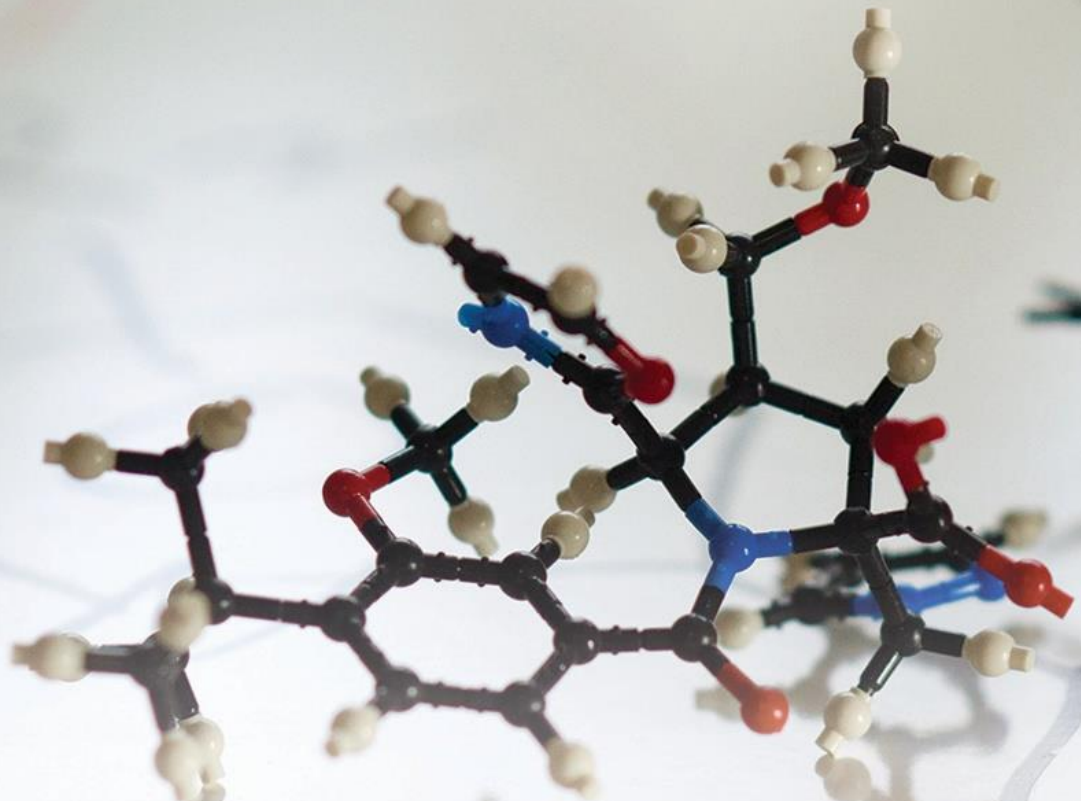
# Corporate Presentation

**July 9, 2020**



ENANTA Pharmaceuticals

**Creating Small Molecule Drugs for Viral Infections and Liver Diseases**

# 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 development 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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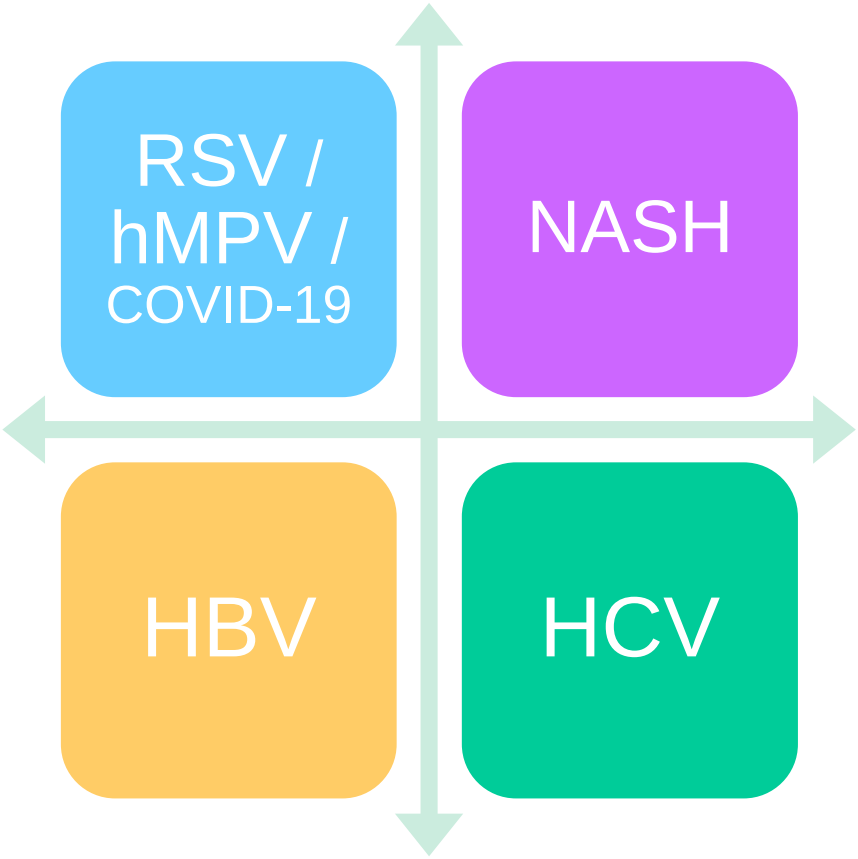
# Investment Highlights

- Virology and liver disease-focused biotech company
- Clinical-stage programs in areas of high unmet medical need:
  - RSV: Phase 2b "RSVP" Study ongoing
  - NASH: Phase 2b "ARGON-2" Study ongoing
  - HBV: Phase 1b Two studies ongoing
- Discovery/preclinical programs in HBV, NASH, RSV, hMPV & COVID-19
- Partnered product marketed in AbbVie's HCV regimen:
  - Glecaprevir – HCV protease inhibitor in MAVYRET®/MAVIRET®
  - $205M in fiscal 2019 royalties on HCV regimens
- Strong balance sheet and royalties fund R&D programs
  - $435M in cash at 3/31/20

# Our Therapeutic Focus

- Leverage our core strength in HCV to become a leader in Viral and Liver diseases
- Multiple new therapeutic areas with goal of building multiple approaches in each



# Broad Virology and Liver Disease Pipeline

| Product Candidate | | Discovery | Preclinical | Phase 1 | Phase 2 | Phase 3 | Market |
|---|---|---|---|---|---|---|---|
| HCV | Protease Inhibitor | glecaprevir – containing pan-genotypic 2-DAA combo (MAVYRET glecaprevir/pibrentasvir) | | | | | |
| RSV | N-protein Inhibitor | EDP-938 | | | | | |
| NASH | FXR Agonist | EDP-305 | | | | | |
| HBV | Core Inhibitor | EDP-514 | | | | | |
| NASH | FXR Agonist Follow-on | EDP-297 | | | | | |
| hMPV | Inhibitor | | | | | | |
| COVID-19 | DAA | | | | | | |
| RSV, HBV, NASH, other Discovery or Preclinical | | | | | | | |

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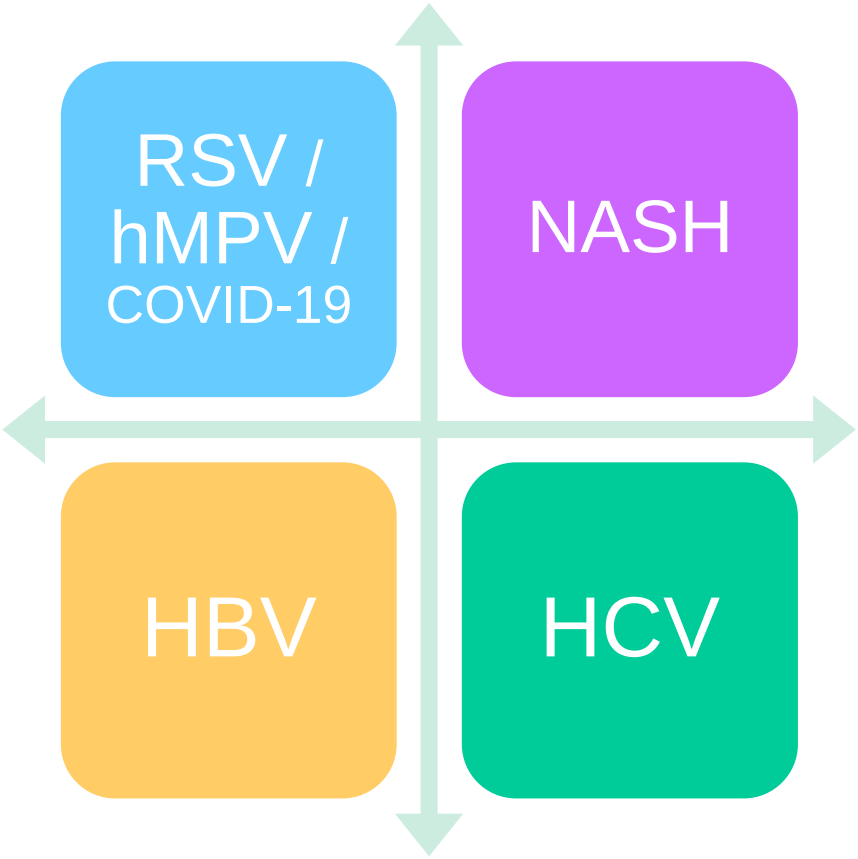


# Respiratory Syncytial Virus (RSV)

- Negative-sense, single-stranded RNA virus of family Pneumoviridae
- Can cause severe lung infections, including bronchiolitis (infection of small airways in the lungs) and pneumonia (an infection of the lungs)
- Higher risk populations for severe illness include:
  - Premature babies
  - Older adults, especially those 65 years and older
  - People with chronic lung disease or certain heart problems
  - People with weakened immune systems (e.g. HIV, organ transplant, chemotherapy)
- Each year in U.S.:
  - > 57,000 children below age 5 are hospitalized for RSV
  - ~ 177,000 older adults are hospitalized, and about 14,000 die
- No safe and effective treatments

Source: CDC



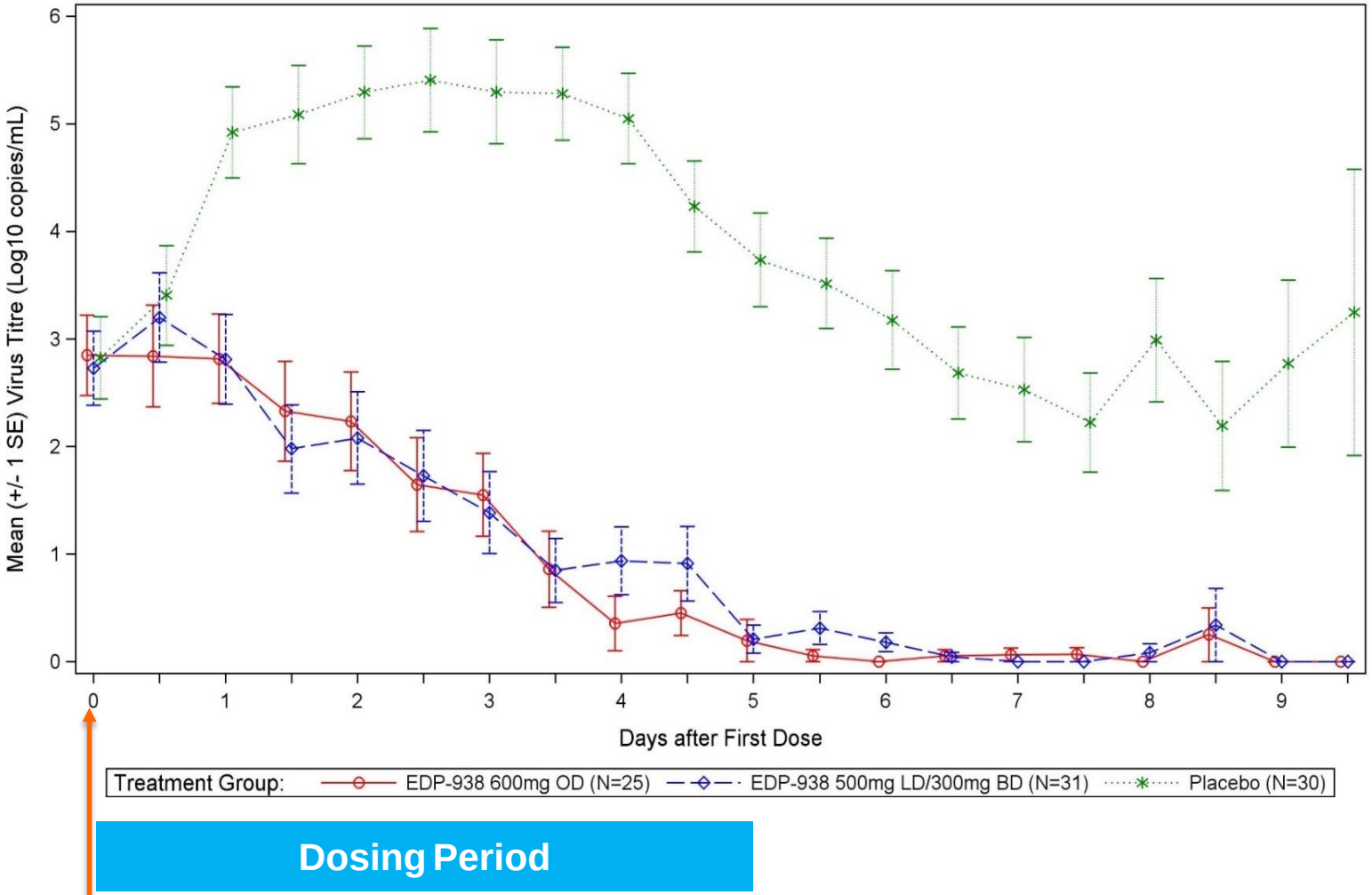
# EDP-938: N-Protein Inhibitor for RSV

- EDP-938 is the only N-inhibitor under clinical evaluation
  - Non-fusion approach directly targets viral replication
- Strong preclinical virological 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 resistant virus from other mechanisms
  - Robust *in vivo* efficacy data
- Phase 2a human challenge study met primary and key secondary efficacy endpoints
- Phase 2b “RSVP” study in adult outpatients ongoing
- Additional Phase 2 RSV studies in pediatric patients and adult transplant patients targeted to begin 4Q 2020

# Robust Antiviral Effect

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

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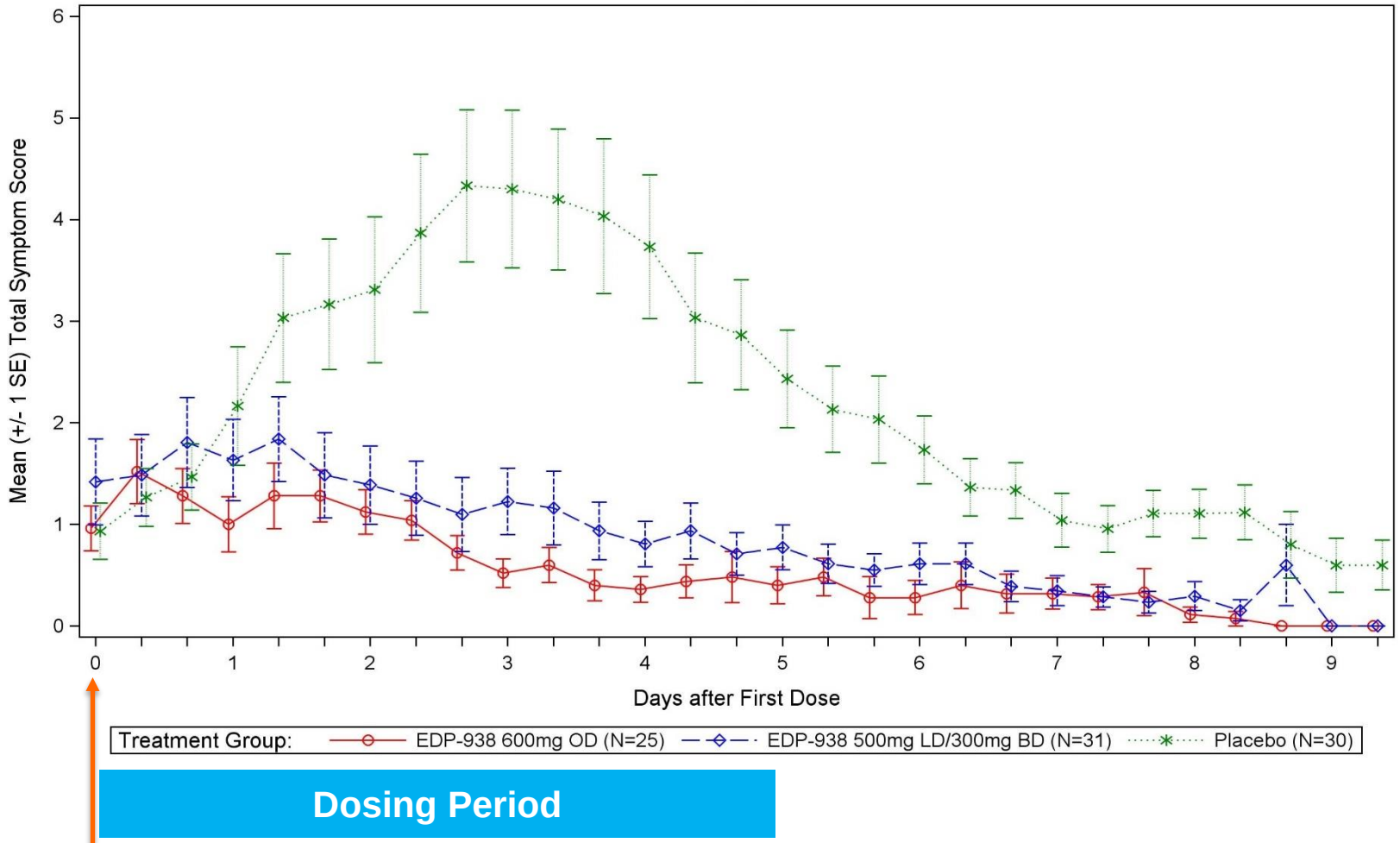
# EDP-938 Shows a Rapid and Sustained Attenuation of RSV Symptoms in Both Active Arms Compared to Placebo (68%, 74%↓ AUC; P<0.001)

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# Summary: EDP-938, A Highly Efficacious and Safe RSV N-Inhibitor

- Phase 1 Results:
  - Safe and well tolerated, no SAEs, AEs were mild
  - At Phase 2 doses, mean trough levels 30x higher than $EC_{90}$ 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
  - EDP-938 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

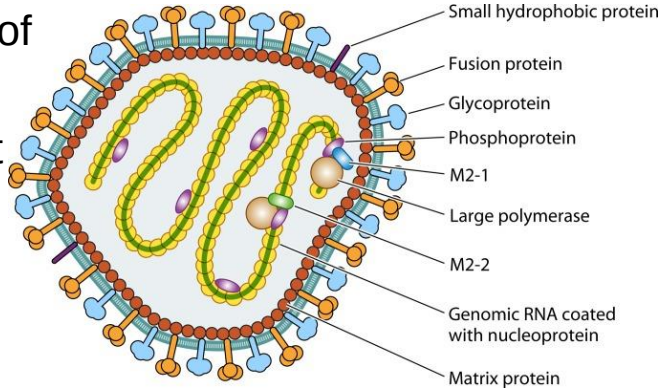

 

# “RSVP” – A Phase 2b Study in Adult Outpatients with RSV


- RSVP Study Design:
  - Randomized, double-blind, placebo-controlled in approximately 70 subjects, up to the age of 75 years
  - 800mg EDP 938 or placebo for 5 days
    - Comparable to 600mg suspension dosage form used in challenge study
  - Subjects will be followed for a total of 14 days
  - Primary Objective: to evaluate the effect of EDP-938 on progression of RSV infection by assessment of clinical symptoms measured over the course of the 14-day study observation period
- Goal: Topline data 3Q 2021

# Human Metapneumovirus (hMPV)

- Paramyxovirus closely related to RSV
  - Has the ability to cause mild to severe disease in people of all ages
  - hMPV replication dependent on several viral proteins that form a multiprotein complex in cells
    - Multiple potential targets for hMPV drug discovery

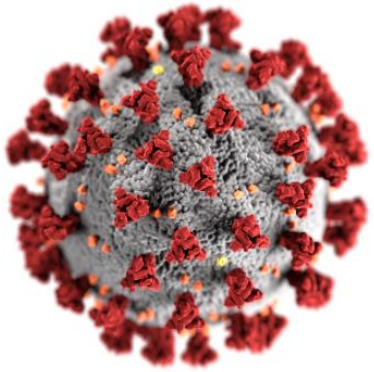



- Important cause of respiratory tract infections (RTIs), particularly in children, the elderly and immunocompromised individuals
  - Second most common cause of lower RTIs in children (behind RSV)
  - Reinfection with hMPV occurs throughout life
- No approved vaccine or therapeutics available
- Enanta nanomolar hMPV inhibitor leads under active optimization

# SARS-CoV-2 (COVID-19)

- Caused by respiratory infection of a new highly pathogenic coronavirus, SARS-CoV-2
  - Belongs to coronaviridae, a family of enveloped RNA viruses that include SARS-CoV and MERS-CoV
  - Has a 30kb single-strand positive RNA genome that encodes 4 structural proteins and 16 nonstructural proteins, including several potential druggable targets



- No approved vaccines or therapeutics available for any of the coronaviruses despite previous outbreaks

- Enanta is leveraging years of antiviral drug discovery expertise to
  - Screen compounds from Enanta library against SARS-CoV-2
  - Initiate novel drug discovery efforts to identify direct-acting antivirals

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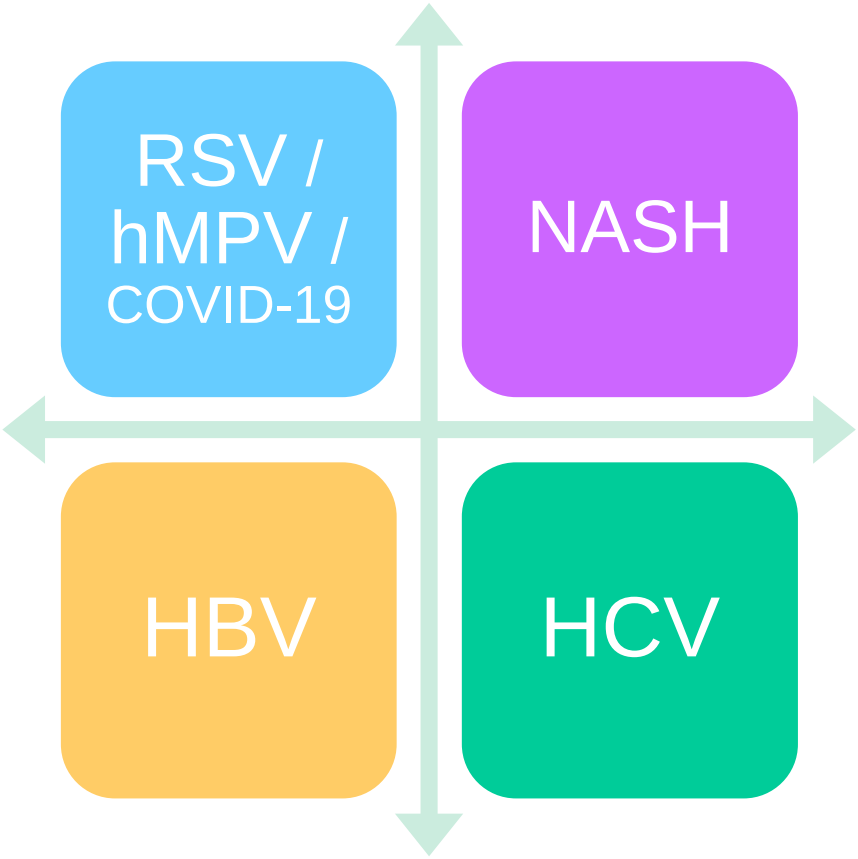


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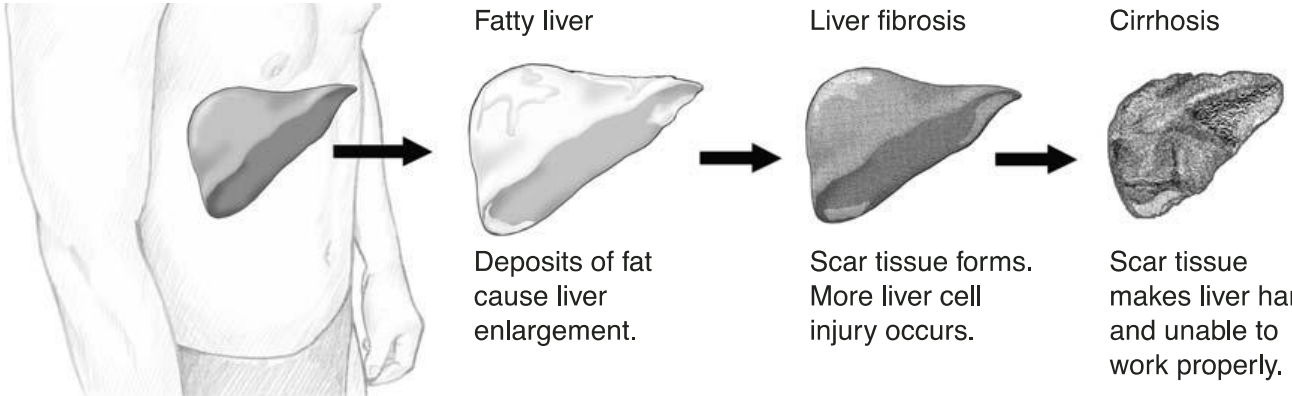
# Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH)

- Number one cause of liver disease in Western Countries
- NAFLD: excessive fat (triglyceride) accumulation in the liver (steatosis)
- A subgroup of NAFLD patients has liver cell injury and inflammation in addition to excessive fat (steatohepatitis), *i.e.* NASH
- NASH is associated with the metabolic syndrome – diseases related to type 2 diabetes, insulin resistance, obesity, hyperlipidemia, and hypertension
- While NAFLD does not correlate with short-term morbidity or mortality, progression to NASH dramatically increases risk of cirrhosis, liver failure and hepatocellular carcinoma

Stages of Liver Injury
(NIDDK)

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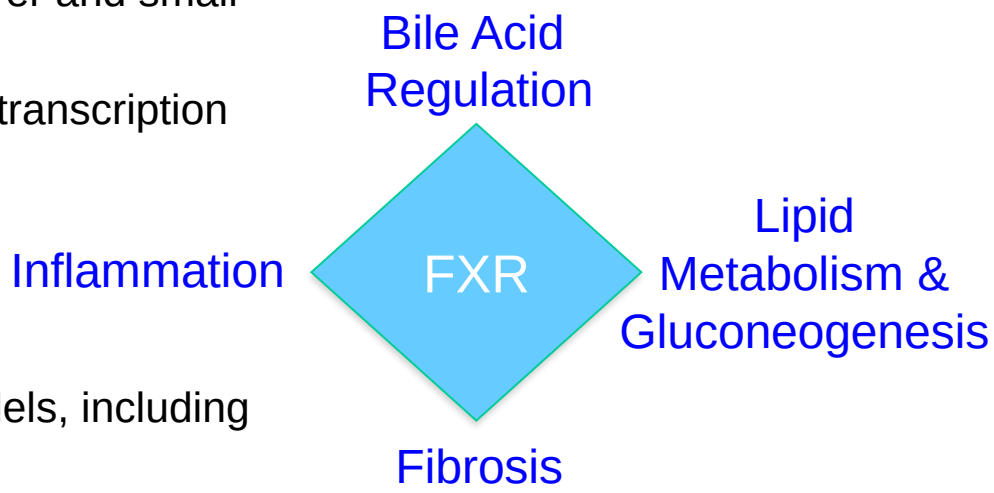
# Enanta's Approach to NASH Agonists of Farnesoid X Receptor (FXR)

- FXR
  - Nuclear receptor
  - Main regulator of bile acid levels in liver and small intestine
  - Responds to bile acids by regulating transcription of key enzymes and transporters
- FXR agonist preclinical PoC
  - Ameliorate pathologies in NASH models, including an effect on fibrosis
- Clinical validation of FXR agonist in NASH with 6-ECDCA (OCA)




Source: Matsubara Mol Cell Endocrinol 2013; Neuschwander-Tetri et al, Lancet, 2014

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# FXR Agonist EDP-305: Introduction

- EDP-305: Non-bile acid
  - Steroidal non-carboxylic acid, modified with additional non-steroidal binding element to enhance potency
- Potent FXR receptor agonist activity *vs* OCA
- Highly selective for FXR *vs* other nuclear receptors
  - And *vs* TGR5 receptor
- Potent and differentiated effects on FXR-dependent gene expression *vs* OCA
  - *E.g.* Shp, Cyp7a1, Bsep, Fgf15/FGF19
  - Human hepatocytes and *in vivo* mouse model
- Efficacy in multiple NASH models
  - STAM™ mouse NASH model and dietary-induced NASH (DIN) mouse model
  - Improvement in hepatocyte ballooning and overall NAFLD Activity Score vs OCA
- Reduced liver fibrosis in rodent models
  - Mdr2-/-, MCD, CDAHFD, thioacetamide and bile duct ligation models


 

# FXR Agonist EDP-305: Phase 2 Studies

- Fast Track Designation granted by FDA for NASH with fibrosis
- Phase 2 studies in NASH
  - ARGON-1 study in NASH complete
    - Design: 12-week dose ranging, randomized, double-blind, placebo-controlled
    - Evaluate safety, tolerability, PK, and efficacy ALT reduction in NASH
- Positive Phase 2a ARGON-1 results warrant further studies in NASH (Phase 2b ARGON-2)


 

# Summary of EDP-305 ARGON-1 Study

- Primary (ALT change) and key secondary (liver fat by MRI-PDFF) endpoints were met at week 12 using 2.5 mg dose
- Strong target engagement as shown by reductions in C4, and increases in FGF-19 and ALP
- Robust reduction in marker of liver injury (GGT)
- Generally safe for up to 12 weeks
  - Majority of TEAEs were mild to moderate
  - Incidence of treatment discontinuation due to pruritus was 1.8% for 1 mg and 20.8% for 2.5 mg
  - Associated with small numeric absolute changes in lipids


 

# EDP-305 Next Steps: ARGON-2, a Phase 2b NASH Study

ARGON-2

- Phase 2b NASH study:
  - Randomized, placebo-controlled in biopsy-proven NASH patients (~ 340)
  - 72-week treatment duration
  - Includes a 12-week interim analysis (to generate dose information more quickly for potential combinations)
  - Primary endpoint: improvement of fibrosis without worsening of NASH and/or NASH resolution without worsening of fibrosis
- Two doses selected to provide strong target engagement and a balanced profile in terms of efficacy and tolerability:
  - 1.5 mg dose: designed to demonstrate stronger biomarker signals of efficacy than seen at 1.0 mg
  - 2.0 mg dose: designed to demonstrate less pruritus than seen at 2.5 mg


 

# EDP-297 – A Potent and Differentiated Follow-on FXR Agonist

- EDP-297 preclinical profile shows:
  - High target-tissue distribution (liver and intestine) *vs* plasma and skin
  - Potency greater than that published on any FXR agonist in clinical development today
- A highly potent *and* highly targeted FXR agonist may allow for lower doses and reduced drug levels at non-targeted tissues
  - Potential to reduce pruritus unless pruritus is FXR-mediated by FXR receptors in liver or intestine
- Planned Phase 1 study to initiate 3Q 2020 and data expected in 2Q 2021


 

# EDP-297 is a Highly Potent FXR Agonist with Excellent Target Tissue Distribution

| Compound | | FXR FL Activation $EC_{50}$ (nM) | Dose (mouse, *po*) | Intestine / Plasma @ 4 hrs ~ Tmax | Liver / Plasma @ 4 hrs ~ Tmax |
|---|---|---|---|---|---|
| OCA | Bile Acid | 130 [1] | 10 mg/kg | 160 | 26 |
| cilofexor | Non-Bile Acid | 41 [2] | 1 mg/kg | 0.6 | 0.9 |
| EDP-305 | Non-Bile Acid | 8 | 1 mg/kg | 7 | 15 |
| tropifexor | Non-Bile Acid | 0.4 [3] | 1 mg/kg | 0.8 | 8 |
| **EDP-297** [4] | Non-Bile Acid | **<0.1** | 1 mg/kg | **265** | **75** |

Enanta data except where noted

1. $EC_{50}$ = 99 nM reported by Intercept
2. Gilead data. Trauner *et al Hepatology* 2019
3. $EC_{50}$ = 0.26 nM reported by Novartis. Tully *et al J. Med. Chem.,* 2019
4. **EDP-297 is undetectable in mouse skin**

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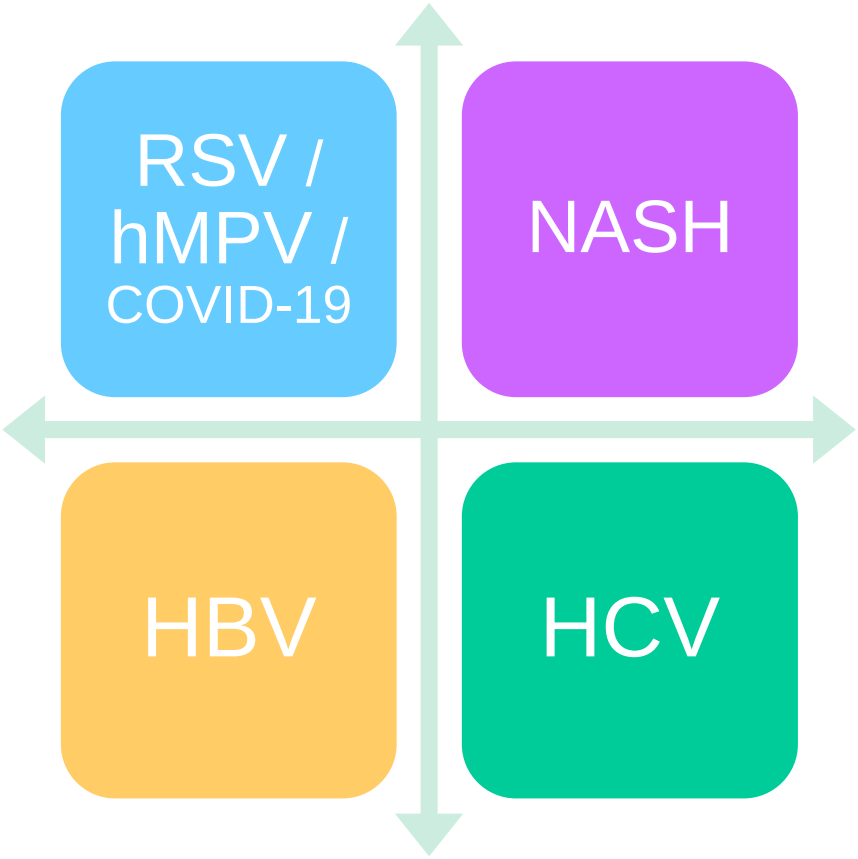


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# HBV Background

- Potentially life-threatening liver infection caused by the hepatitis B virus
- Current treatments rarely give true cures
  - **Interferon** gives better results (~10%), but with side effects
  - **RT inhibitors** very effective at reducing viral load, but offer very low cure rates (1% or lower) and must be taken for life to improve cirrhosis or hepatocellular carcinoma (HCC) outcomes
- Prevalence estimates
  - US: ~850,000 - 2 million
  - US + Japan + major EU populations: ~4.9 million
  - Worldwide: ~250 million

- Estimated 15-25% of patients with chronic HBV infection will develop chronic liver diseases including cirrhosis, HCC or liver decompensation

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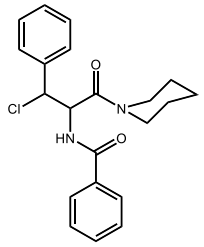
Sources: WHO, CDC, Datamonitor

# Core inhibitors: Introduction

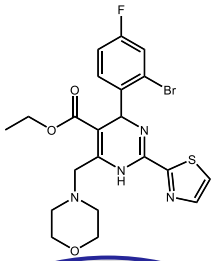
**(Also called capsid assembly modulators, core protein allosteric modulators, capsid inhibitors)**

- Novel class of replication inhibitor
- Act at multiple steps in HBV lifecycle
  - Prevent proper uncoating, nuclear import, assembly, and recycling

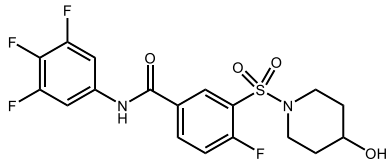
Phenylpropemides (AT-130)



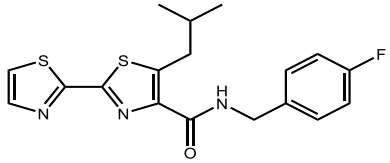
HAPs (GLS4)

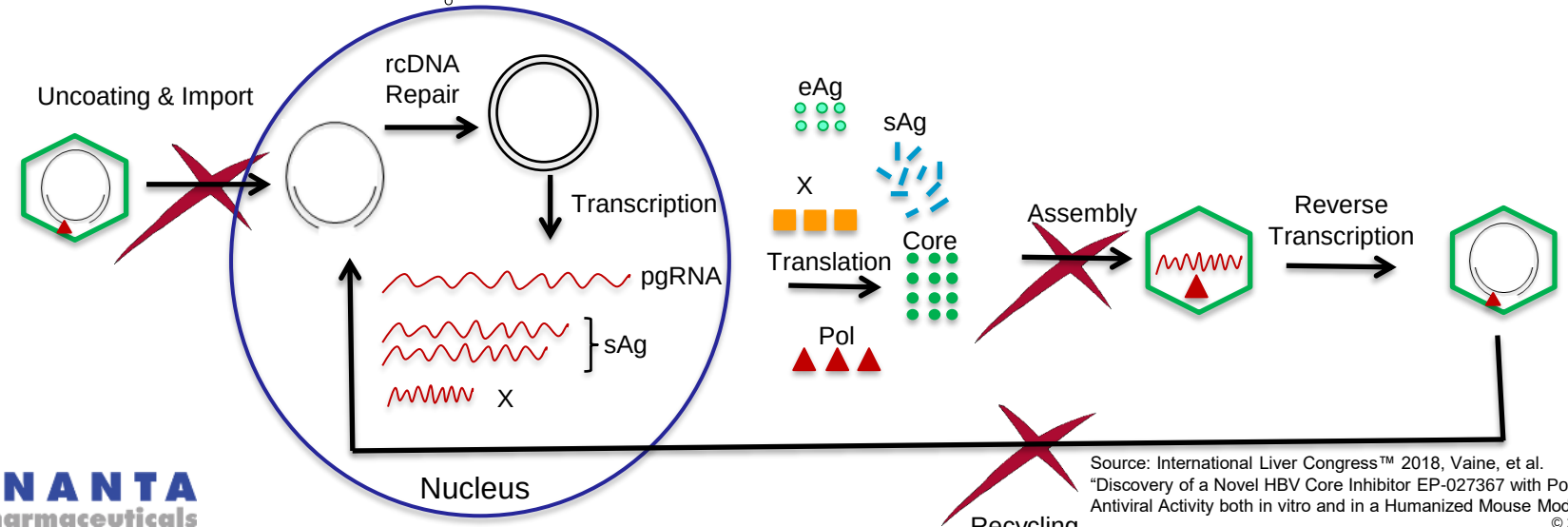


Sulfamoylbenzamides (SBA-R01)



Isothiafludine (NZ-4)






Source: International Liver Congress™ 2018, Vaine, et al. "Discovery of a Novel HBV Core Inhibitor EP-027367 with Potent Antiviral Activity both in vitro and in a Humanized Mouse Model"



# Core Inhibitor EDP-514 is a Potent Inhibitor of HBV Replication

- EDP-514 is active in multiple HBV stable cell lines

| | HBV Stable Cell Line $EC_{50}$ (nM) | | |
|---|---|---|---|
| | HepAD38 | HepDE19 | HepG2.2.15 |
| Intracellular Viral DNA | 18 | 27 | 17 |
| Encapsidated pgRNA | 25 | 3 | 5 |
| HBeAg | 20 | 34 | >500* |

* In HepG2.2.15 cells, HBeAg is transcribed off transgene and is not dependent on viral replication

Viral DNA measured by qPCR
Encapsidated pgRNA measured by modified pulldown and qPCR
HBeAg measured by commercial ELISA kit

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# EDP-514 Prevents *de novo* Formation of cccDNA in Primary Human Hepatocytes

- EDP-514 prevents cccDNA establishment when present at early time points in infection (HBsAg as surrogate marker)

| Compound | HBsAg $EC_{50}$ (nM) | | HBV DNA $EC_{50}$ (nM) | |
|---|---|---|---|---|
| | d0 Addition | d3 Addition | d0 Addition | d3 Addition |
| EDP-514 | 35 | >1000 | 10 | 6 |
| Entecavir | >1000 | >1000 | 0.25 | 0.21 |

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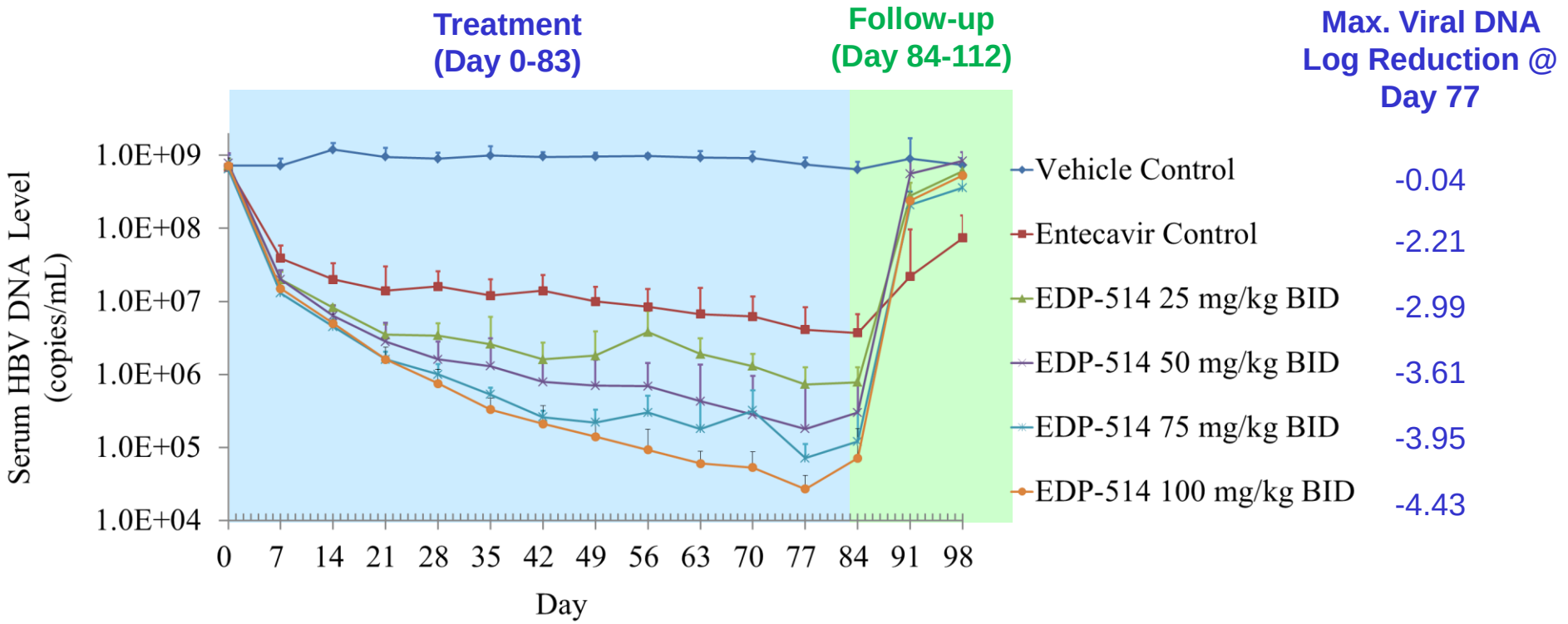
# EDP-514 is Efficacious in the Humanized Liver Mouse Model

- uPA/SCID mice were infected with genotype C HBV and subsequently treated with EDP-514 BID at indicated doses for 12 weeks

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# HBV Core Inhibitor EDP-514 Summary

- A novel core inhibitor that displays potent anti-HBV activity at multiple points in the HBV lifecycle
- *In vitro*:
  - Potent anti-HBV activity in HBV expressing stable cell lines
  - Capable of preventing the establishment of cccDNA
  - Potent 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
- Fast Track designation by FDA


 

# EDP-514 Phase 1 Development

- Phase 1
  - Part 1 Complete: Evaluated safety, tolerability PK of SAD/MAD doses in healthy volunteers
    - EDP-514 was generally safe and well tolerated
    - PK profile supportive of once daily dosing
    - Data to be presented at EASL in August 2020
  - Part 2 Initiated: Assessing safety and antiviral activity in NUC-suppressed patients
    - Topline results anticipated in 2Q 2021
- Additional Phase 1b study in viremic HBV patients
  - Initiated; preliminary data anticipated in 1H 2021


 

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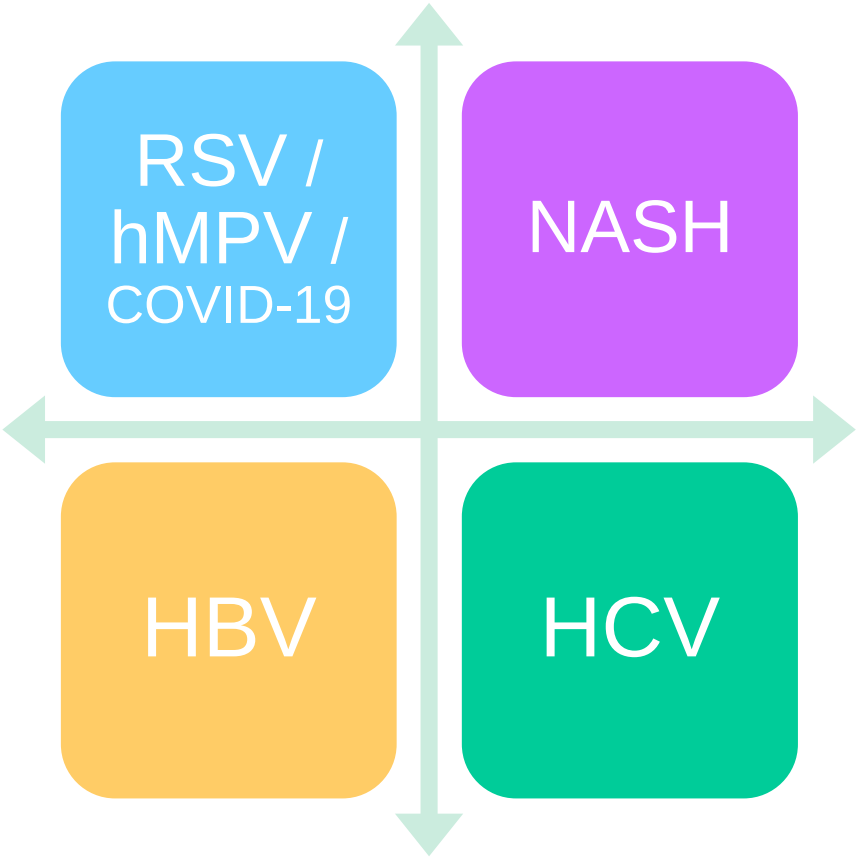


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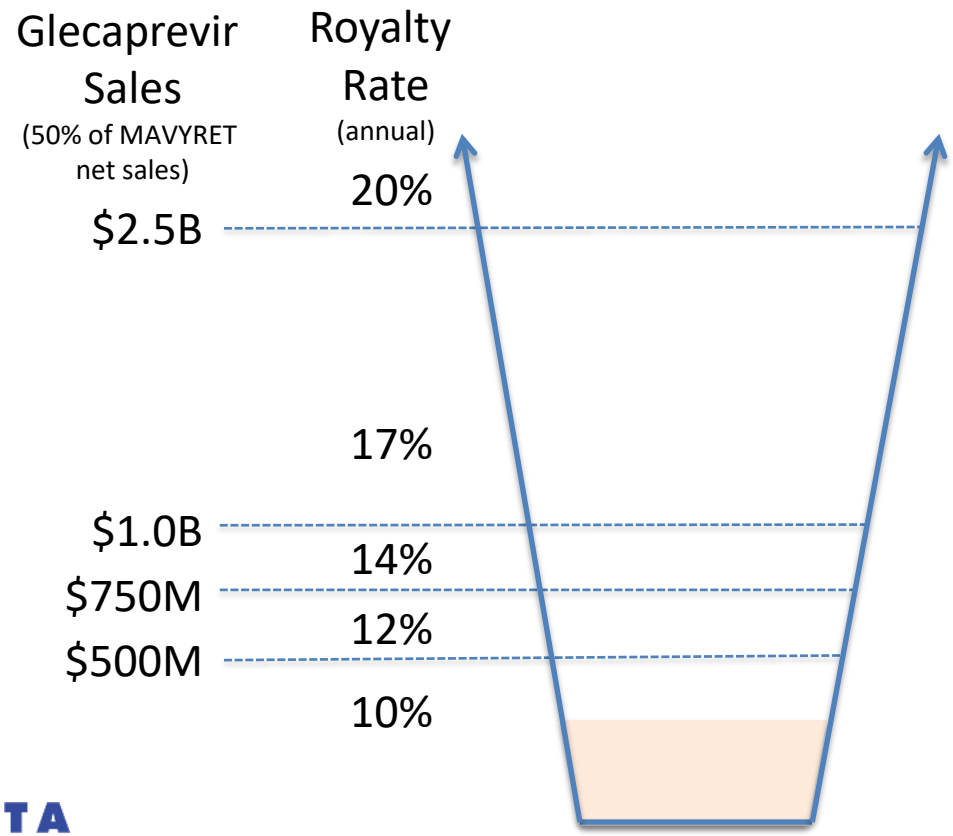
# Glecaprevir– Our Licensed Protease Inhibitor for Hepatitis C Virus

| 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 2020 HCV royalties

- Q4 $TBD
- Q3 $TBD
- Q2 $TBD
- Q1 $27.6M

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

# Financial Highlights

| ($ In millions) | Fiscal Year Ended Sept. 30, 2019 | Fiscal 2Q20 |
|---|---|---|
| Total Revenues | $205.2 | $27.6 |
| R&D Expenses | $142.2 | $32.6 |
| G&A Expenses | $26.3 | $6.9 |
| Net Income (Loss) | $46.4 | $(6.0) |
| Net Income (Loss) per Diluted Common Share | $2.21 | $(0.30) |
| **Balance Sheet** | | |
| Cash, Cash Equivalents and Marketable Securities | $400.2 | $435.4 |



 

# Key Catalysts and Funding

- RSV N-inhibitor EDP-938; also hMPV and COVID-19 Inhibitor Leads
  - Goal: Data from RSVP Phase 2b adult outpatient study 3Q 2021
  - Goal: Initiate two Phase 2 RSV studies in pediatric and transplant patients 4Q 2020
  - Advance COVID-19 drug discovery
  - Optimize nanomolar hMPV inhibitor leads
- NASH: FXR Agonists EDP-305 and EDP-297
  - Resumed ARGON-2 Phase 2b in NASH; 12-week interim analysis in 2021
  - Initiate Phase 1 for EDP-297 (follow-on FXR) targeted for 3Q 2020
  - Advance non-FXR compounds for NASH
- HBV: Core Inhibitor EDP-514
  - Present positive Phase 1 data in healthy volunteers at EASL, August 2020
  - Initiated Phase 1b in viremic HBV patients; preliminary data anticipated in 1H 2021
  - Resumed Phase 1b in NUC-suppressed HBV patients; topline results anticipated in 2Q 2021
  - Funding from double-digit HCV royalties on glecaprevir (MAVYRET®)


 

# ENANTA Pharmaceuticals

Creating Small Molecule Drugs for Viral Infections and Liver Diseases
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