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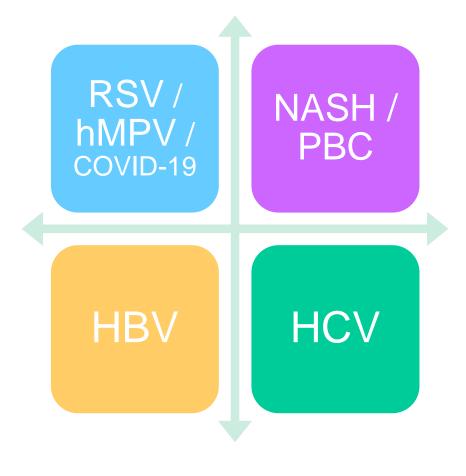
#### **Investment Highlights**

- Virology & liver disease-focused biotech company
- Four clinical-stage programs in areas of high unmet medical need:
  - RSV: Phase 2b "RSVP" Study initiated
  - NASH: Phase 2a "ARGON-1" Study completed
  - PBC: Phase 2 "INTREPID" Study ongoing
  - HBV: Phase 1 Study ongoing
- Discovery/preclinical programs in NASH, HBV, RSV, hMPV and 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
  - \$415M in cash at fiscal year end 12/31/19



#### **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 bisease ripellite							
Product	: Candidate	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Market
HCV	Protease Inhibitor	glecaprevir – containing pan-genotypic 2-DAA combo			MAVYRET : glecaprevir/pibrentasvir		

Inhibitor

N-protein

**FXR Agonist** 

**FXR** Agonist

Core Inhibitor

**FXR** Agonist

Follow-on

**Inhibitor** 

DAA

RSV, HBV, NASH, other Discovery or Preclinical

**Inhibitor** 

**RSV** 

**NASH** 

**PBC** 

**HBV** 

**NASH** 

**hMPV** 

COVID-19

**EDP-938** 

**EDP-305** 

**EDP-305** 

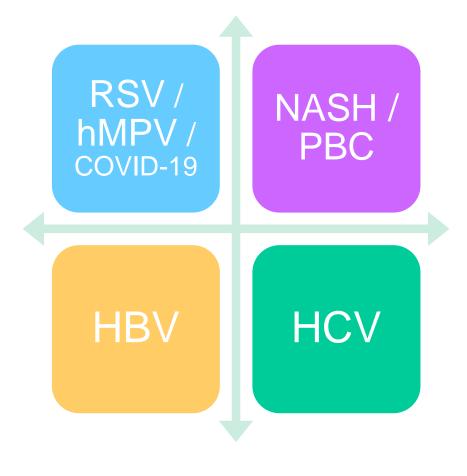
**EDP-514** 

**EDP-297** 

<b>Broad Virology and</b>	Liver	Disease	<b>Pipeline</b>

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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

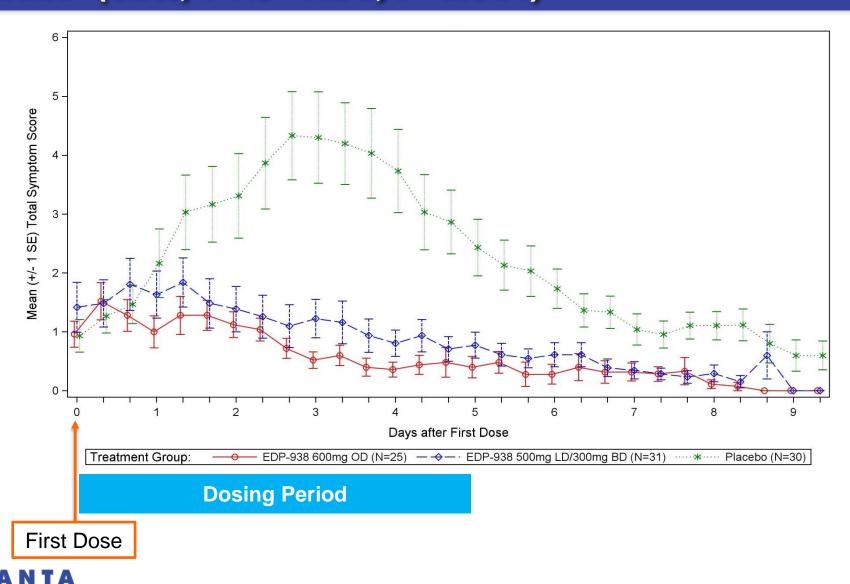


#### **Robust Antiviral Effect**

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



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



### 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<sub>90</sub> 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<sub>trough</sub> concentrations were approximately >20-40x higher than EC<sub>90</sub>
  - 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 1H 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, & immunocompromised individuals
    - 2nd 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



Small hydrophobic protein

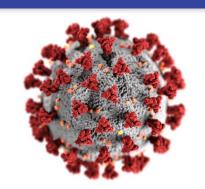
Fusion protein

Glycoprotein Phosphoprotein

Large polymerase

#### SARS-CoV-2 (COVID-19)

- COVID-19 is 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 infected >180K people and caused 7.2K deaths worldwide in 3 months (March 16)



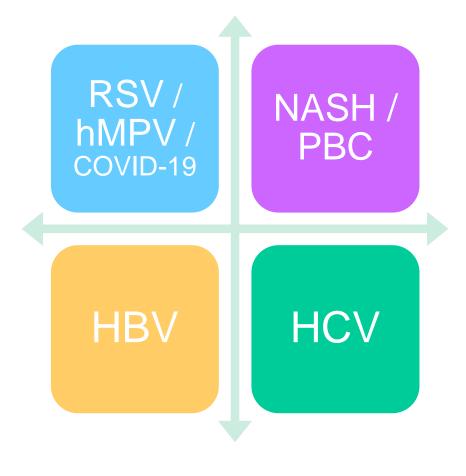
Source: CDC Public Health Image Library

- Has a 30kb single-strand positive RNA genome that encodes 4 structural proteins and 16 nonstructural proteins, including several potential druggable targets
- There are 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



#### **Our Therapeutic Focus**

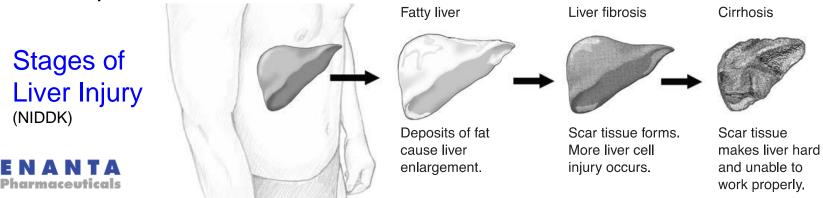
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## Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH)

- 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, but progression to NASH dramatically increases risks of cirrhosis, liver failure, and hepatocellular carcinoma



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#### Enanta's Approach to NASH and PBC-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

Inflammation

- FXR agonist preclinical PoC
  - ameliorate pathologies in NASH and PBC models, including an effect on fibrosis

Bile Acid

Regulation

 Clinical validation of FXR agonist in NASH and PBC with 6-ECDCA (OCA)



#### **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<sup>TM</sup> 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 PBC and for NASH with fibrosis
- Phase 2 studies in NASH and PBC
  - ARGON-1 study in NASH complete
  - INTREPID study in PBC ongoing (data targeted by early 2Q 2020)
  - Design: 12-week dose ranging, randomized, double-blind, placebocontrolled
  - Evaluate safety, tolerability, PK, and efficacy (ALP reduction in PBC and 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 2.5mg 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 1mg and 20.8% for 2.5mg
  - associated with small numeric absolute changes in lipids



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



- Initiate Ph2b NASH study by early 2Q 2020:
  - 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 & 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 <u>and</u> 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 initiating mid-calendar 2020 and data expected in 1H 2021



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

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

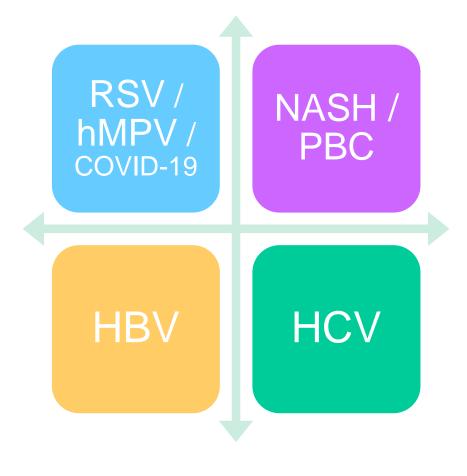
Enanta data except where noted

- 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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#### **HBV Background**

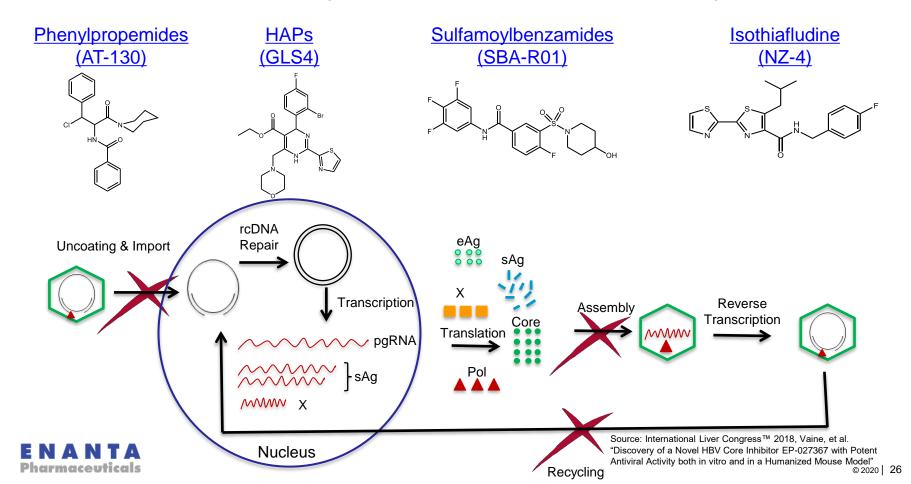
- Potentially life-threatening liver infection caused by the hepatitis B virus
- Current treatments rarely give true cures
  - Interferon gives better results (~10%), but with side effects
  - RT inhibitors very effective at reducing viral load, but offer very low cure rates (1% or lower) and must be taken for life to improve cirrhosis or 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



#### **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

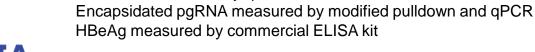


### Core Inhibitor EDP-514 is a Potent Inhibitor of HBV Replication

EDP-514 is active in multiple HBV stable cell lines

	HBV Stable Cell Line EC <sub>50</sub> (nM)			
	HepAD38	HepDE19	HepG2.2.15	
Intracellular Viral DNA	18	27	17	
Encapsidated pgRNA	25	3	5	
HBeAg	20	34	>500*	

<sup>\*</sup> In HepG2.2.15 cells, HBeAg is transcribed off transgene and is not dependent on viral replication



Viral DNA measured by qPCR



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

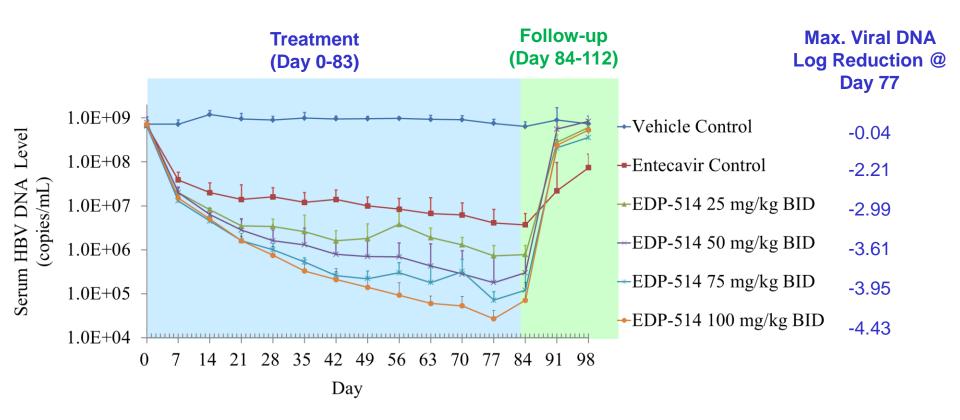
 EDP-514 prevents cccDNA establishment when present at early time points in infection (HBsAg as surrogate marker)

Compound	HBsAg EC <sub>50</sub> (nM)		HBV DNA EC <sub>50</sub> (nM)		
	d0 Addition	d3 Addition	d0 Addition	d3 Addition	
EDP-514	35	>1000	10	6	
Entecavir	>1000	>1000	0.25	0.21	



### 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





#### **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 cells 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



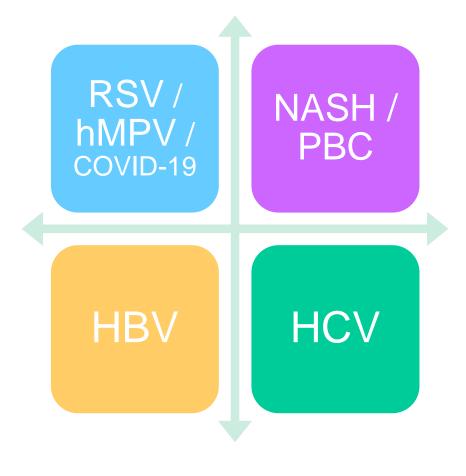
#### **EDP-514 Phase 1 Development**

- 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 2020
  - Part 2 Initiated: Assess safety and antiviral activity in NUCsuppressed patients
- Additional Phase 1b study in viremic HBV patients is expected to initiate in 2Q 2020



#### **Our Therapeutic Focus**

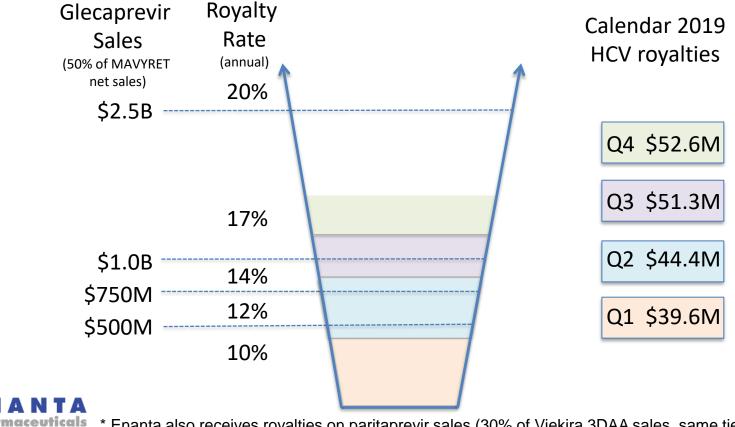
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#### **Glecaprevir- Our Licensed Protease Inhibitor for Hepatitis C Virus**

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



### Financial Highlights

(\$ In millions)	Fiscal Year Ended Sept. 30, 2019	Fiscal 1Q20
Total Revenues	\$205.2	\$52.6
R&D Expenses	\$142.2	\$32.8
G&A Expenses	\$26.2	\$6.9
Net Income	\$46.4	\$13.4
EPS (per diluted share)	\$2.21	\$0.65
<b>Balance Sheet</b>		
Cash, Cash Equivalents and Marketable Securities	\$400.2	\$414.7



#### **Key Catalysts and Funding**

- RSV N-inhibitor EDP-938 and hMPV Inhibitor Leads
  - Goal: Data from RSVP Phase 2b adult outpatient study 1H 2021
  - Initiate additional Phase 2 RSV studies in infants and transplant 4Q 2020
  - Initiate COVID-19 drug discovery
  - Optimize nanomolar hMPV inhibitor leads
- NASH / PBC: FXR Agonists EDP-305 and EDP-297
  - Initiate ARGON-2 Phase 2b in NASH by early 2Q 2020
  - Phase 2 data from INTREPID study for PBC by early 2Q 2020
  - Initiate Phase 1 for EDP-297 (follow-on FXR) in mid-2020
  - Advance non-FXR compounds for NASH
- HBV: Core Inhibitor EDP-514
  - Phase 1 data in healthy volunteers at EASL 2020
  - Initiate Phase 1b in viremic HBV patients in 2Q 2020
  - Data from Phase 1b in nuc-suppressed HBV patients in 1Q 2021
- Funding by double-digit HCV royalties from glecaprevir (MAVYRET®)



