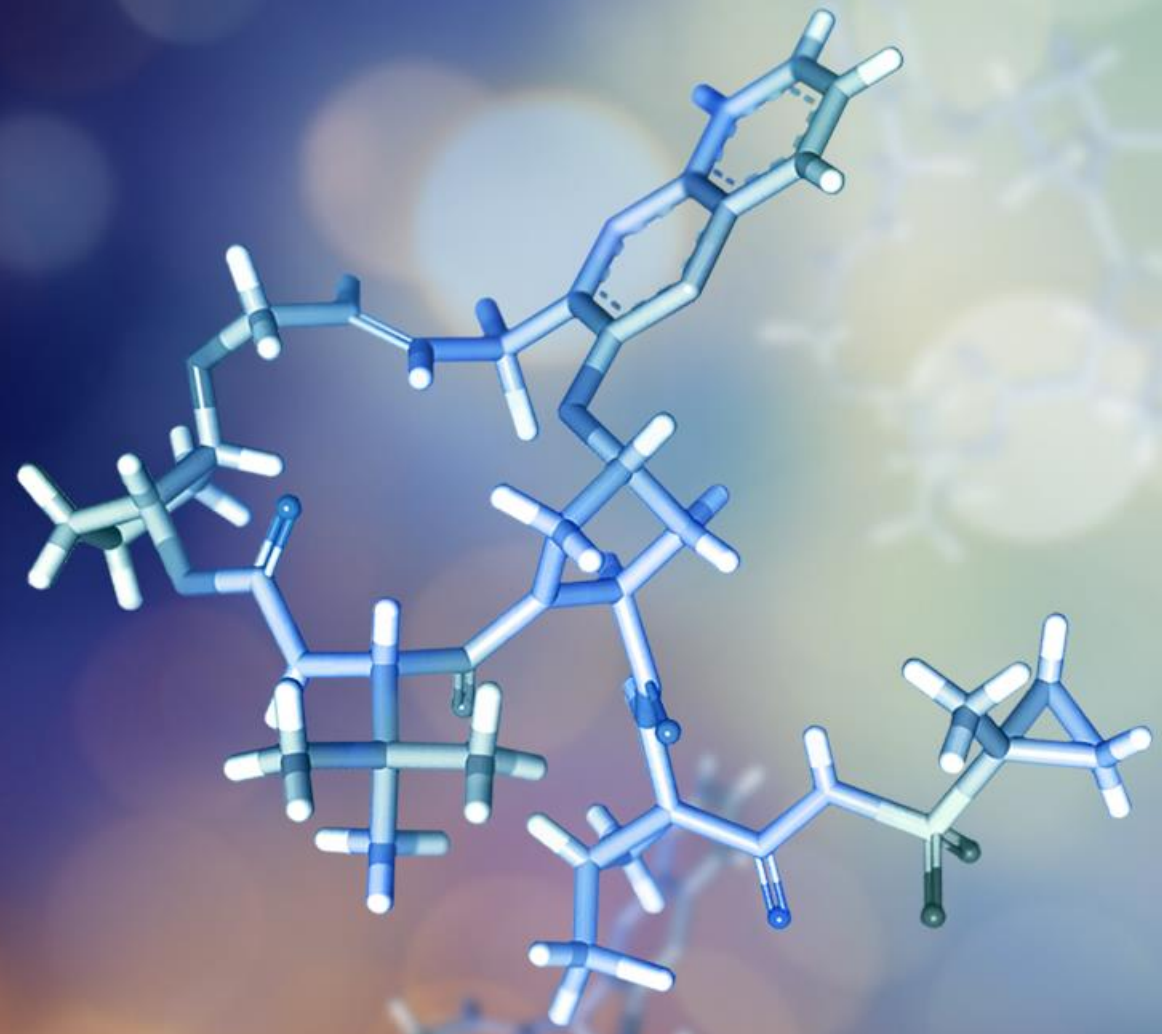
# ENANTA Pharmaceuticals

CREATING SMALL MOLECULE DRUGS
FOR VIRAL INFECTIONS AND LIVER DISEASES



## Corporate Presentation

January 6, 2022

# Forward Looking Statements Disclaimer

This presentation contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our research and development programs, our business and the industry in which we operate. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would,” and other similar expressions that are predictions of or indicate future events and future trends, as well as other comparable terminology. These forward-looking statements include, but are not limited to, statements about overall trends, royalty revenue trends, research and clinical development plans and prospects, liquidity and capital needs and other statements of expectations, beliefs, future plans and strategies, anticipated events or trends, and similar expressions. These forward-looking statements are based on our management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management’s beliefs and assumptions. These forward-looking statements are not guarantees of future performance or results and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this presentation may turn out to be inaccurate.

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# A Proven Approach to Drug Discovery

Using a proven, chemistry-driven approach to develop best-in-class small molecule drugs for virology and liver disease

**Robust Clinical Stage Pipeline**

**RSV:** Phase 2b in adult patients (RSVP)

Phase 2b in adult stem cell transplant patients (RSVPTx)

Phase 2 in pediatric patients (RSVPEDs)

**HBV:** Two Phase 1b studies completed (core inhibitor)

**COVID-19:** Phase 1 (protease inhibitor) to initiate in February 2022

**Proven Track Record of Success**

**Glecaprevir** – HCV protease inhibitor in MAVYRET®/MAVIRET®

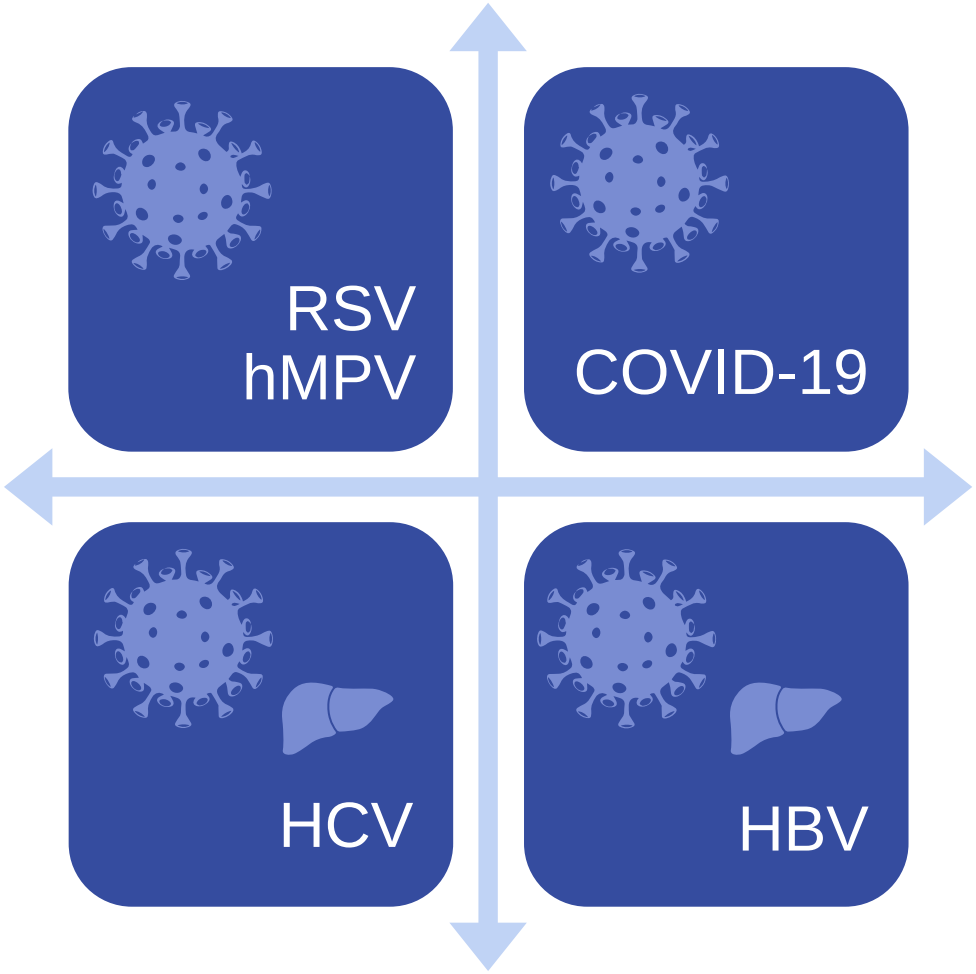
**$97M in fiscal 2021 royalties** on HCV regimens

**Strong Balance Sheet**

**Strong balance sheet and royalties** to fund robust pipeline

**$352M in cash** at 9/30/21

# Our Therapeutic Focus




Leveraging our core strength in Hepatitis C to become a leader in oral treatments for **viral** infections and **liver** diseases

Several new therapeutic areas with goal of building multiple approaches in each

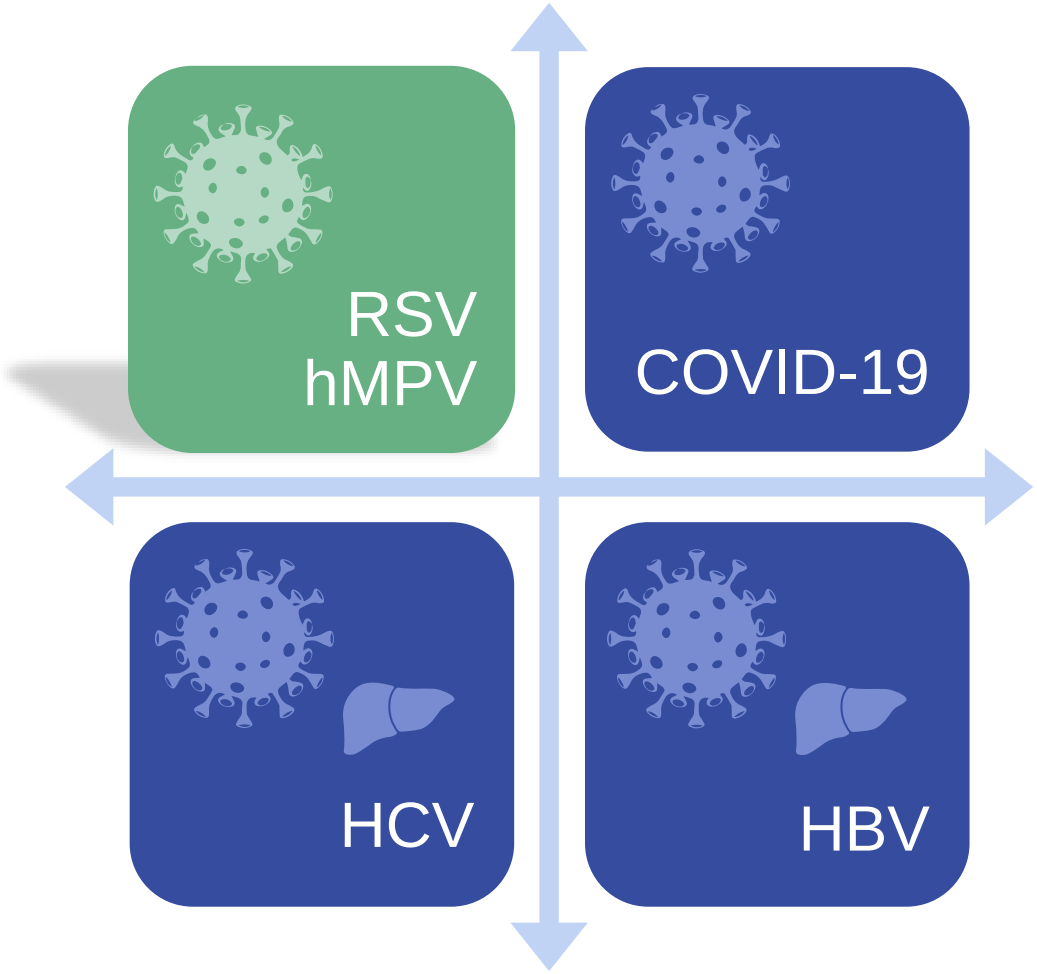
# Enanta Pipeline

| | | PRODUCT CANDIDATE | DISCOVERY | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | MARKET |
|---|---|---|---|---|---|---|---|---|
| Virology: Liver | HCV | Protease Inhibitor | Glecaprevir-containing pangenotypic 2-DAA combo | | | | | MAVYRET glecaprevir/pibrentasvir |
| | HBV | Core Inhibitor | EDP-514 | | | | | |
| Virology: Respiratory | RSV | N-Protein Inhibitor | EDP-938 *RSVP* | | | | | |
| | | | EDP-938 *RSVPEDs* | | | | | |
| | | | EDP-938 *RSVTx* | | | | | |
| | | L-Protein Inhibitor | EDP-323 | | | | | |
| | hMPV | Non-Fusion Inhibitor | | | | | | |
| | COVID-19 | Protease Inhibitor | EDP-235 | | | | | |
| Discovery or Preclinical | RSV, HBV, other | | | | | | | |
| For Out-license | NASH | FXR Agonists | EDP-305 (Phase 2), EDP-297 (Phase 1) | | | | | |

*Fixed-dose combination contains glecaprevir and AbbVie's NS5A inhibitor, pibrentasvir. Marketed by AbbVie as MAVYRET® (U.S.) and MAVIRET® (ex-U.S.).

# Our Therapeutic Focus

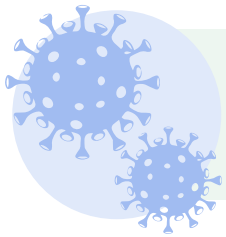



Leveraging our core strength in Hepatitis C to become a leader in oral treatments for **viral** infections and **liver** diseases

Several new therapeutic areas with goal of building multiple approaches in each

# Respiratory Syncytial Virus (RSV)



Causes severe lung infections, including bronchiolitis (infection of small airways in the lungs) and pneumonia (an infection of the lungs). No safe and effective treatments.

Higher risk populations for severe illness:

- Young infants and children
- Premature babies
- Older adults especially those 65+ years
- People with chronic lung disease or certain heart problems
- People with weakened immune systems (e.g. HIV, organ transplant, chemotherapy)

**RSV at a Glance**

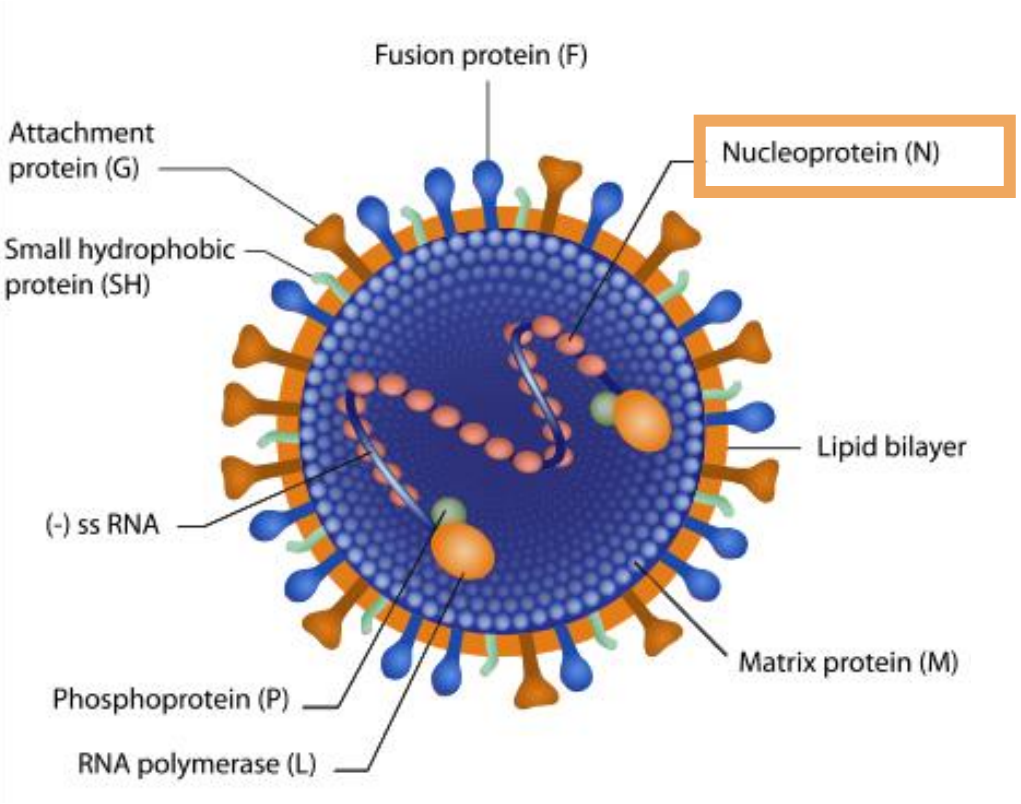
| Children < 5 years[1,2] | Adults > 65 years[3] |
|---|---|
| 33M global cases | |
| 3M global hospitalizations | 177K US hospitalizations |
| 120K global deaths | 14K US deaths |
| 2.1M U.S. hospitalizations/ outpatient visits, of which 78% are older than 1 year | |

Sources: 1.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5592248/ 2. https://www.nejm.org/doi/full/10.1056/NEJMoa0804877 3. https://www.cdc.gov/rsv/high-risk/older-adults.html

# EDP-938: N-Protein Inhibitor for RSV

- EDP-938 is the only N-inhibitor under clinical evaluation
  - Non-fusion approach directly targets viral replication vs. entry
  - Granted Fast Track Designation by FDA
- Strong preclinical virologic profile:
  - Nanomolar inhibitor of both RSV-A and RSV-B activity
  - Maintained antiviral potency across all clinical isolates tested
  - Demonstrated high-barrier to resistance *in vitro*
  - Synergy with other drug mechanisms (e.g. fusion and L-inhibitors)
  - Active against virus variants resistant to other mechanisms
  - Robust *in vivo* efficacy data



# EDP-938 Development Program

## Phase 1 Results

- Safe and well tolerated, no SAEs, AEs were mild
- At Phase 2 doses, mean trough levels 30x higher than EC90 of EDP-938 against RSV-infected human cells

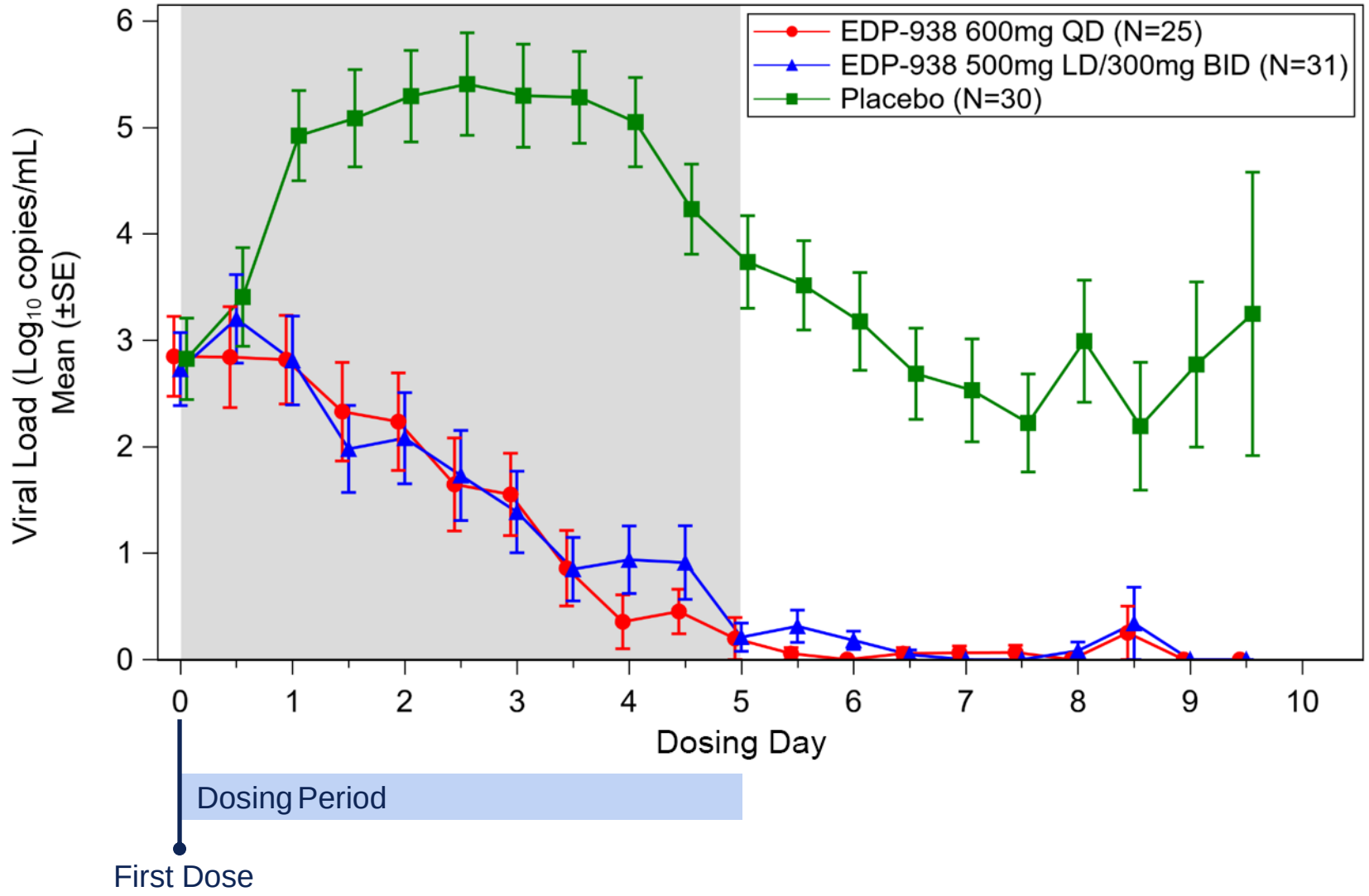
## Phase 2a Challenge Study Results

- Primary and key secondary efficacy endpoints were achieved ($p<0.001$) at both dose levels after 5 days of dosing
  - Primary endpoint: Reduction in area under the curve (AUC) viral load in the intent-to-treat-infected population (ITT-I)
  - Secondary endpoint: Reduction in Total Symptom Score (TSS)
- Mean $C_{trough}$ concentrations were approximately >20-40x higher than $EC_{90}$
- Well tolerated with safety profiles similar to placebo
- Consistent profile observed in >250 subjects exposed to EDP-938 for up to 7 days in Phase 1 and Phase 2a

# EDP-938 Robust Antiviral Effect

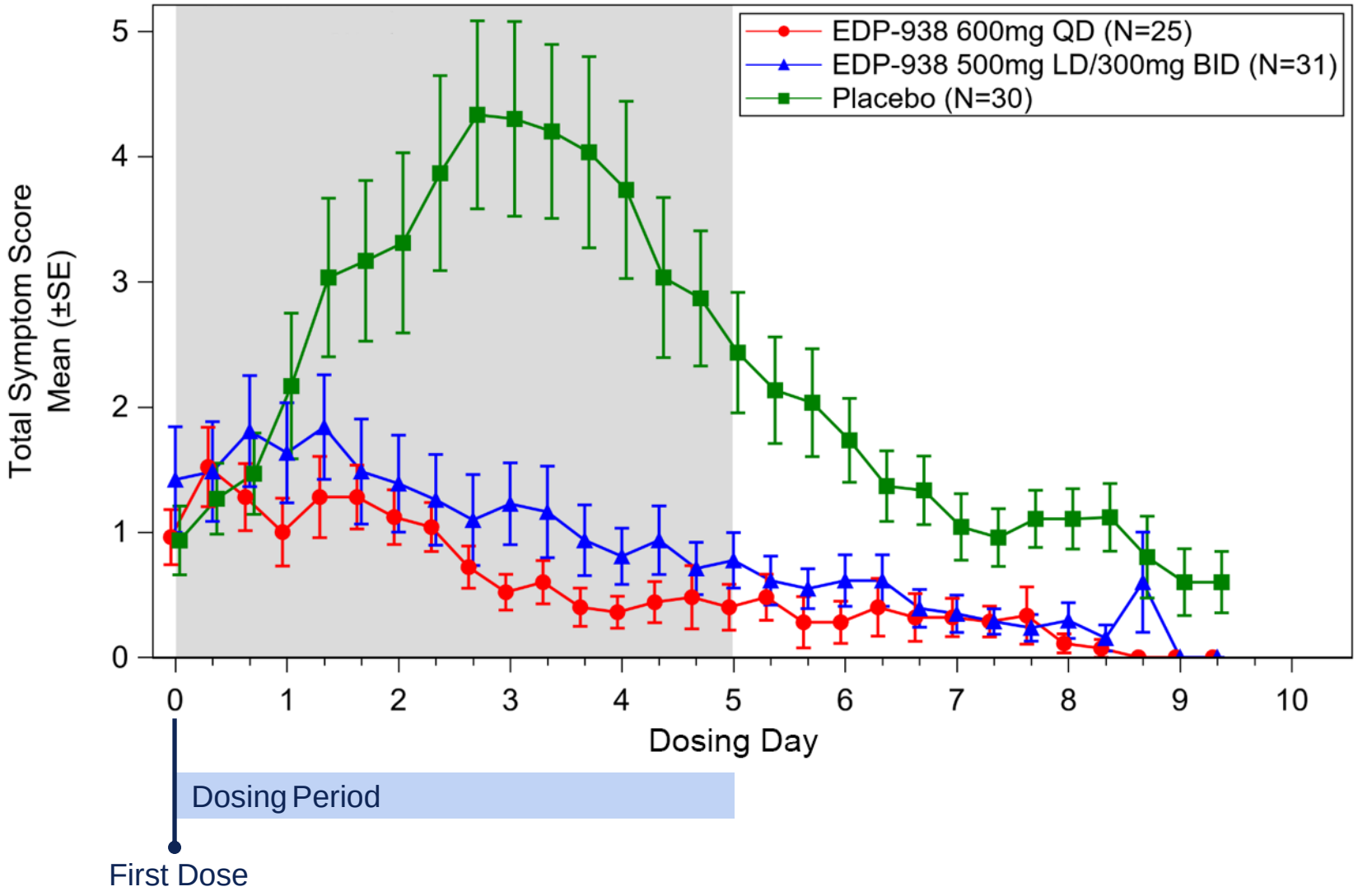
Rapid and Sustained Reduction in Viral Load in Both Active Arms Compared to Placebo (71%, 74% ↓ AUC; P<0.001)



# EDP-938 Robust Symptom Reduction

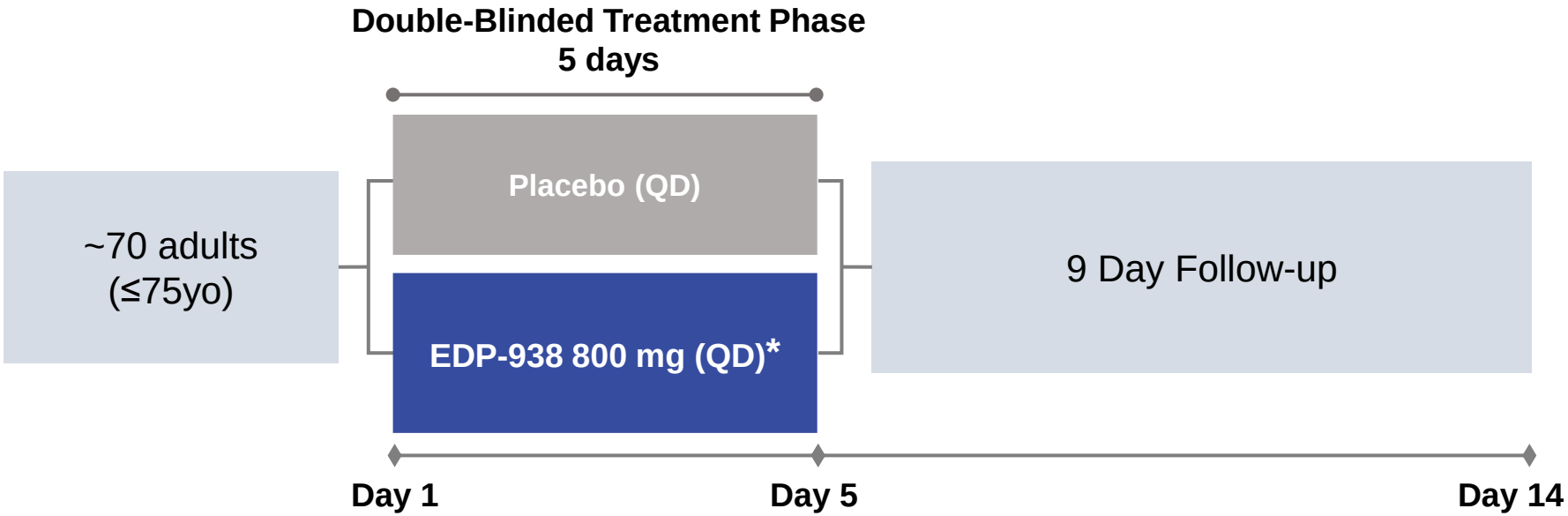
Rapid and Sustained Attenuation of RSV Symptoms in Both Active Arms Compared to Placebo (68%, 74% ↓ AUC; P<0.001)



# RSVP: A Phase 2b Study of EDP-938 in Adult Outpatients With RSV

RSVP!




- **Primary Objective:**

  Effect of EDP-938 on progression of RSV infection by assessment of clinical symptoms measured over the 14-day study period

- **Secondary Objective:**

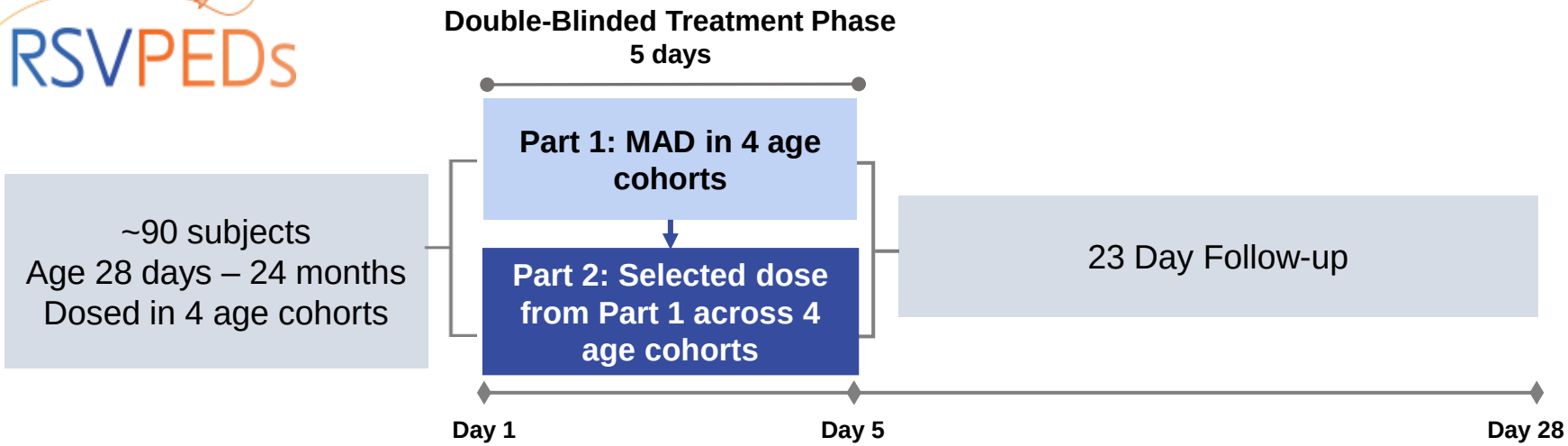
  Antiviral efficacy, safety and PK of EDP-938

*Equivalent to 600mg suspension dosage form used in challenge study

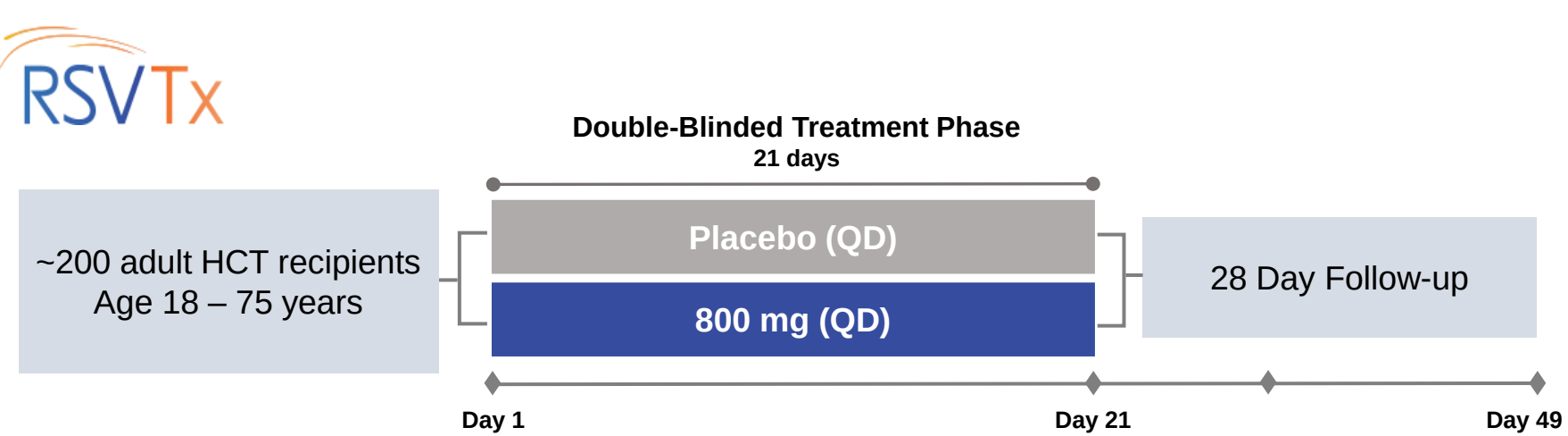
# Two Additional Phase 2 Clinical Trials: RSVPEDs and RSVTx

## RSVPEDs




- **Primary Objective, Part 1:** Safety and PK of EDP-938
- **Primary Objective, Part 2:** Antiviral activity of EDP-938

## RSVTx




- **Primary Objective:** Effect of EDP-938 on development of LRTC in HCT subjects with acute RSV URTI
- **Secondary Objectives:** Viral load, progression to respiratory failure or all-cause mortality, PRO, PK and safety

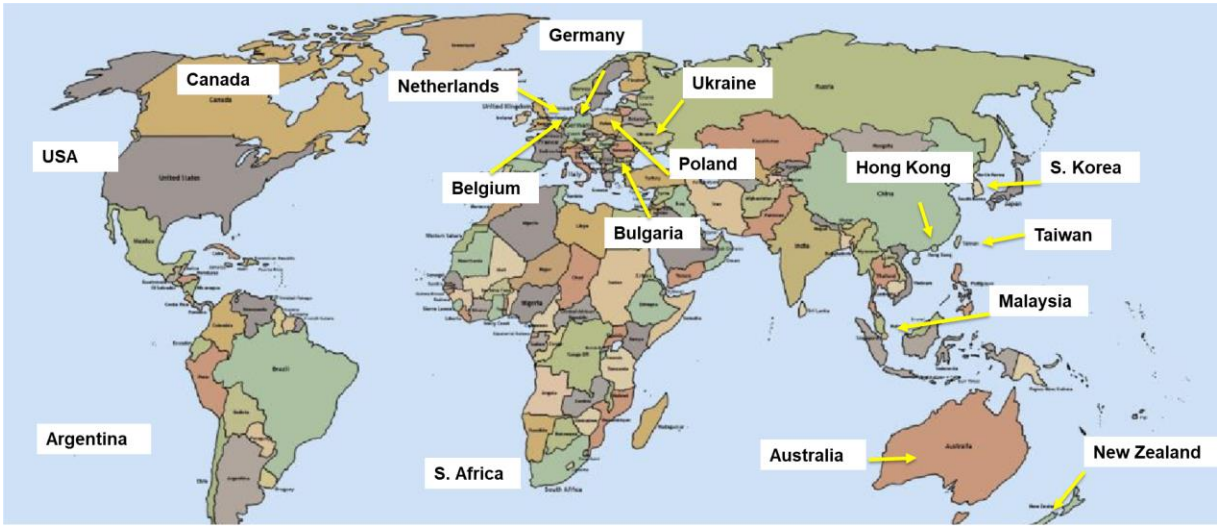
LRTC: lower respiratory tract complication; HCT: hematopoietic cell transplant; URTI: upper respiratory tract infection; PRO: patient reported outcomes; PK: pharmacokinetics

# Capitalizing on RSV During Northern Hemisphere Season

- RSV, like influenza, did not emerge during the usual late-fall and winter RSV season in the Northern Hemisphere in 2020-2021
- In Summer 2021, the CDC issued a health advisory to notify clinicians and caregivers about increased interseasonal RSV activity across parts of the Southern United States[1]
- Capitalized on RSV spikes and completed enrollment in RSVP in December 2021, with topline data expected in Q2 2022
- RSVPEDs and RSVTx, initiated during the pandemic, will continue to enroll into 2023

**RSVP Clinical Trial Sites**

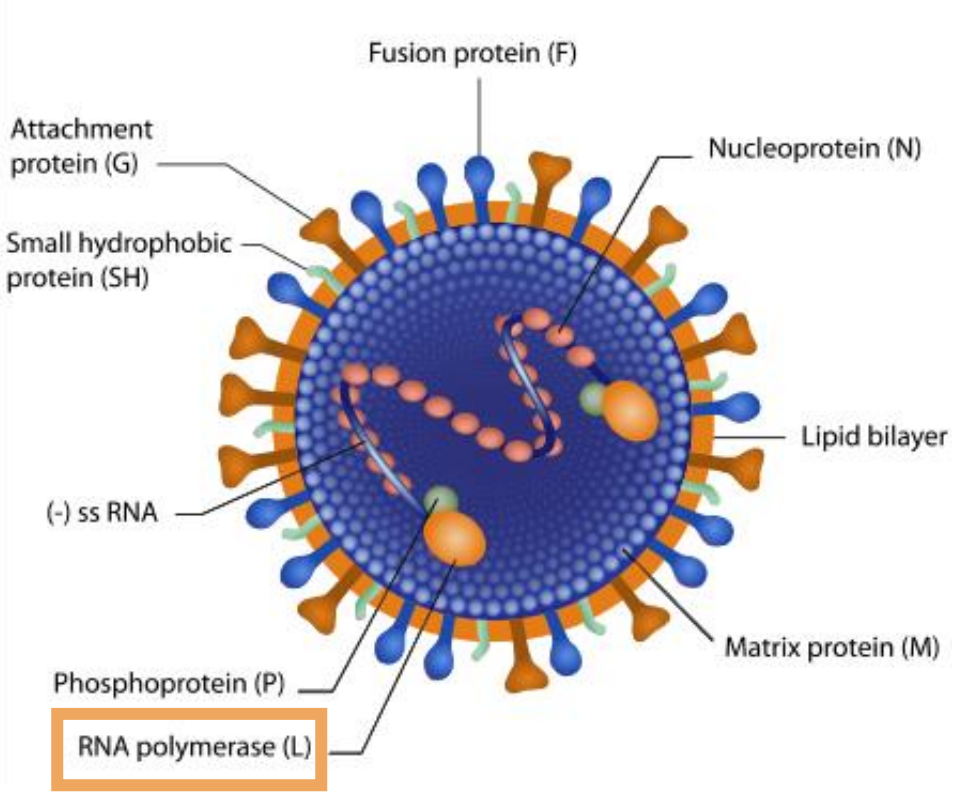



Sources: 1. CDC Health Advisory

# EDP-323: RSV L-Protein Inhibitor

- Novel, oral, selective direct-acting antiviral targeting the RSV L-protein
  - RSV L-protein is a viral RNA-dependent RNA polymerase that contains multiple enzyme activities required for RSV replication
- Potential to be used alone or in combination with other classes of RSV inhibitors, such as EDP-938
  - Additive to synergistic with F-, N-, L- inhibitors and ribavirin
  - Not expected to have cross resistance with other mechanisms
- Nanomolar potency against RSV-A and RSV-B

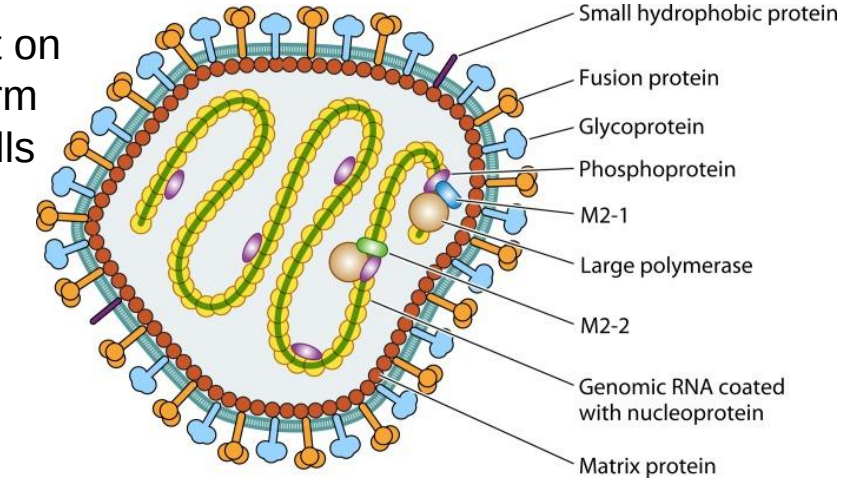


# Human Metapneumovirus (hMPV)

Important cause of respiratory tract infections (RTIs), particularly in children, the elderly and immunocompromised individuals

- Paramyxovirus closely related to RSV
  - hMPV replication dependent on several viral proteins that form a multiprotein complex in cells
  - Multiple potential targets for hMPV drug discovery
- No approved vaccine or therapeutics available
- Enanta nanomolar hMPV inhibitor leads under active optimization




## hMPV at a Glance

Serious respiratory infections can occur in children under 5 years old

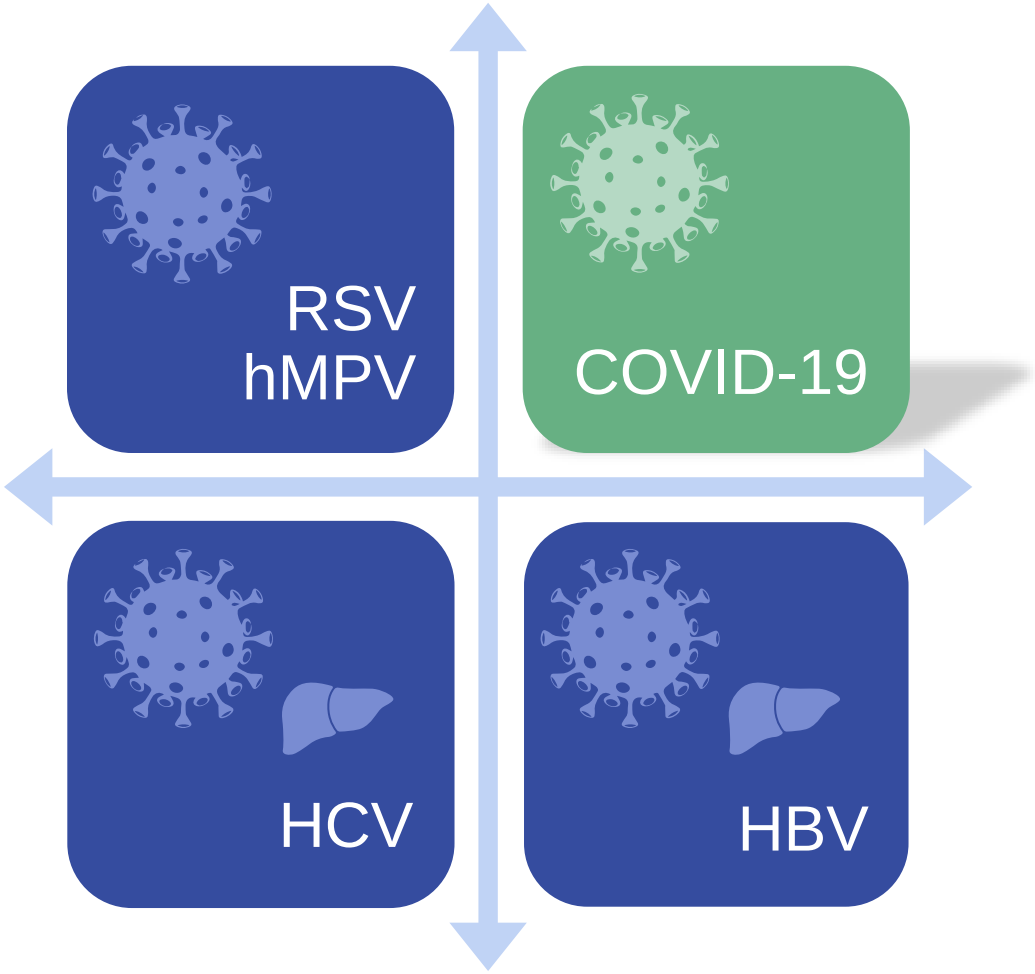
Second most common cause of lower RTIs in children (behind RSV)

Reinfection with hMPV occurs throughout life

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1539100/

# Our Therapeutic Focus

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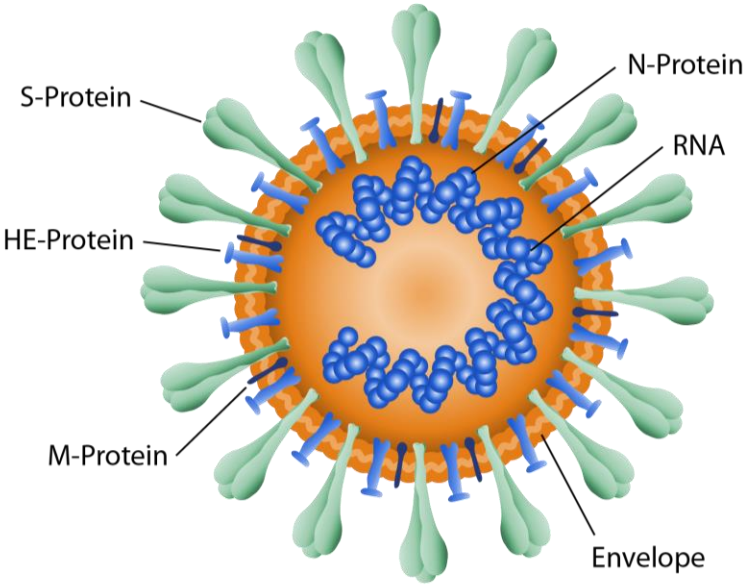
# EDP-235: Oral Protease Inhibitor Specifically Designed for COVID-19

- Novel, oral, direct-acting antiviral specifically designed to target the SARS-CoV-2 protease
- Potent inhibition of SARS-CoV-2 3CLpro enzyme ($IC_{50}$ = 5.8 nM)
  - Activity retained against proteases from SARS-CoV-2 variants
- Potent and selective inhibition of SARS-CoV-2 replication in multiple cellular models, including primary human airway epithelial cells ($EC_{90}$ = 33nM)
- Active against other human coronaviruses
- High barrier to resistance observed preclinically
- Predicted human efficacious dose of 100 to 500mg once-daily
  - Good oral bioavailability (95% in rats), target tissue distribution (lung to plasma AUC ratio >4), and long half-life (16 hours)
- Entering the clinic in February 2022



# EDP-235: Highly Potent 3CLpro Inhibitor and Retains Activity Against SARS-CoV-2 Variants

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| Assay | | Lineage | Potency (nM) |
|---|---|---|---|
| Biochemical Activity | 3CLpro FRET ($IC_{50}$) | A *[Original] / B.1.617.2 [Delta]** | **5.8** ± 3.7 |
| | | B.1.1.318 (T21I) | **2.0** ± 0.1 |
| | | B.1.351 (K90R) *[Beta]* | **2.8** ± 0.9 |
| | | B.1.617.3 (A194S) | **5.7** ± 0.5 |
| | | C.36.3 (G15S) | **4.7** ± 2.5 |
| | | P.2 (L205V) *[Zeta]* | **3.4** ± 1.0 |
| Cellular Activity | HuH-7, SARS-CoV-2 Replicon | A | **4.5** ± 1.7 |
| | Vero E6, CPE ($EC_{50}$) | A (+P-gpi) *[Original]* | **5.1** ± 0.3 |
| | pHAEC, Viral yield or qPCR ($EC_{90}$) | B.1 | **33** |
| | Vero E6, Viral yield ($EC_{50}$) | B.1 | **12.1** ± 5.6 |
| | Vero E6, Viral yield ($EC_{50}$) | B.1.1.7 *[Alpha]* | **46** |
| | Vero E6, Viral yield ($EC_{50}$) | B.1.351 *[Beta]* | **44** |

FRET = fluorescence resonance energy transfer; CPE = cytopathic effect; P-gpi = P-glycoprotein inhibitor CP-100356 (2 µM); pHAEC = primary human airway epithelial cells; qPCR = quantitative polymerase chain reaction.
*The 3CLpro sequences for the ancestral A lineage and B.1.617.2 (Delta) variant are identical

Source: Jiang *et al.,* ISIRV Poster #120, Oct 19, 2021

 

# EDP-235 Preclinical Profile Suggests Potential for Best-in-Class Antiviral Treatment for SARS-CoV-2 Infection

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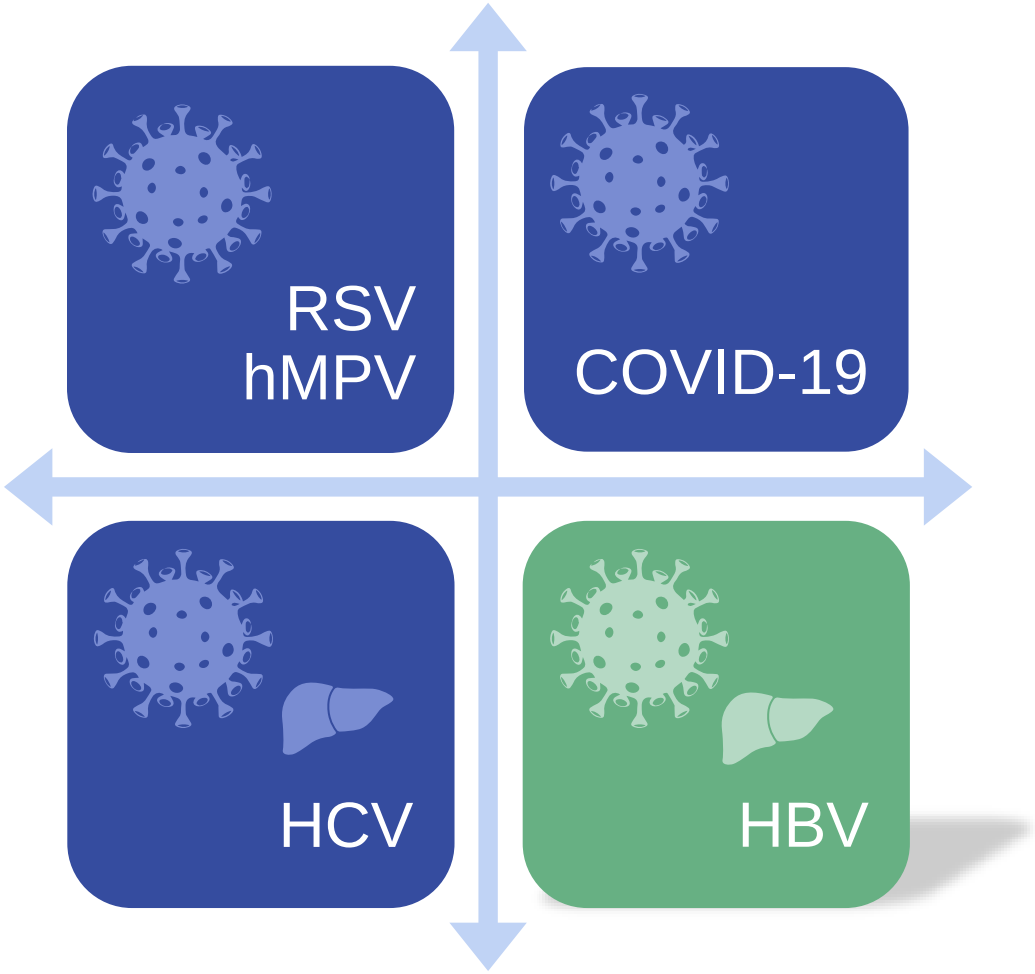
| Preclinical Properties | | EDP-235[1] | PF-07321332[2] | PBI-0451[3] | S-217622[4] | Molnupiravir[5] | AT-527[6] |
|---|---|---|---|---|---|---|---|
| Mechanism | | **Protease** | Protease | Protease | Protease | Polymerase | Polymerase |
| Potency | Enzyme $IC_{50}$ (nM) | **5.8** | 19 | 20 – 30 | 13 | n/a | n/a |
| | Vero Cell $EC_{50}$ (nM) | **5.1** | 75 | n/a | 370 | 1410* | 470** ($EC_{90}$ in pHAEC) |
| Oral Bioavailability[7] | | **95%** | 34 – 50% | n/a | 97% | 36 – 56% | n/a |
| Lung Penetration[8] | | **4.1** | 0.8[9] | ~1 | n/a | 1.8 | 1.2 (monkeys) 0.8 (humans) |
| Projected Efficacious Dose | | **100 – 500 mg QD** | 250 mg/100 mg **RTV** q12h | 500 mg BID or 1500 mg QD | QD | 800 mg BID | 1100 mg BID |

*Data from N-hydroxycytidine (NHC): molnupiravir prodrug of NHC
**Data from AT-511 (AT-527 is the hemi-sulfate salt of AT-511)
pHAEC: primary human airway epithelial cells
RTV: ritonavir

1. Jiang *et al.,* ISIRV Poster #120, Oct 19, 2021
2. Owen *et al.*, medRxiv, July 2021; Pfizer 2Q2021 earnings presentation
3. Pardes Corporate Presentation, June 2021
4. Shionogi R&D Day, Sept 28, 2021, Tachibana, *et al.,* ISIRV oral presentation, Oct 20, 2021
5. Grobler *et al.,* ID Week 2021, Poster 543; Painter *et al.,* Antiviral Research Nov 2019
6. Good *et al., AAC*, 2021; Atea 2Q2021 earnings presentation; Atea press releases Oct 19, 2021, Nov 11, 2021
7. Oral bioavailability in rats for EDP-235, PF-07321322 and S-217622; in mice for molnupiravir
8. AUC lung to plasma ratio in rats for EDP-235, PF-07321332, in mice for molnupiravir; $C_{12}$ lung to plasma ratio in monkeys and humans for AT-527
9. Data for PF-07321332 generated by Enanta

# Our Therapeutic Focus

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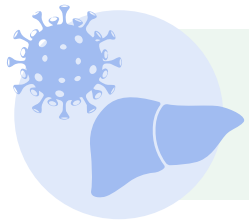
# Hepatitis B Virus (HBV)



Potentially life-threatening liver infection caused by the hepatitis B virus

- In 2019, hepatitis B resulted in an estimated 820,000 deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer)[1]
- Current treatments rarely give true cures
  - **Interferon** is ~10% effective, but with side effects[2]
  - **Reverse-transcriptase inhibitors** effective at reducing viral load, but low cure rates (1% or lower) and treatment for life to improve cirrhosis or HCC outcomes[3]

| HBV at a Glance | |
|---|---|
| **US** | 850K – 2M people[4] |
| **Europe and European Economic Area** | ~4.7M people[5] |
| **Worldwide** | ~290M people[6] |

Sources: 1. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b 2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5401664/ 3. https://pubmed.ncbi.nlm.nih.gov/30342034/
4.https://jamanetwork.com/journals/jama/fullarticle/2738558 5.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5356432/ 6.https://pubmed.ncbi.nlm.nih.gov/29599078/

# EDP-514: HBV Core Inhibitor

- A novel core inhibitor that displays potent anti-HBV activity at multiple points in the HBV lifecycle
- Granted Fast Track Designation by FDA

***In vitro***

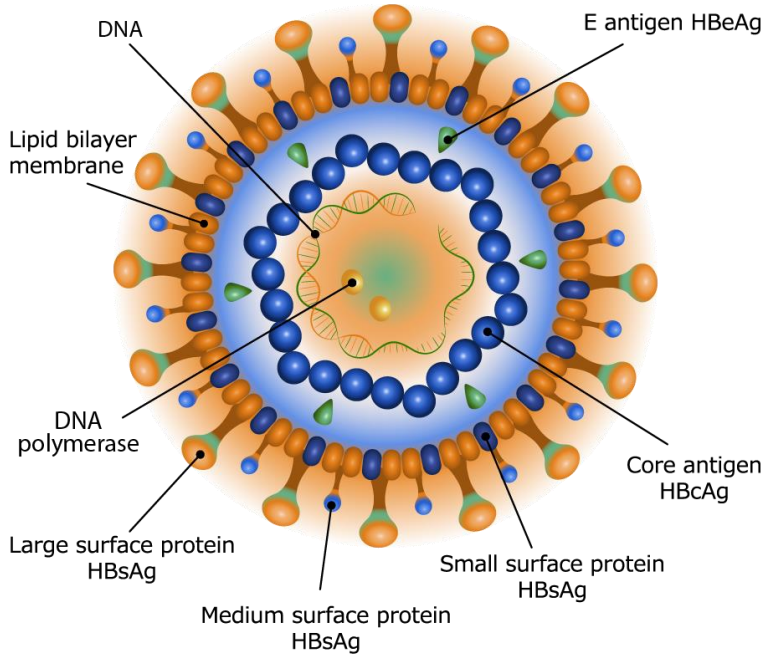
- Potent anti-HBV activity in HBV expressing stable cell lines
- Capable of preventing the establishment of cccDNA
- Pan-genotypic activity

***In vivo***

- Favorable tolerability and pharmacokinetic profile
- Over 4-log reduction in HBV viral titers with 12 weeks of treatment in a chimeric liver mouse model

***Phase 1a***

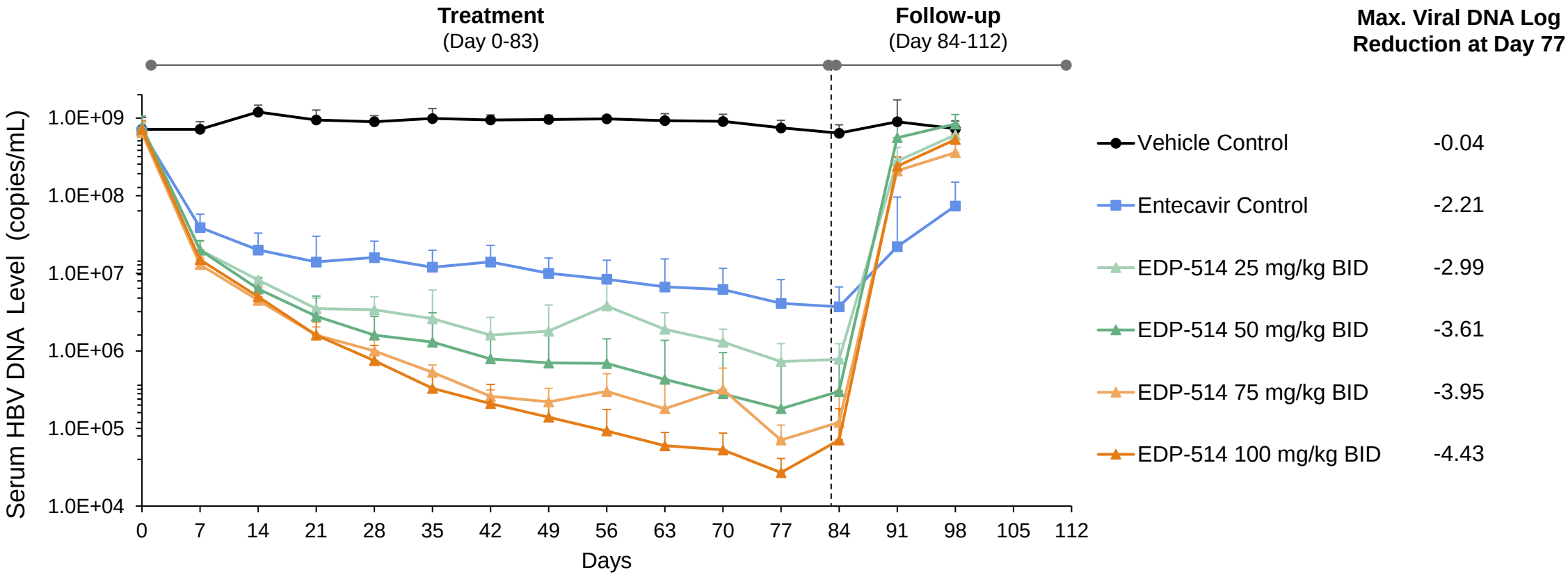
- Healthy volunteer SAD/MAD
- Generally safe and well tolerated for up to 14 days
  - All reported treatment emergent adverse events of mild severity
- Pharmacokinetics supportive of once-daily dosing with no food effect



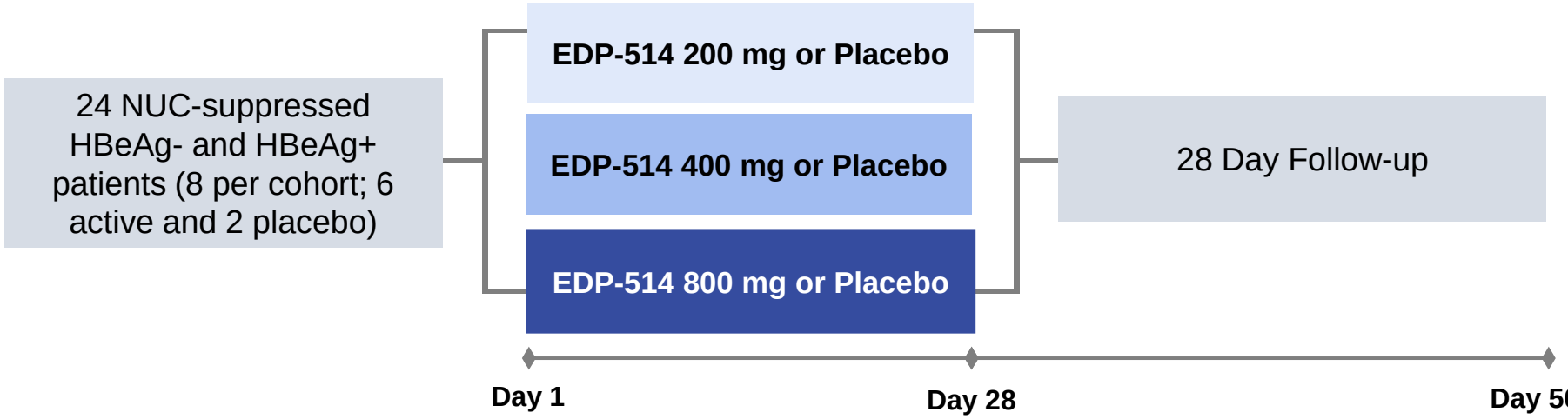
# EDP-514: Efficacious in the Humanized Liver Mouse Model

- uPA/SCID mice were infected with genotype C HBV and dosed with EDP-514 for 12 weeks



# EDP-514 Phase 1: Positive Data in NUC-Suppressed Patients




- **Primary Objective:** Safety and tolerability
- **Secondary Objective:** PK and antiviral activity

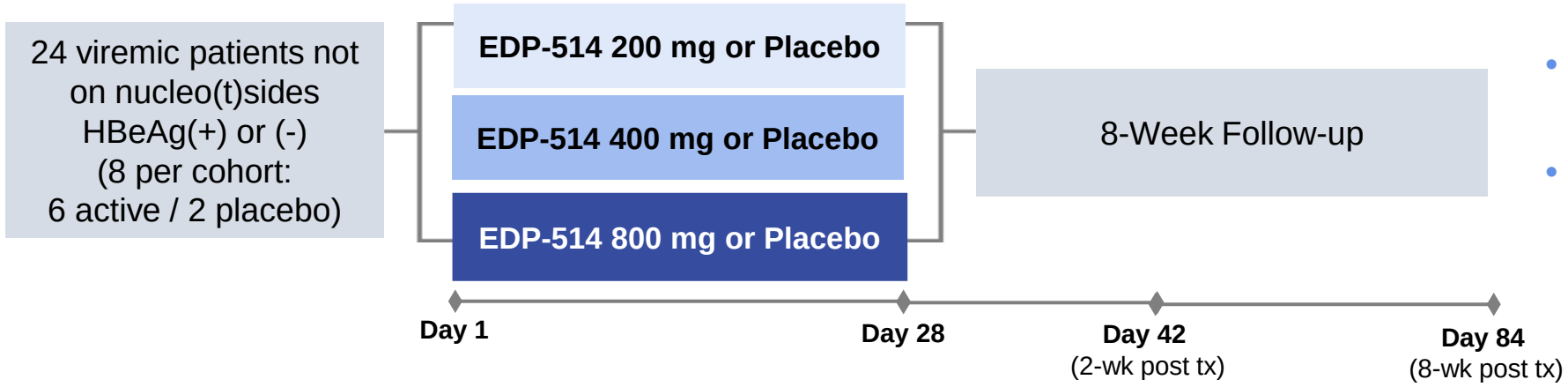
## Positive data from three dose cohorts: 200 mg, 400 mg and 800 mg of EDP-514

- EDP-514 was safe and well-tolerated in NUC-suppressed subjects at all doses up to 28 days
- Pharmacokinetics supportive of once-daily dosing, with trough concentrations up to ~20-fold the $paEC_{50}$
- Mean reduction in HBV RNA of up to ~1 log compared with 0.2 log in placebo
  - Maximum reduction of 2.3 log (HBeAg-) and 2.8 log (HBeAg+) was observed in patients receiving EDP-514 as compared with 1.2 log in placebo

$paEC_{50}$: protein-adjusted $EC_{50}$

# EDP-514 Phase 1b: Positive Data in Viremic HBV Patients




- **Primary Objective:** Safety and tolerability
- **Secondary Objective:** PK and antiviral activity

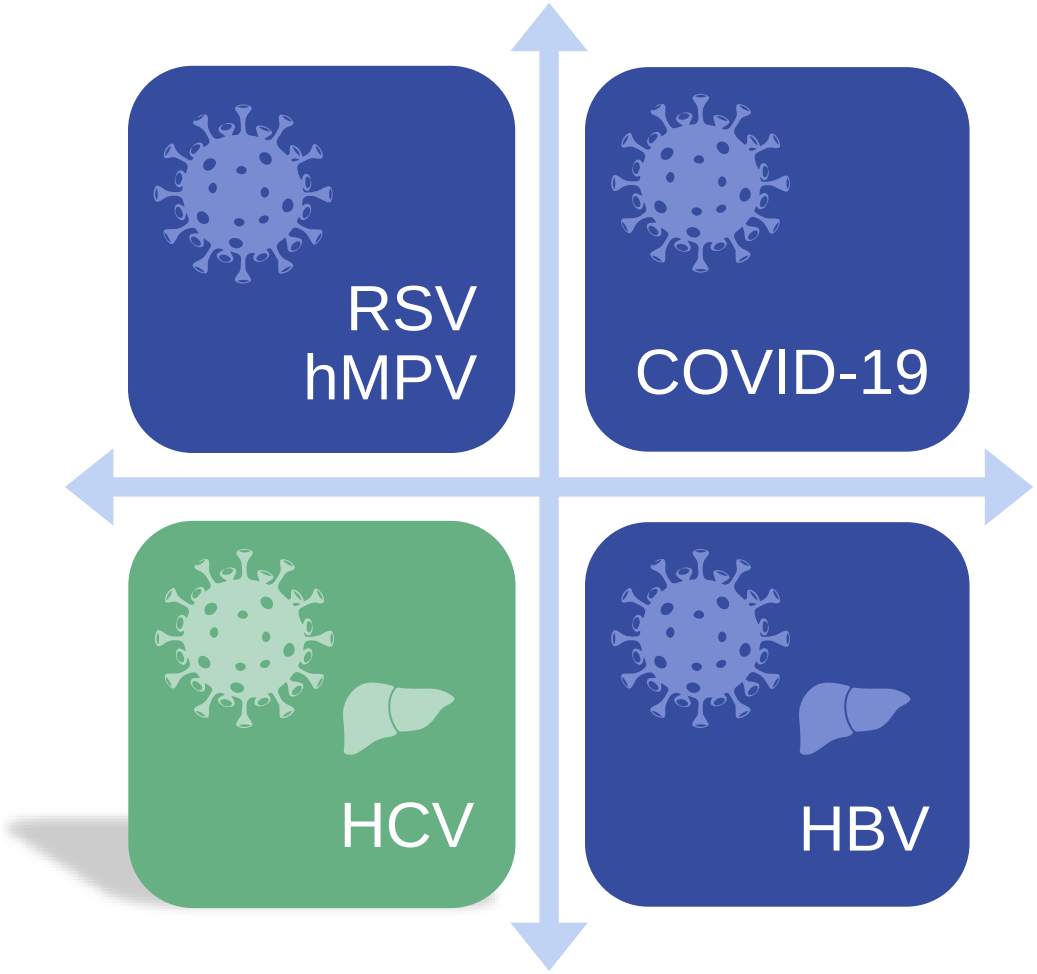
## Positive data from three dose cohorts: 200 mg, 400 mg and 800 mg of EDP-514

- EDP-514 was safe and well tolerated in viremic chronic HBV patients dosed for 28 days
  - No severe or serious TEAEs; no liver enzyme elevations or other clinically significant laboratory abnormalities
  - Safety profile remains consistent across healthy subjects and NUC-suppressed patients
- Pharmacokinetics supportive of once-daily dosing, with trough concentrations up to ~20-fold the $paEC_{50}$
- Mean reduction in HBV DNA of 2.9, 3.3, 3.5 log in the 200 mg, 400 mg, and 800 mg groups compared with 0.2 log in placebo
- Mean reduction in HBV RNA of 2.9, 2.4, 2.0 log in the 200 mg, 400 mg, and 800 mg groups compared with 0.02 log in placebo

$paEC_{50}$: protein-adjusted $EC_{50}$, <LLOQ: Below the lower level of quantification, <LOD: Below the limit of detection

# Our Therapeutic Focus



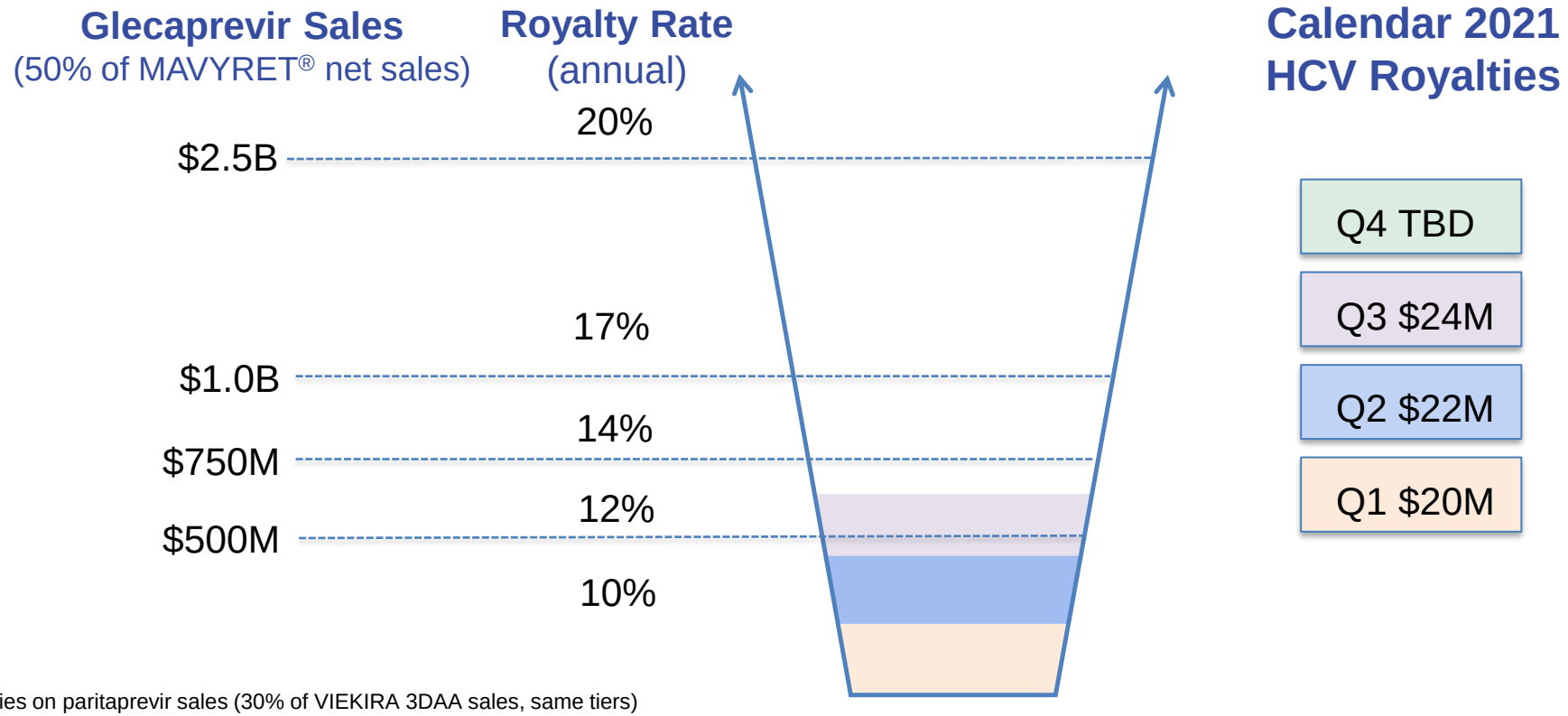

Leveraging our core strength in Hepatitis C to become a leader in oral treatments for **viral** infections and **liver** diseases

Several new therapeutic areas with goal of building multiple approaches in each

# Glecaprevir: Our Licensed Protease Inhibitor for Hepatitis C Virus

| Product | Regimen | Enanta Asset | Economics* |
|---|---|---|---|
| MAVYRET glecaprevir/pibrentasvir 100 mg/40 mg tablets | 2-DAA (ABBV) | glecaprevir (PI) | Double-digit royalty on 50% of net sales |




**Calendar 2021 HCV Royalties**

- Q4 TBD
- Q3 $24M
- Q2 $22M
- Q1 $20M

*Enanta also receives royalties on paritaprevir sales (30% of VIEKIRA 3DAA sales, same tiers)

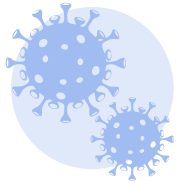
# Financial Highlights

| ($ in millions except per share amounts) | Fiscal Year Ended Sept. 30, 2021 | Fiscal Quarter Ended Sept. 30, 2021 |
|---|---|---|
| Total Revenues | $97.1 | $23.6 |
| R&D Expenses | $174.1 | $48.9 |
| G&A Expenses | $32.5 | $8.4 |
| Net Loss | $(79.0) | $(24.6) |
| Net Loss per Diluted Common Share | $(3.92) | $(1.22) |
| **Balance Sheet** | | |
| Cash, Cash Equivalents and Marketable Securities | $352.4 | $352.4 |

# Key Catalysts 2022

## Virology Respiratory



### RSV: N-Protein Inhibitor EDP-938 and L-Protein Inhibitor EDP-323

- ☐ Report data for RSVP Phase 2b trial of EDP-938 in Q2 2022
- ☐ Continue recruitment for RSVPEDs and RSVTx clinical trials for EDP-938
- ☐ Initiate Phase 1 trial for EDP-323 in 2H 2022

### SARS-CoV-2

- ☐ Initiate Phase 1 trial for EDP-235 in February 2022

### hMPV

- ☐ Nominate clinical development candidate in 2H 2022

## Virology Liver

### Hepatitis B Virus

- ☐ Select third mechanism for HBV combination regimen with EDP-514

# ENANTA
## Pharmaceuticals

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