, S. Chen, T. Ngo, A. Ahmad, M. Turnak, S. Rottinghaus
Enanta Pharmaceuticals, Inc., Watertown, MA, USA

Contact: Christopher Harris, MD
charris@enanta.com | (617) 607-0800
4 Kingsbury Avenue, Watertown, MA 02472

BACKGROUND

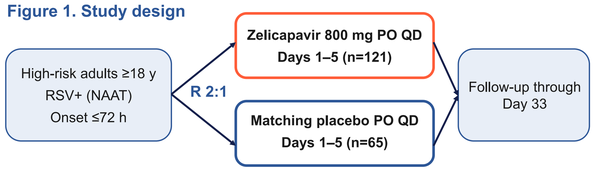
- Older adults and adults with chronic cardiopulmonary conditions are at elevated risk of severe respiratory syncytial virus (RSV) disease; RSV-related hospitalization is followed by increased risk of cardiorespiratory events[1]
- No RSV antiviral has previously demonstrated efficacy in high-risk adults
- Zelicapavir (EDP-938) is an investigational, once-daily oral N-protein inhibitor
  - Strong preclinical profile
    - Nanomolar potency against RSV-A and RSV-B
    - Antiviral potency across all clinical isolates tested
    - High barrier to resistance
  - Prior analyses in high-risk adults[2] and children[3] reported shorter time to complete symptom resolution
  - Granted Fast Track designation



Objective: Evaluate time to Complete Resolution and time to Sustained Resolution of RSV symptoms with zelicapavir vs placebo

METHODS

Figure 1. Study design



Phase 2b, randomized, double-blind, placebo-controlled; 84 sites, 12 countries; Nov 2022–Jun 2025 (NCT05568706); IRB-approved; GCP; written informed consent. n = all dosed. PO, orally; QD, once daily; R, randomization.

Endpoint definitions

Respiratory Infection Intensity and Impact Questionnaire (RiiQ™), daily: 13 RSV symptoms, including 4 lower respiratory tract disease (LRTD) symptoms, of the 29 items; each scored 0–3

- **Resolution (primary; LRTD):** each symptom ≤1 at 2 consecutive timepoints
- **Complete Resolution:** all symptoms 0 at 2 consecutive timepoints
- **Sustained Resolution:** all symptoms absent and remaining absent through Day 33

- **Population:** adults with ≥1 risk factor: age ≥65 y, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), or asthma (age 65–74 y and/or asthma alone capped at 20%). Excluded: anticipated hospitalization, COPD with FEV1 ≤35%, immunocompromise (incl. transplant), HIV
- **Analysis sets:** safety (all dosed); modified intent-to-treat (mITT; central-lab RSV+); HR3 (mITT excluding age <65 y with asthma only, and 65–74y with no other condition)
- **Analysis:** Kaplan-Meier medians; Cox hazard ratios (HR); unresolved patients censored at Day 33

Table 1. Baseline characteristics (186 dosed)

n (%) unless noted	Zel N=121	PBO N=65	HR3 Zel N=92	HR3 PBO N=50
Age, y, median	71	72	73	73
Female	74 (61.2)	49 (75.4)	52 (56.5)	38 (76.0)
CHF	27 (22.3)	8 (12.3)	26 (28.3)	8 (16.0)
COPD	45 (37.2)	25 (38.5)	43 (46.7)	24 (48.0)
Asthma	32 (26.4)	16 (24.6)	13 (14.1)	9 (18.0)
Onset ≤48 h	78 (64.5)	42 (64.6)	58 (63.0)	32 (64.0)

RESULTS

Time to Complete Resolution

- Time to Complete Resolution was a pre-specified analysis
- Median time to Complete Resolution was 0.5–7.2 days shorter with zelicapavir

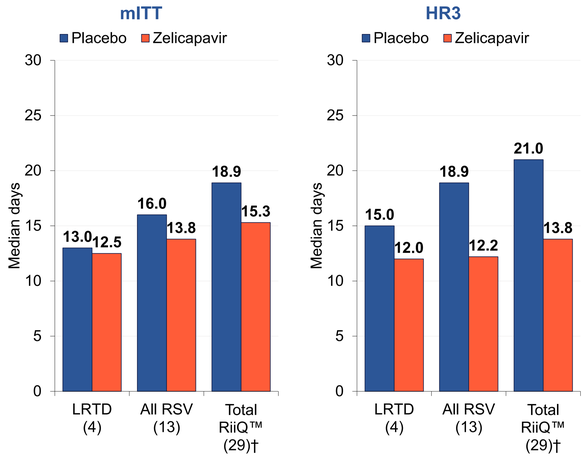


Figure 2. Median days to Complete Resolution. Δ (days): mITT 0.5 / 2.2 / 3.6; HR3 3.0 / 6.7 / 7.2

Table 2. Time to Complete Resolution by RiiQ™

Measure	Pop.	Zel vs PBO, median d	Δ d	HR (95% CI)
All RSV (13)	HR3	12.2 vs 18.9	6.7	1.18 (0.78–1.80)
All RSV (13)	mITT	13.8 vs 16.0	2.2	1.08 (0.74–1.56)
Total RiiQ™ (29)†	HR3	13.8 vs 21.0	7.2	1.31 (0.84–2.05)
Total RiiQ™ (29)†	mITT	15.3 vs 18.9	3.6	1.19 (0.81–1.75)
LRTD (4)	HR3	12.0 vs 15.0	3.0	0.98 (0.66–1.46)
LRTD (4)	mITT	12.5 vs 13.0	0.5	0.90 (0.63–1.29)

HR >1 favors zelicapavir. Analyzed n: mITT 114 vs 59; HR3 91 vs 49. †Post hoc. Primary endpoint (LRTD resolution to mild/absent): median 5.0 vs 4.1 days; HR 0.84 (95% CI 0.60–1.17)

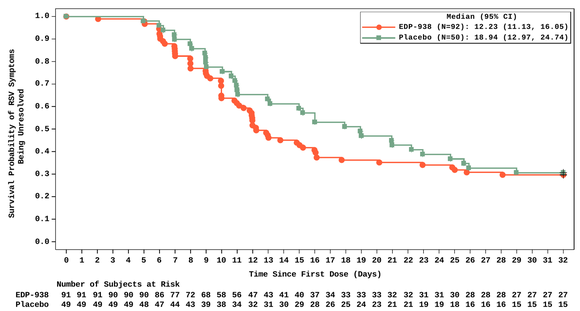


Figure 4. Kaplan-Meier: Time to Complete Resolution of all 13 RSV symptoms, HR3 population

RESULTS

Time to Sustained Resolution

- Time to Sustained Resolution was an ad hoc analysis
- Median time to Sustained Resolution was 2.8–7.8 days shorter with zelicapavir

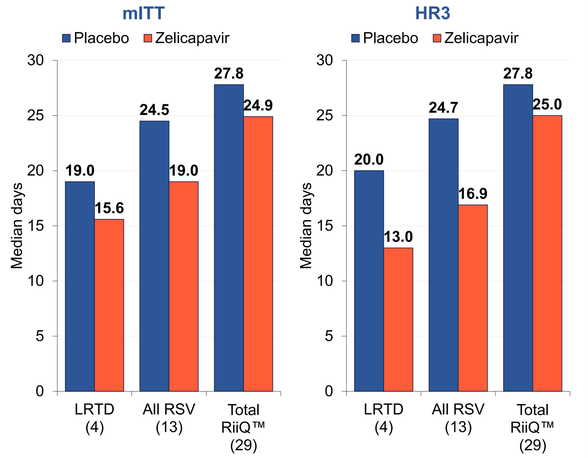


Figure 3. Median days to Sustained Resolution. Δ (days): mITT 3.4 / 5.5 / 2.9; HR3 7.0 / 7.8 / 2.8

Table 3. Time to Sustained Resolution by RiiQ™

Measure	Pop.	Zel vs PBO, median d	Δ d	HR (95% CI)
All RSV (13)	HR3	16.9 vs 24.7	7.8	1.17 (0.76–1.80)
All RSV (13)	mITT	19.0 vs 24.5	5.5	1.13 (0.77–1.66)
Total RiiQ™ (29)†	HR3	25.0 vs 27.8	2.8	1.26 (0.80–2.00)
Total RiiQ™ (29)†	mITT	24.9 vs 27.8	2.9	1.22 (0.82–1.83)
LRTD (4)	HR3	13.0 vs 20.0	7.0	1.06 (0.70–1.60)
LRTD (4)	mITT	15.6 vs 19.0	3.4	0.97 (0.67–1.40)

HR >1 favors zelicapavir. Analyzed n: mITT 114 vs 59; HR3 91 vs 49. †Post hoc.

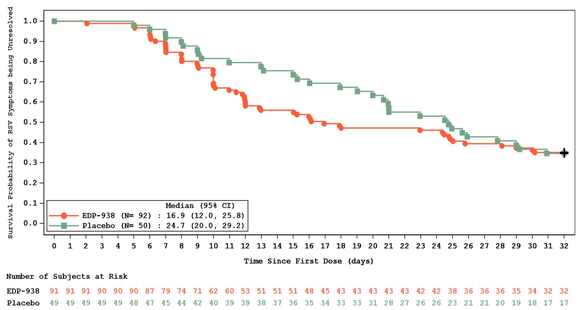


Figure 5. Kaplan-Meier: Time to Sustained Resolution of all 13 RSV symptoms, HR3 population

RESULTS

Table 4. Supporting endpoints (previously reported)

mITT	Zel n=115	PBO n=60	p
PGI-S Resolution, median d (95% CI)	8.98 (7.97–9.98)	10.90 (9.00–14.99)	0.0446
All-cause Hospitalization	2 (1.7%)	3 (5.0%)	—
RSV-related Hosp. (investigator reported)	0	3 (5.0%)	—
Deaths	0	1	—
Undetectable VL, mITT, Day 5	27 (23.5%)	6 (10.0%)	0.0198
Undetectable VL, HR3, Day 5	22/92 (23.9%)	5/50 (10.0%)	0.0292

PGI-S, Patient Global Impression of Severity; VL, viral load. No ICU admission or mechanical ventilation.

Table 5. Treatment-emergent adverse events (TEAEs)

Safety population, n (%)	Zel N=121	PBO N=65
Any TEAE	27 (22.3)	16 (24.6)
Drug-related	7 (5.8)	3 (4.6)
Grade ≥3 / serious	1 (0.8) / 2 (1.7)	5 (7.7) / 4 (6.2)
Led to discontinuation / death	0 / 0	1 (1.5) / 1 (1.5)
Diarrhea / asthma / nausea	4 / 3 / 1	1 / 1 / 2

CONCLUSIONS

- Treatment of an adult population at high risk for complications from RSV disease had shorter median times to Complete Resolution of all 13 RSV symptoms of 2.2 days (mITT) and 6.7 days (HR3) compared to placebo
- Additionally, zelicapavir treatment was associated with shorter median times to Sustained Resolution of 5.5 days (mITT) and 7.8 days (HR3)
- TEAEs occurred in 22.3% of zelicapavir and 24.6% of placebo patients
- **Complete Resolution and Sustained Resolution warrant further evaluation in confirmatory RSV treatment trials**

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- Zelicapavir is investigational for the treatment of respiratory syncytial virus disease.
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