



# Antiviral Therapies

Corporate Presentation  
June 2018

# Forward Looking Statements

---

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the anticipated timing of our drug development programs, including 2018 milestones, and anticipated completion or initiation of studies, IND filings, and opportunities in the hepatitis C and influenza antiviral markets. Forward-looking statements are prefaced by words such as "expect," "plan," "intend," "anticipate," and similar words. Forward-looking statements are based on our current expectations and assumptions regarding our business, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. Our actual results may differ materially from those contemplated by the forward-looking statements for a variety of reasons, including delays in manufacturing created by third parties, the ability of clinical research organizations to recruit patients, and the failure to obtain adequate financing to fund our programs. Also see the risk factors contained in the Prospectus Supplement dated April 30, 2018, and our Form 10-K for the year ended December 31, 2017. We caution you, therefore, against relying on any of these forward-looking statements. They are neither statements of historical fact nor guarantees or assurances of future performance. We do not intend to nor do we undertake any duty to update these forward-looking statements.

# Corporate Overview

---

## Highlights

**Clinical Stage Antiviral Company**

**Wholly Owned Product Portfolio**

**Proprietary Drug Discovery Platform**

## Target Diseases

**Hepatitis**

**Influenza**


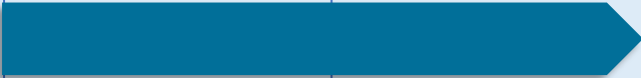

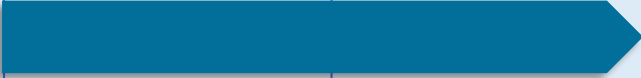

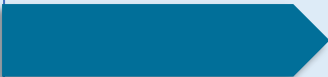
**Norovirus  
Gastroenteritis**

# Investment Highlights

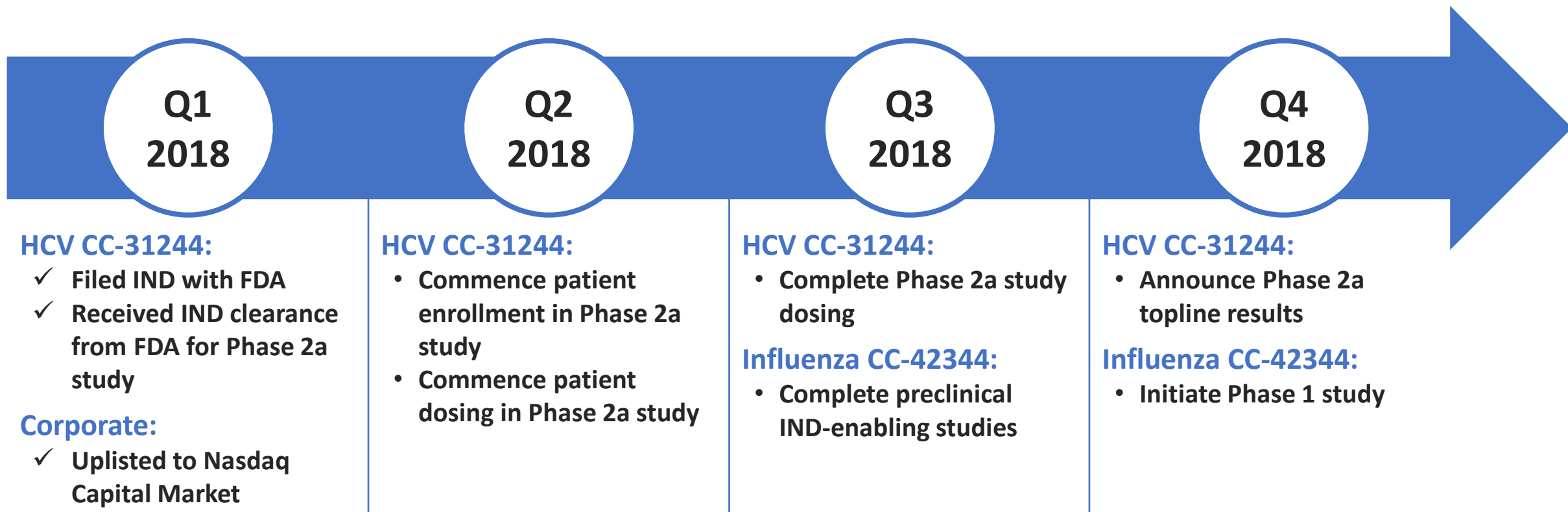
---

- Nobel Prize winning expertise leveraged to design first- and best-in-class antiviral drug candidates addressing well established and growing markets
- Lead program CC-31244 for the treatment of hepatitis C infection entering Phase 2a in Q2 2018
  - Received IND clearance from FDA in Q1 2018
  - Topline data expected before year end
  - Exploring partnering opportunities in strategic territories
- Influenza candidate, CC-42344 is a novel PB2 inhibitor scheduled to enter Phase 1 in Q4 2018 for the treatment of influenza
  - Shown excellent antiviral activity against influenza A strains, including avian pandemic strains and Tamiflu resistant strains
- Company positioned to achieve multiple clinical and regulatory milestones in the near-term
- Recently uplisted to Nasdaq Capital Market

# Robust Development Pipeline

Program		Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Hepatitis C (HCV)	<b>CC-31244</b> (Pan-genotypic NS5B NNI)					
	<b>CC-2850</b> (Pan-genotypic NS5B Nuc)					
	<b>CC-2069</b> (Pan-genotypic NS5A inhibitor)					
Influenza	<b>CC-42344</b> (Influenza A PB2 inhibitor)					
	<b>Influenza A/B inhibitor</b>					
Norovirus	<b>Noro Polymerase Inhibitor</b>					

# Near-Term Milestones Expected to Drive Value



# Seasoned Management Team

---

## Gary Wilcox, Ph.D.

*Vice Chairman and Chief Executive Officer*

Over 35 years of executive biotech leadership experience and played a key role in the development of Cialis

**icòs**<sup>®</sup>

**XOMA**

**Cialis**<sup>®</sup>  
tadalafil

**UCLA**  
University of California, Los Angeles

---

## Sam Lee, Ph.D.

*President*

20 years of anti-infective drug discovery research experience and played a key role in the early development of phosphoinositide 3-kinase (PI3K) delta inhibitors

**icòs**<sup>®</sup>

**Zydelig**

---

## James J. Martin, MBA, CPA

*Chief Financial Officer*

25 years of finance and management experience including providing financial leadership to commercial-stage, publicly traded health science companies

**nims**

**MOTUS**<sup>GI</sup>™



**VBI VACCINES**



# Board of Directors

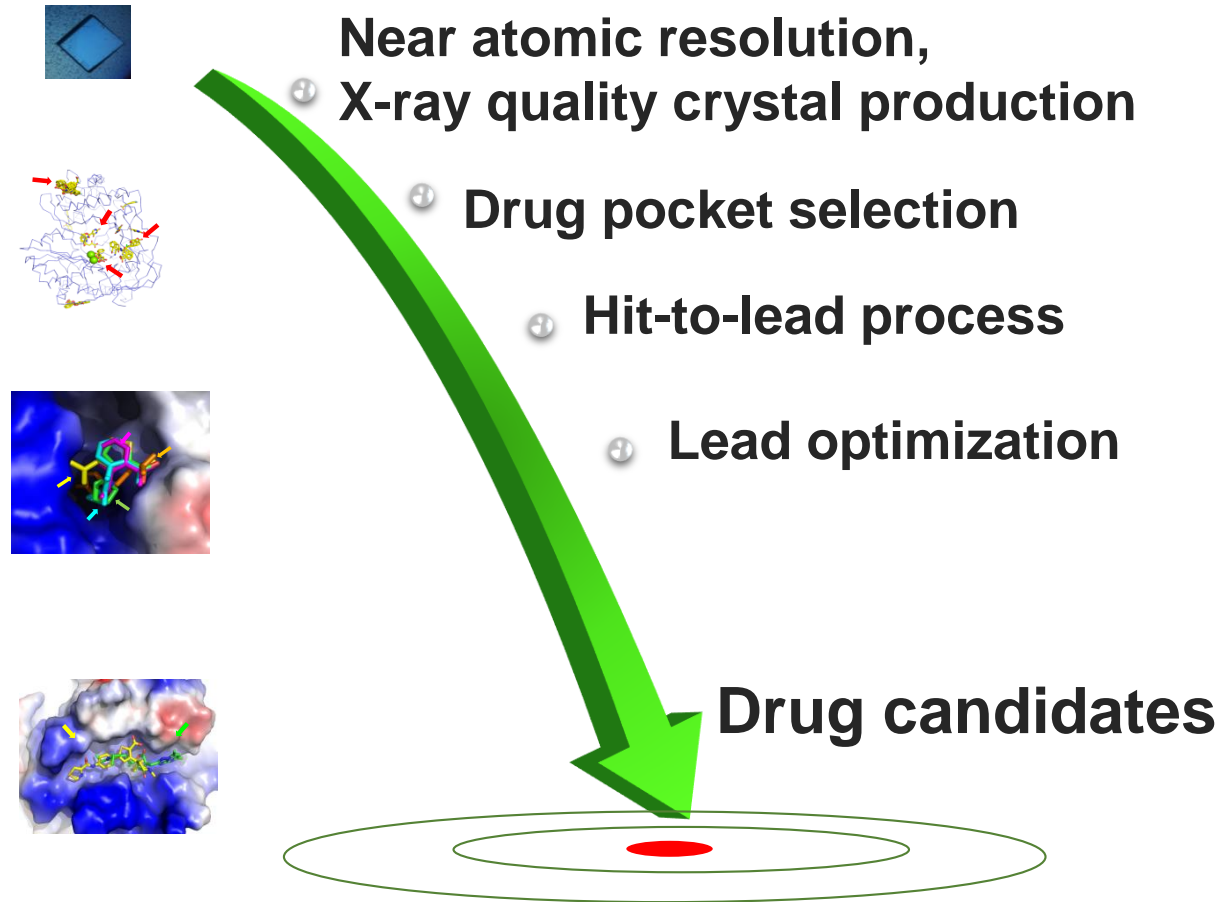
<b>Raymond F. Schinazi, Ph.D.</b> <i>Chairman</i>	Frances Winship Walters Professor of Pediatrics, Director, Laboratory of Biochemical Pharmacology and Director, HIV Cure Scientific Working Group at Emory University
<b>Gary Wilcox, Ph.D.</b> <i>Vice Chairman and Chief Executive Officer</i>	Vice Chairman and Chief Executive Officer, Cocrystal Pharma, Inc.
<b>David S. Block, M.D.</b> <i>Director</i>	President and Chief Executive Officer of Gliknik Inc.
<b>Phillip Frost, M.D.</b> <i>Director</i>	Chairman and CEO of OPKO Health, Inc.
<b>Jane Hsiao, Ph.D.</b> <i>Director</i>	Vice Chairman and Chief Technical Officer of OPKO Health, Inc.
<b>Steve Rubin</b> <i>Director</i>	Executive Vice President-Administration and a director of OPKO Health, Inc.



# Cocrystal Technology

## Nobel Prize Winning Technology

---

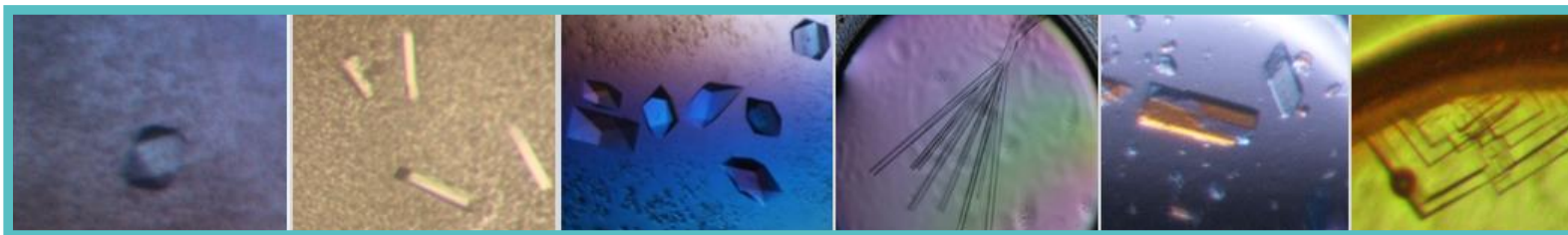


# CC-31244: Broad Spectrum HCV NNI

## Demonstration of Cocrystal's Enabling Technology

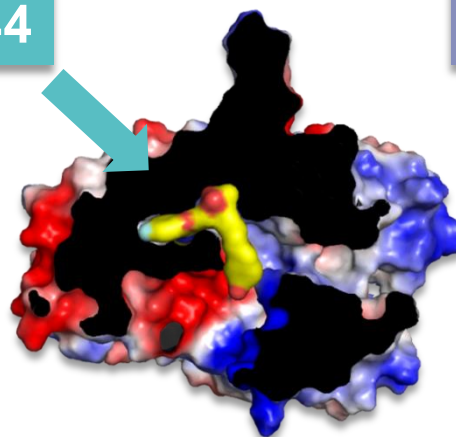
---

HCV GT1 – GT6 NS5B polymerase crystals



CC-31244

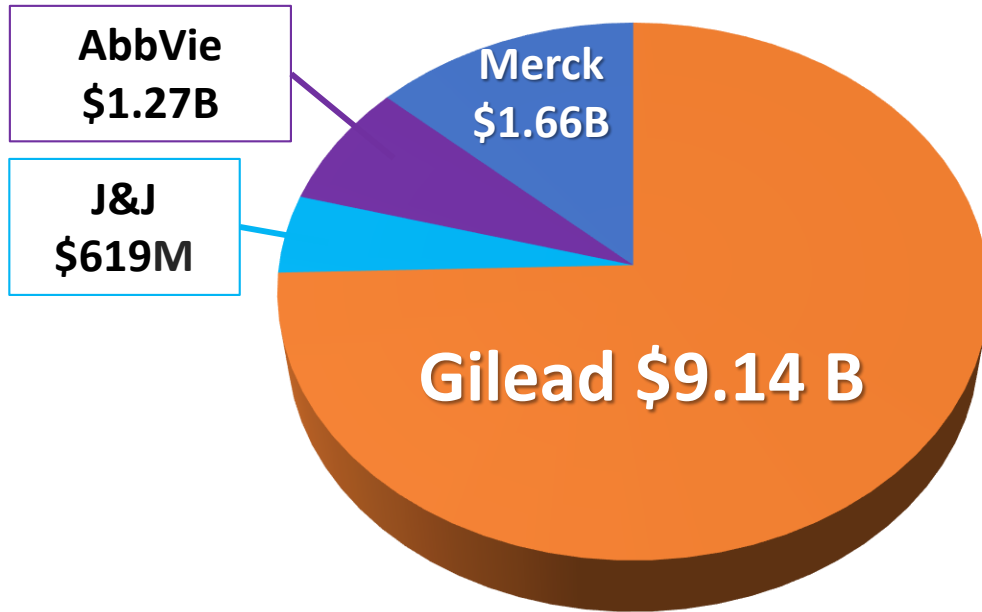
HCV NS5B polymerase



Proven track record for broad spectrum antiviral leads

# Hepatitis C Treatment Market Share

2017 Annual Sales: \$12.69 Billion



■ Gilead (Harvoni, Epclusa, Sovaldi, Vosevi)

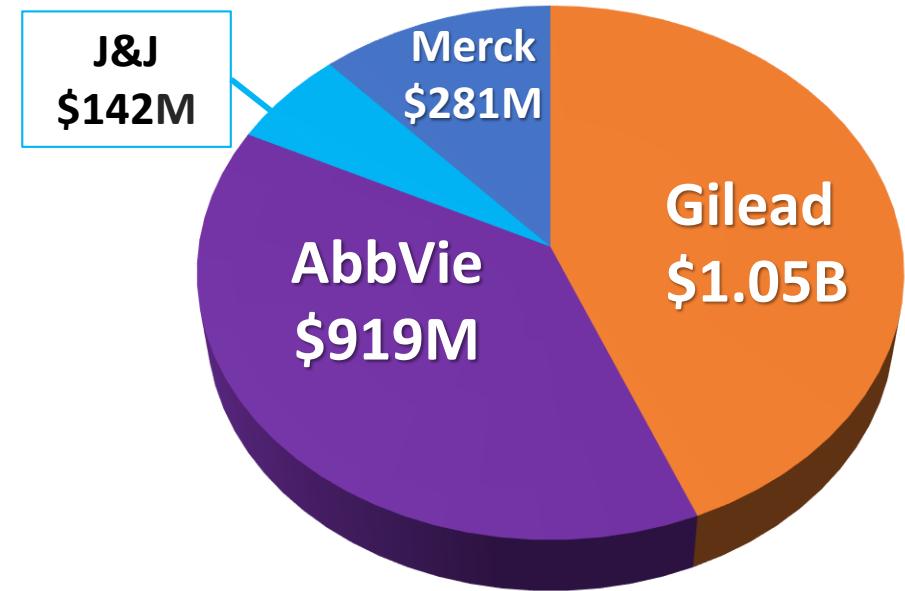
■ J&J (Olysio)

■ AbbVie (Viekira, Mavyret)

■ Merck (Zepatier)

Source: 2017 Form 10-K

Q1 2018 Sales: \$2.39 Billion



Source: 2018 Form 10-Q

# AbbVie's Mavyret Demonstrated a Shorter Treatment: From 12 Weeks To 8 Weeks

Approved broad spectrum HCV combination therapy

Nuc + NS5A inhibitor



**Gilead's EPCLUSA**  
(sofosbuvir 400mg/  
velpatasvir 100 mg)  
**12-week treatment**  
**Approved June 2016**



PI + NS5A inhibitor

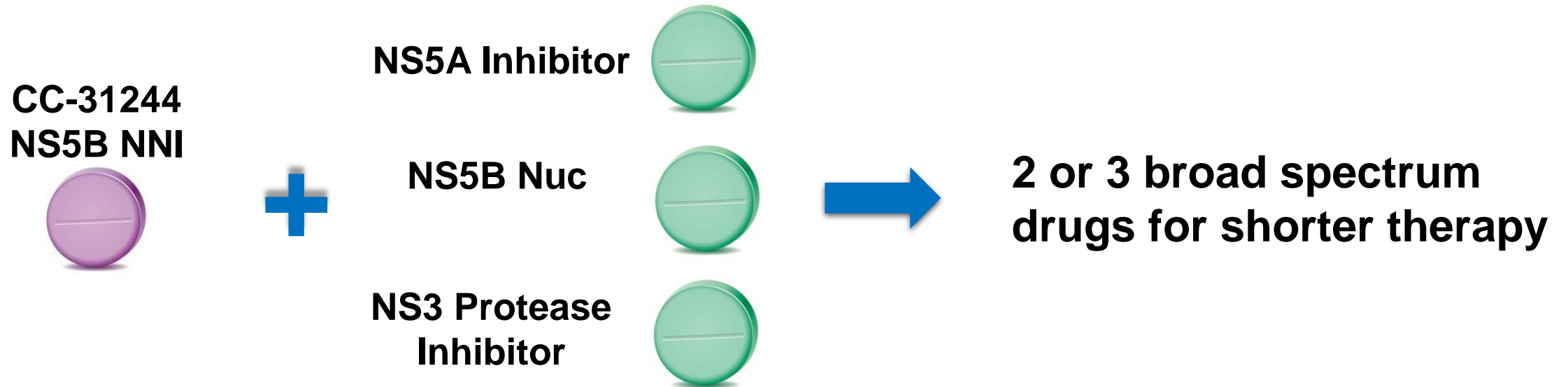


**AbbVie's Mavyret**  
(glecaprevir 100 mg/  
pibrentasvir 40 mg)  
**8-week treatment**  
**Approved August 2017**



# Cocrystal's HCV Strategy: Shorter Combination Therapy

Multiple opportunities in developing shorter combination therapy with approved HCV drugs



# Cocrystal's Next Wave Combination Therapy: CC-31244 with Approved HCV Drugs

---

- Potential best-in-class HCV NNI with a strong profile
  - Broad spectrum, potent NS5B polymerase inhibitor
  - Developed by Cocrystal's proprietary structure-based discovery platform
  - High barrier to drug resistance
  - Effective against known NNI drug resistant variants
  - Liver targeting
- Acceptable safety and efficacy profiles in Phase 1 studies
- Potential for a shorter therapy with existing HCV combination therapy
- Received IND clearance from FDA in Q1 2018
- Phase 2a scheduled to commence Q2 2018

# Phase 1a Study Completed

Single ascending doses  
(complete)



20 mg	50 mg	100 mg	200 mg*	400 mg
N = 40; 30 CC-31244, 10 placebo; * food effect assessed				

Multiple ascending doses  
(complete)



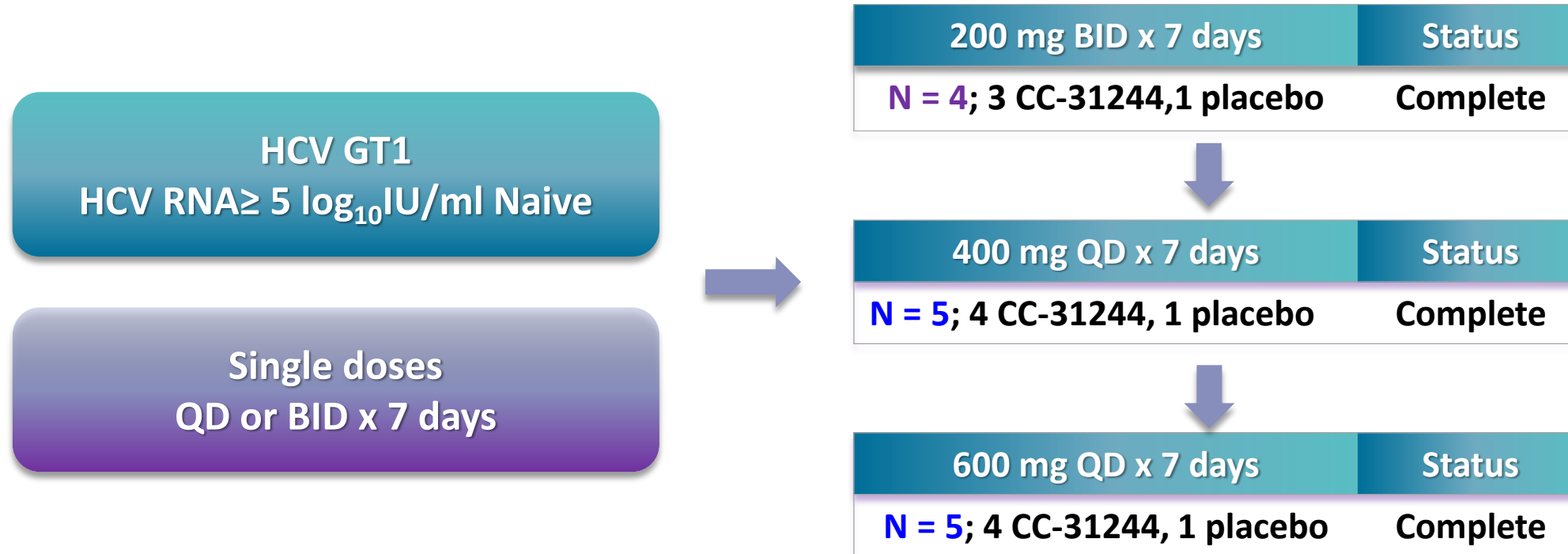
200 mg BID	400 mg QD
N = 16; 12 CC-31244, 4 placebo x 7 days	

## Endpoints

- Safety: adverse events (AEs) and laboratory abnormalities



# Phase 1b Study Completed

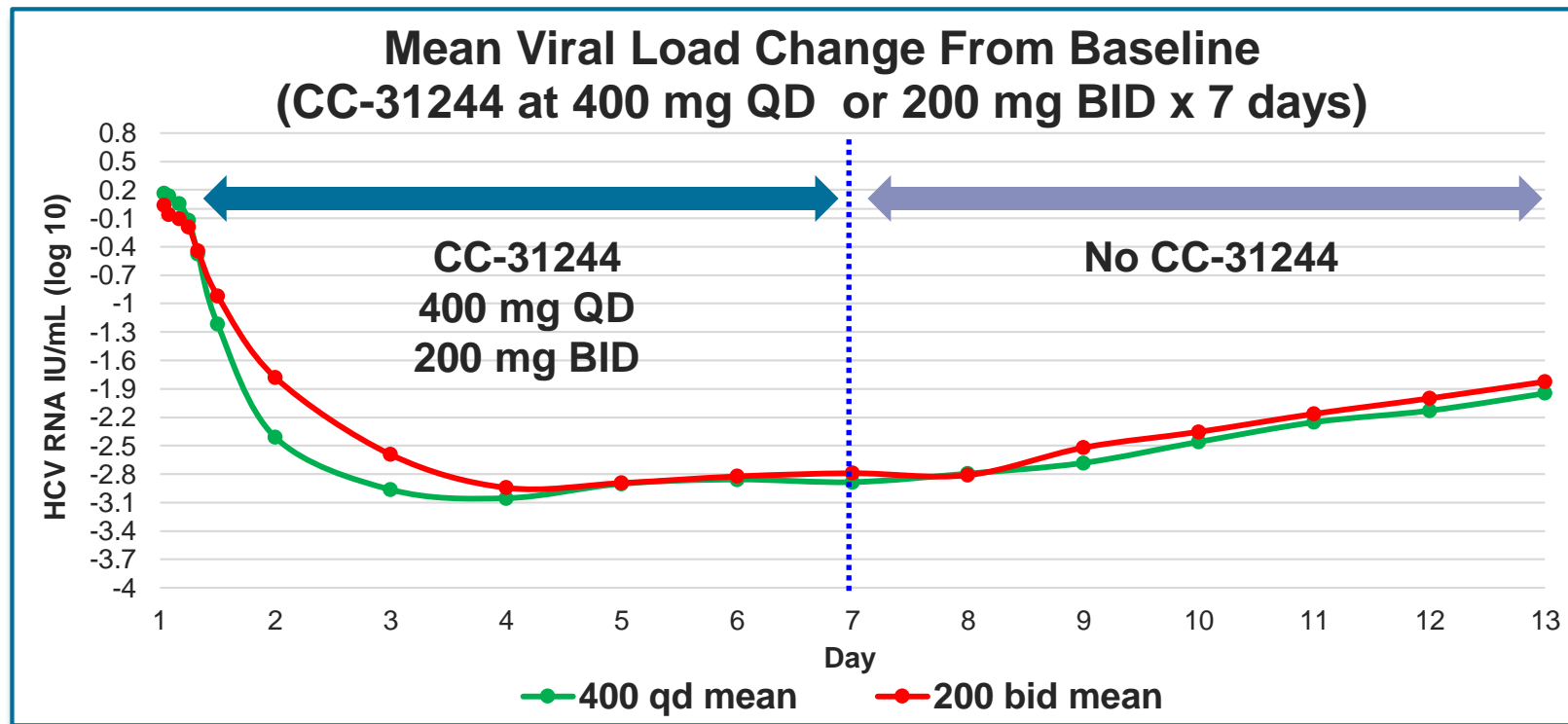


## Endpoints

- Efficacy: changes in HCV RNA viral load
- Safety: adverse events (AEs) and laboratory abnormalities

# Superior Viral Load Reduction

- HCV RNA viral load decline of 3 logs by 48 hours
- After the NNI treatment, the viral load levels were slowly increased



# Best-in-Class Potential of Any NNI

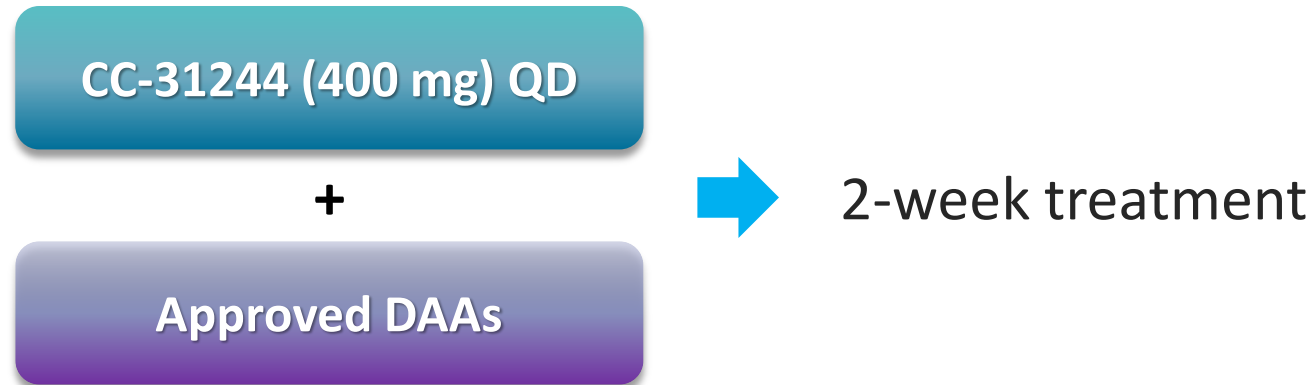
Drug	Genotype	Dose (mg)	Treatment Duration (days)	Viral load reduction (Log <sub>10</sub> IU/ml)
<b>CC-31244</b> ←	<b>Genotype 1-6</b> ←	<b>400</b> ←	<b>7 (QD)</b>	<b>-3.0</b>
<b>ABT-333*</b> (Dasabuvir)	Genotype 1	400	3 (BID)	-1.08
		800	3 (BID)	-0.95
<b>GS-9190</b> (Tegobuvir)	Genotype 1	40	3 (BID)	-1.0
		120	3 (BID)	-1.5

(\* : approved DAA)

# CC-31244 Phase 2a Study Design

---

- An open-label, Phase 2a study evaluating the safety, tolerability and preliminary efficacy of CC-31244 with approved HCV DAAs



- Endpoints
  - Efficacy: changes in HCV RNA viral load
  - Safety: adverse events (AEs) and laboratory abnormalities
- Expect to commence patient enrollment in Q2 2018

# HCV Summary and Conclusion

---

- Showed an acceptable safety profile in both healthy volunteers and GT1 patients up to 400 mg x 7 days
- No serious adverse events or discontinuations due to adverse events
- Demonstrated HCV RNA viral load reduction of ~ 3 logs by 48 hours
- Demonstrated a sustained post-treatment antiviral effect after the 7-day treatment
- Potential to be an important DAA in shorter HCV combination regimens

# New Antivirals For Influenza

---



- High mortality rate:
  - 1918 Spanish Flu, 20-100 million deaths
  - 1957 Asian Flu, 1-1.5 million deaths
  - 1968 Hong Kong Flu, 0.75-1 million deaths
  - 2009 Swine Flu, 0.15-0.5 million deaths
- Emerging influenza viruses
  - Highly virulent avian influenza viruses
  - Tamiflu-resistant influenza viruses
- Delayed vaccine development

# Great Opportunity in Influenza Antiviral Market

---

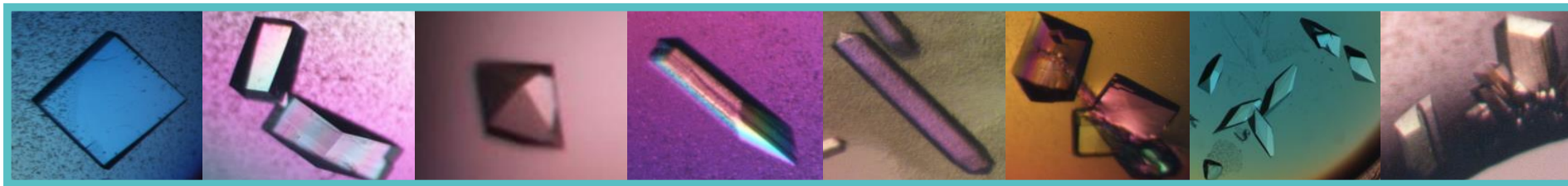
- Seasonal and pandemic infection
  - 3-5 million cases of severe illness per year
  - 250,000 – 500,000 deaths worldwide\*
- Approved influenza therapies have major limitation
- Multiple product routes of delivery, inhalation, oral, and intravenous (IV)
- Stock piling and prophylactic market in addition to standard of care

\*Reference: <https://www.cdc.gov/flu/about/disease/burden>

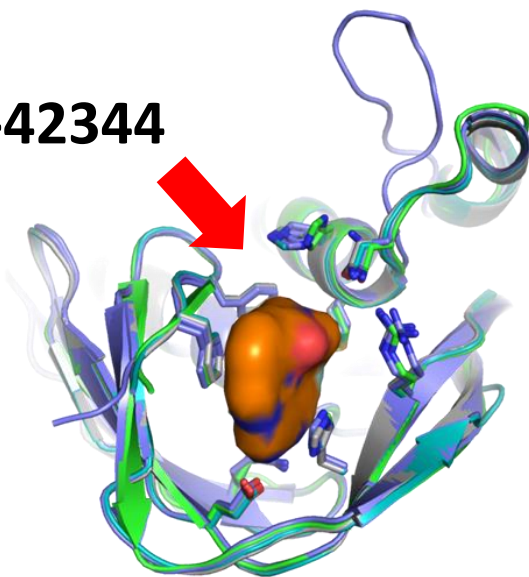


# Influenza A Preclinical Lead CC-42344

## Influenza Crystals



**CC-42344**



- Potent and favorable PK profiles
- Excellent anti-influenza activity against pandemic, seasonal, and Tamiflu resistant influenza strains
- Binds a highly conserved site
- Novel mechanism of action
- IND filing scheduled in 2018

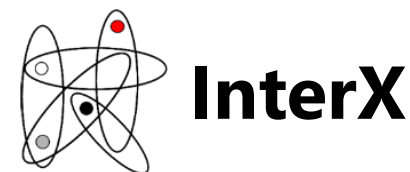
# Early Stage Programs

---

- Influenza A/B Inhibitor Program
  - Influenza cocrystals developed
  - Structure-based lead discovery ongoing
  - IND filing in 2019
- Noro Polymerase Inhibitor
  - Structure-based NNI discovery ongoing
  - Multiple polymerase crystals developed
  - Noro nucleoside lead discovery ongoing
  - IND filing in 2019

# Cocrystal-HitGen-InterX Collaboration: Aimed at Rapid Lead Discovery Process

---



- Combines synergistic drug discovery platforms developed by Cocrystal-HitGen-InterX
- Break through hit-to-lead process
- High quality novel leads will be developed

# Selected Value Indicators Suggest Potential Significant Upside

Company Name	Ticker	Market Cap (M)*	Overview	Status
Arrowhead Pharmaceuticals	ARWR	\$938	Develops medicines to treat intractable diseases by silencing the genes that cause them	2 Phase 1 6 Preclinical
Arbutus BioPharma	ABUS	\$323	Biopharmaceutical company developing a cure for patients suffering from chronic hepatitis B infection	1 Phase 2 2 Preclinical 3 Discovery
Chimerix	CMRX	\$218	Developing novel antivirals for the growing population of immunocompromised patients,	1 Phase 3 2 Phase 2 1 Phase 1
Sinovac Biotech	SVA	\$445	Biopharmaceutical company that develops vaccines that protect against human infectious diseases	1 NDA post Phase 3 preliminary data 1 IND approval 2 IND filed
Spring Bank Pharmaceuticals	SBPH	\$178	Discovery and development of a novel class of therapeutics using a proprietary small molecule nucleic acid hybrid, or SMNH	2 Phase 2 3 Preclinical

\*As of 5/31/2018

# Financial Snapshot – Nasdaq: COCP

---

**\$67.3MM**

Market cap\*

**29.9MM**

Common shares  
outstanding

**60K**

Average daily  
volume\*\*

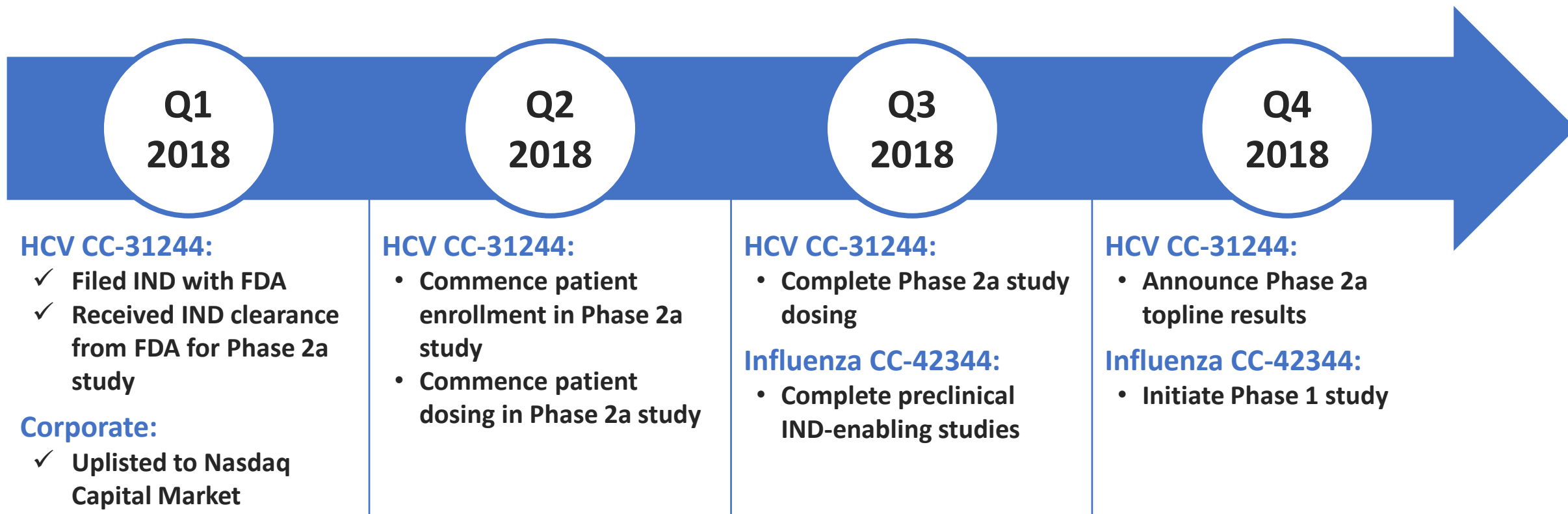
\* Based on May 31, 2018 closing price of \$2.25 per share.

\*\* Based on May 31, 2018 Yahoo Finance.

# COCP Capitalization Table

Capitalization Table (As of May 31, 2018)	# of Shares	WAEP	\$ Value	% of Fully Diluted
Common Shares Outstanding (Directors & Officers)	15,219,800			49.75%
Common Shares Outstanding (Other)	14,703,276			48.06%
Warrants	243,375	\$10.28	\$2,501,895	0.80%
Stock Options	425,637	\$12.44	\$5,294,924	1.39%
<b>Fully Diluted Shares Outstanding</b>	<b>30,592,088</b>			<b>100%</b>

# Near-Term Milestones Expected to Drive Value





# Thank You!



NASDAQ: COCP

[www.cocrystalpharma.com](http://www.cocrystalpharma.com)



# Appendix

# Scientific Advisors

Roger Kornberg, Ph.D. <i>Chief Scientist, Chairman of Scientific Advisory Board</i>	Professor of Structural Biology at Stanford University School of Medicine. Nobel Laureate in Chemistry, Member of the National Academy of Sciences, and the American Academy of Arts and Sciences
Michael Levitt, Ph.D.	Stanford University School of Medicine. Professor, Department of Structural Biology. Nobel Laureate in Chemistry, Member of the National Academy Sciences, and fellow of the Royal Society, London
Baek Kim, Ph.D.	Director of Center for Drug Discovery, Professor of Pediatrics, Department of Pediatrics, Emory School of Medicine. Clinical and Translational Science and HIV/HSV Pathogenesis
Bob Lehman, Ph.D.	Stanford University School of Medicine. Professor, Department of Biochemistry. Member of the National Academy Sciences
Gary Schoolnik, M.D.	Stanford University School of Medicine. Professor & Chief, Division of Geographic Medicine & Infectious Diseases; Professor, Microbiology & Immunology
Roland Strong, Ph.D.	Fred Hutchinson Cancer Research Center. Professor, Department of Structural Biology
Christophe Verlinde, Ph.D.	University of Washington. Associate Professor, Department of Structural Biology

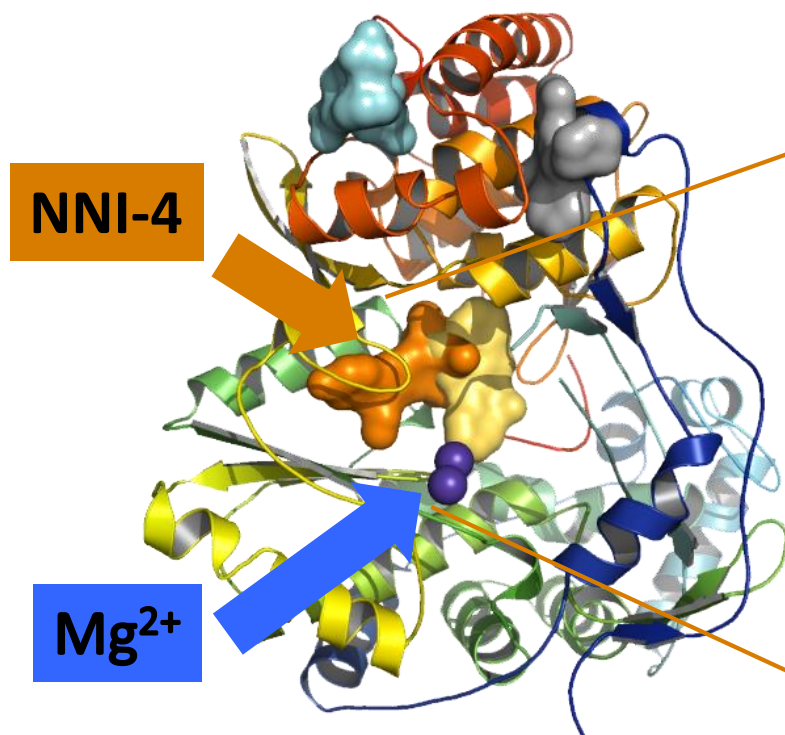
# Cocrystal Patent Portfolio

---

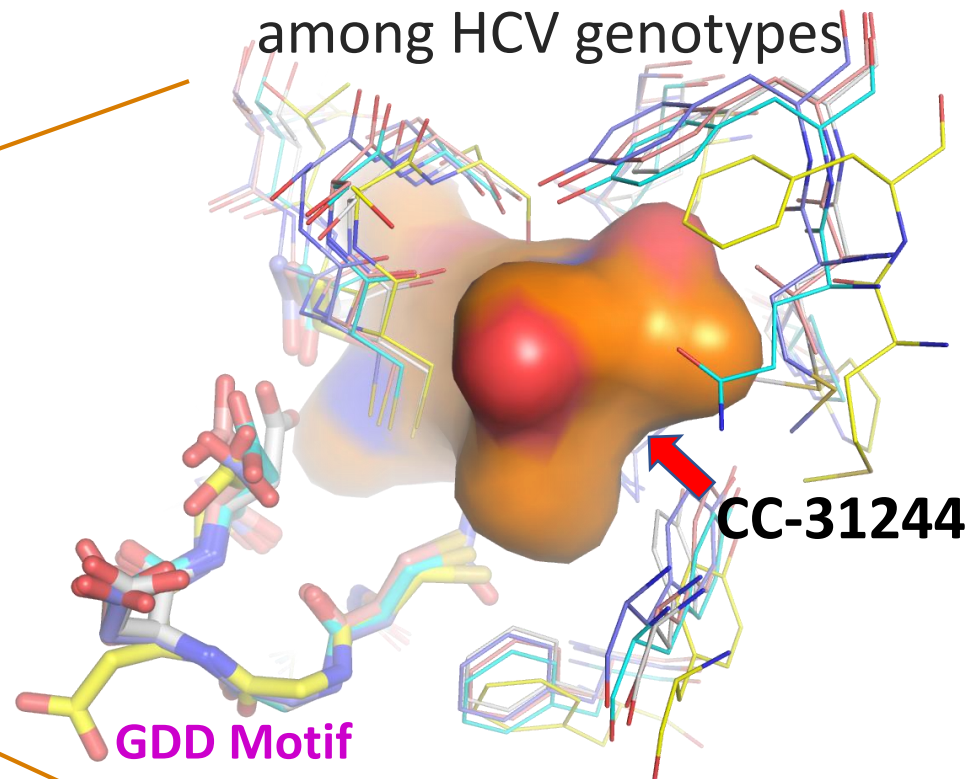
- HCV: 15 patents including three PCT applications
- Influenza: 2 patent applications filed
- Noro: patent application(s) will be filed in 2018

# CC-31244 Binds To a Highly Conserved Drug Binding Site (NNI-4) of NS5B Polymerase

(A) HCV NS5B polymerase



(B) Highly conserved NNI-4 site among HCV genotypes



# CC-31244: Pan-genotypic NS5B NNI

- **CC-31244 HCV replicon EC<sub>50</sub> fold change, <6 fold**

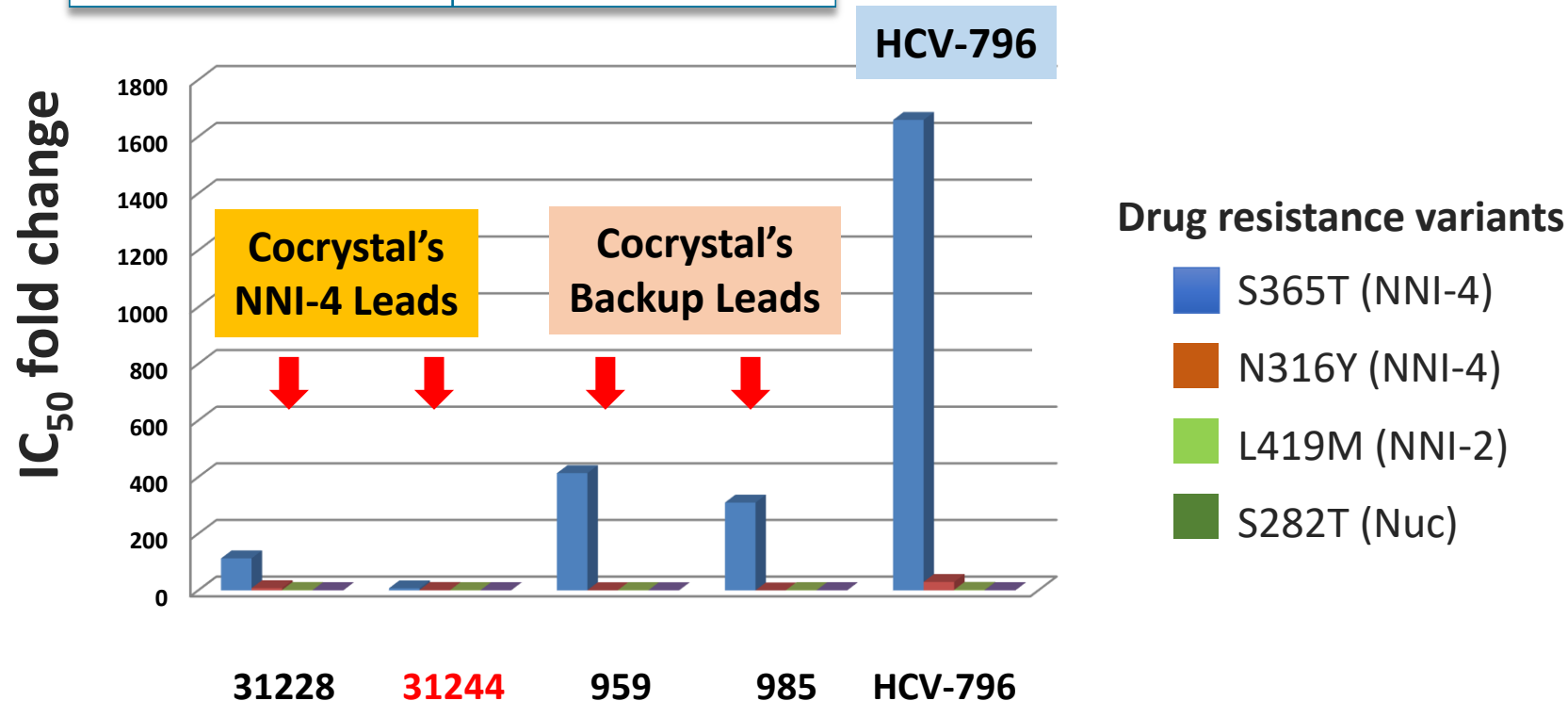
HCV replicon/chimeric replicon EC<sub>50</sub> results

Genotype	CDI-31244 EC <sub>50</sub> , mM	EC <sub>50</sub> Fold change	Sofosbuvir EC <sub>50</sub> , mM	EC <sub>50</sub> fold change
1b	0.005	1.0	0.042	1.0
1a	0.009	1.8	0.034	0.8
2b	0.026	5.2	0.028	0.66
3a	0.011	2.2	0.14	3.2
4a	0.021	4.2	0.047	1.1
5a	0.002	0.4	0.075	1.7



# CC-31244 Exhibits Excellent Activity Against Common NNI and Nuc Drug Resistant Variants

NNI	IC <sub>50</sub> fold change
CC-31244	<5
HCV-796	>1,500

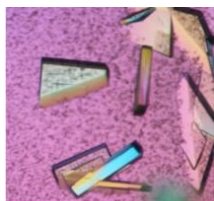


# GT1b NS5B C445F: The Major Drug Resistance Variant of CC-31244

- HCV GT1b replicons containing NS5B variants identified by CC-31244 resistant colony selection

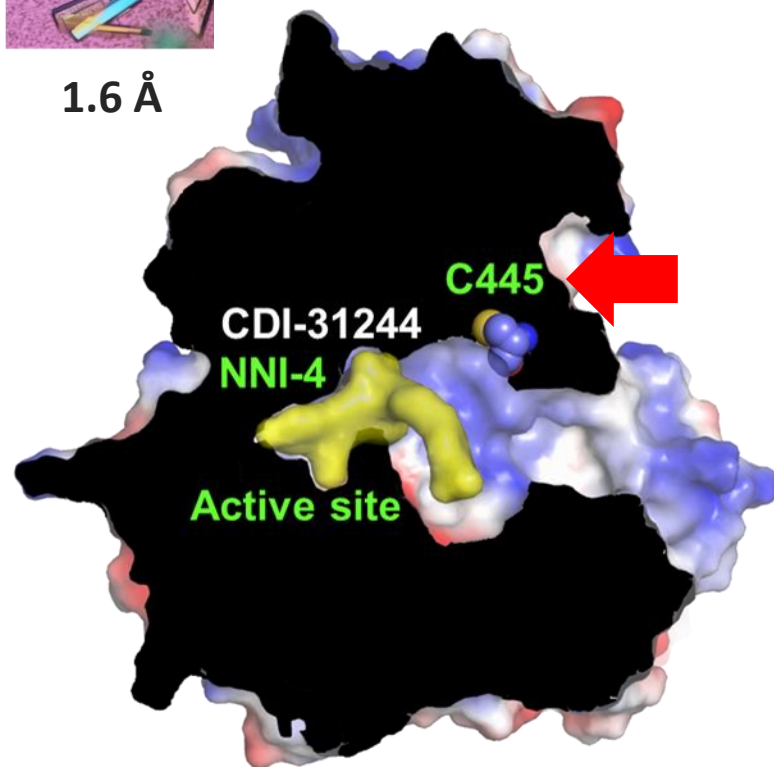
HCV replicon	GT1b C445F/S549G EC <sub>50</sub> μM	GT1b EC <sub>50</sub> μM	EC <sub>50</sub> fold change
CC-31244	0.08	0.005	16 ←
Purified NS5B polymerase	GT1b C445F IC <sub>50</sub> μM	GT1b IC <sub>50</sub> μM	IC <sub>50</sub> fold change
CC-31244	0.23	0.24	0.94 ←

# CC-31244 Binding Mode: GT1b Drug Resistant NS5B C445F



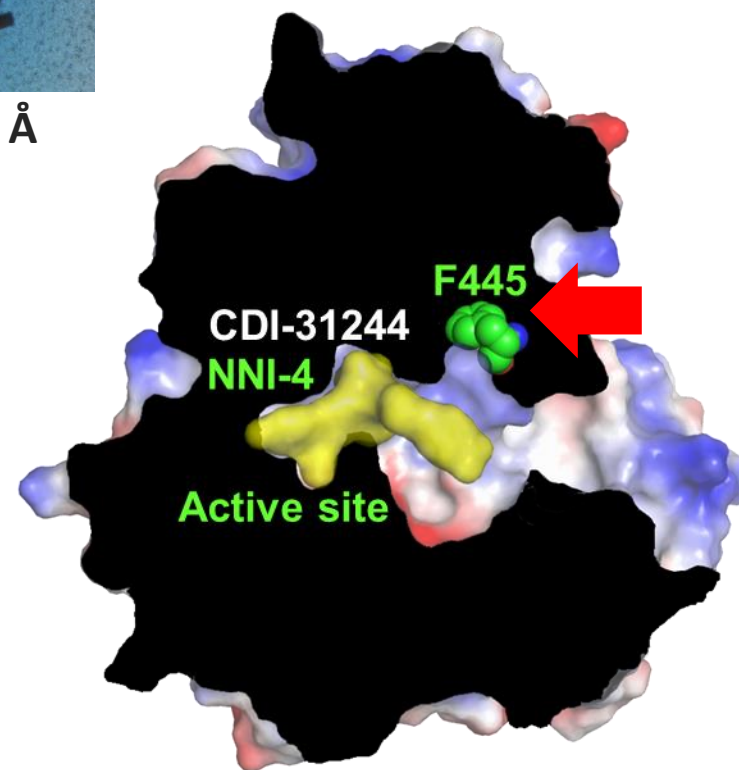
1.6 Å

(A) GT1b wild type



1.7 Å

(B) GT1b C445F



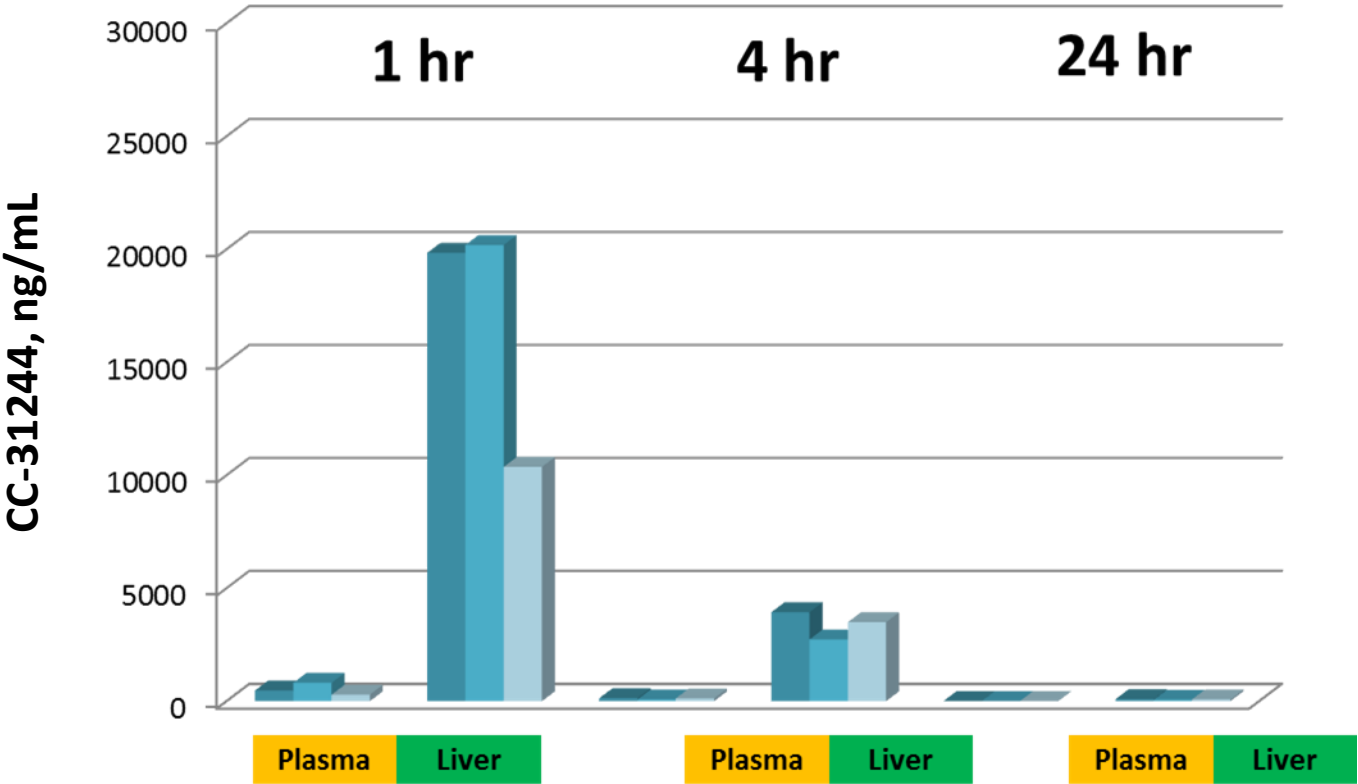
# CC-31244 Exhibits Excellent Liver Targeting

## Rat liver study

Avg: 27  $\mu$ M  
(x5,400 EC50)

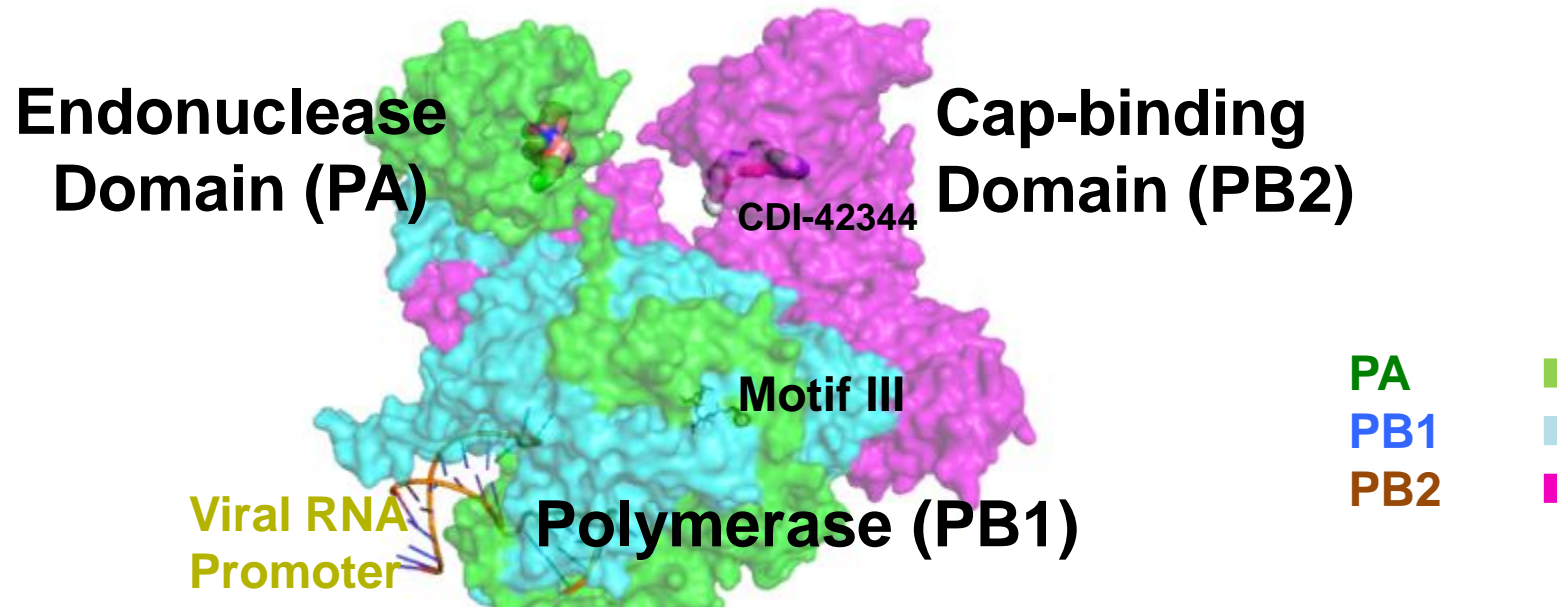
Avg: 5.44  $\mu$ M  
(x1,088 EC50)

Avg: 0.124  $\mu$ M  
( x24.8 EC50)



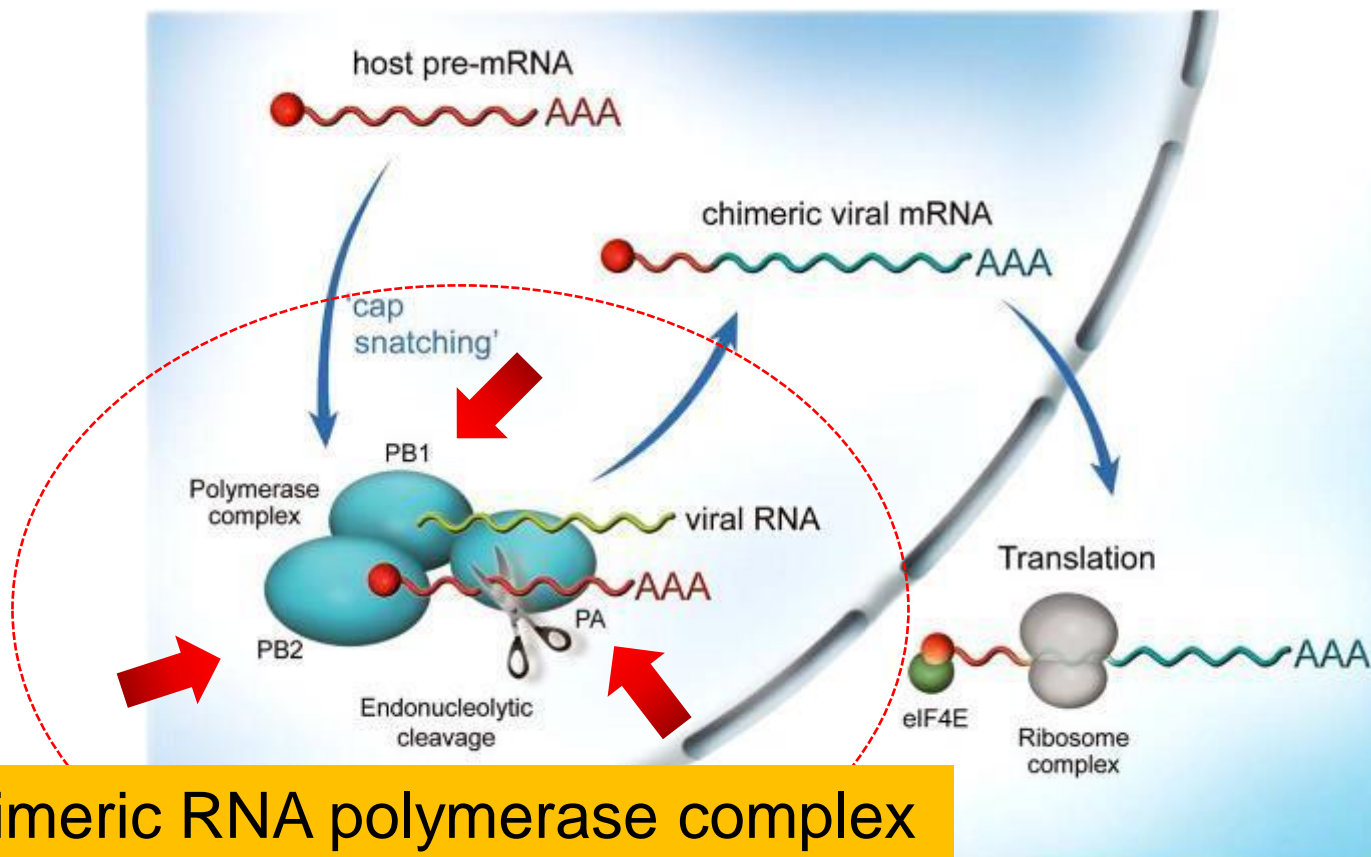
# Cocrystal Influenza Program

- Influenza A PB2 lead, CC-42344: IND filing scheduled in 2018
- Influenza A/B PA: Discovery stage



# Polymerase Complex (PB2:PA:pb1) Is Essential For Influenza Viral Replication

- Polymerase: cap binding (PB2) + endonuclease (PA) + polymerase (PB1)



# CC-42344 Met Preclinical Lead Selection Criteria

Properties	Selection criteria
<b>Pharmacological properties</b>	<ul style="list-style-type: none"><li><input type="checkbox"/> Good antiviral activity (EC50, single digit nanomolar)</li><li><input type="checkbox"/> High-affinity binding to a highly conserved drug binding site</li><li><input type="checkbox"/> Broad spectrum against seasonal and pandemic influenza strains</li><li><input type="checkbox"/> Excellent antiviral activity against Tamiflu resistant influenza strains</li><li><input type="checkbox"/> Selective</li></ul>
<b>Pharmacokinetics</b>	<ul style="list-style-type: none"><li><input type="checkbox"/> Favorable PK properties</li><li><input type="checkbox"/> Adequate half-time and biodistribution</li><li><input type="checkbox"/> Potential for inhalation, oral, and IV administration</li></ul>
<b>Chemical properties</b>	<ul style="list-style-type: none"><li><input type="checkbox"/> Stable molecule</li><li><input type="checkbox"/> Suitable for API scale up and manufacturing</li></ul>
<b>Safety and toxicity</b>	<ul style="list-style-type: none"><li><input type="checkbox"/> Excellent profile for ADMET</li><li><input type="checkbox"/> Absence of obvious cytotoxicity and cardiac toxicity</li><li><input type="checkbox"/> Absence of obvious toxicity in animal studies</li></ul>


# Approved Influenza Antivirals

Antiviral	Developer	MOA/Dosing
<b>Oseltamivir</b> (Tamiflu)	Gilead/ Genentech	Oral neuraminidase Inhibitor/75 mg bid for five days
<b>Zanamivir</b> (Relenza)	Biota/ GSK	Inhaled neuraminidase inhibitor/ 5 mg inhalation bid for five days
<b>Peramivir</b> (Rapivab)	Biocryst/ Shionogi	A single-dose intravenous neuraminidase inhibitor/600 mg IV
<b>Favipiravir</b> (Avigan, T-705) (Approved in Japan)	Toyama	Nuc, polymerase inhibitor/1,200 mg bid, followed by 600 mg bid for five days
<b>Baloxavir marboxil</b> (Xofluza, <b>S-033188</b> ) (Approved in Japan)	Shionogi/ Roche	Oral PA (endonuclease) inhibitor/ 80 mg orally once



# Influenza Clinical Landscape: CC-42344 Can Be Developed For Inhalation, IV, and Oral

- Key players: J&J (PB2 and PA) AND Shionogi/Roche (PA)
- Other companies: Merck, Gilead, and Novartis

Antiviral	Developer	Route	Stage	MOA/Indication
Pimodivir (VX-787 or JNJ-636233872)	J&J	Oral (600 mg/ twice-daily)	Phase 2	PB2 inhibitor/ Influenza A
S-033188	Shionogi/ Roche	Oral (80 mg/ Once-daily)	Approved in Japan	PA inhibitor/ Influenza A&B
AL-794	J&J	Oral (50, 150 mg/ twice-daily)	Phase 1	PA inhibitor/ Influenza A&B
 CC-42344	COCPharm	Inhalation, Intravenous, Oral	Preclinical	PB2 inhibitor/ Influenza A

# In Vitro Potency Comparison: Cocrystal's Leads vs VX-787

Influenza strain	J&J	Cocrystal Preclinical Lead	Cocrystal's backup PB2 inhibitors				
	VX-787 EC50 nM	42344 EC50 nM	42343 EC50 nM	42487 EC50 nM	42500 EC50 nM	42530 EC50 nM	42534 EC50 nM
<b>Pandemic H1N1</b> Influenza A/CA/07/2009	2.4	0.12	5	0.9	2.7	ND	ND
H1N1 Influenza PR/8/34	1	1	1.2	1.2	2	0.5	5
<b>Pandemic H5N1</b> Influenza A/VN/1193/ 2004	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2	<3.2

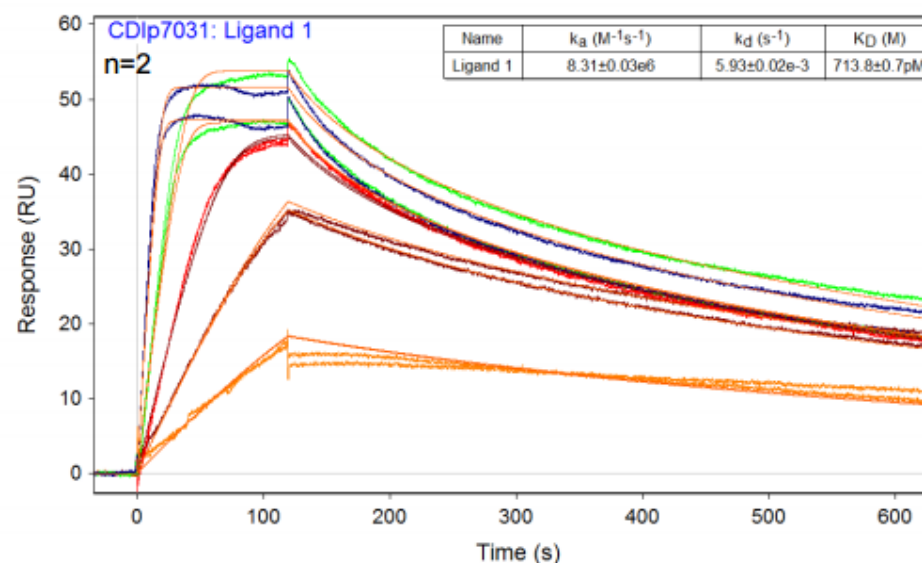
# CC-42344 Shows Broad Spectrum Antiviral Activity Against Pandemic Influenza Strains

Influenza Serotype	Strain	CC-42344 EC50, nM	VX-787 EC50, nM
H5N1	Duck/MN/1524/81	8.6	0.07
H5N1- Amantadine resistant	Duck/MN/1524/81	<3.2	<3.2
H5N1	Gull/PA/4175/83	4.5	0.17
H5N1	Hong Kong/213/2003	<3.2	<3.2
H5N1	Thailand/16/2004	<3.2	<3.2
H5N1	A/VN/1194/2004	1.3	6.6
H7N7	Netherlands/219/2013	5.6	<3.2
H7N9	Shanghai/2/2013	5.4	<3.2
H7N9	Anhui/1/2013	<3.2	<3.2
H7N9	Taiwan/1/2013	<3.2	<3.2

# CC-42344 Exhibits Greater Affinity Than VX-787

- Highly sensitive biophysical method (SPR technology) was applied to determine the affinity ( $K_d$ ) of CC-42344 to the PB2 protein

Compound ID	$K_D$
VX-787	37.4 nM
CC-42344	9.90 nM



Sample H1N1 Sensorgram data