CRYSTAL PHARMA, INC.

Discovery of Potent, Highly Selective, Broad Spectrum Antivirals

Fred Hutch/Merck
Infectious Disease Summit
May 10, 2018

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Forward Looking Statements

This presentation contains forward-looking statements, the anticipated timing of our drug development programs, including near-term milestones, and anticipated completion or initiation of studies, IND filings, and opportunities in the hepatitis C and influenza antiviral markets. Forward-looking statements also 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 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

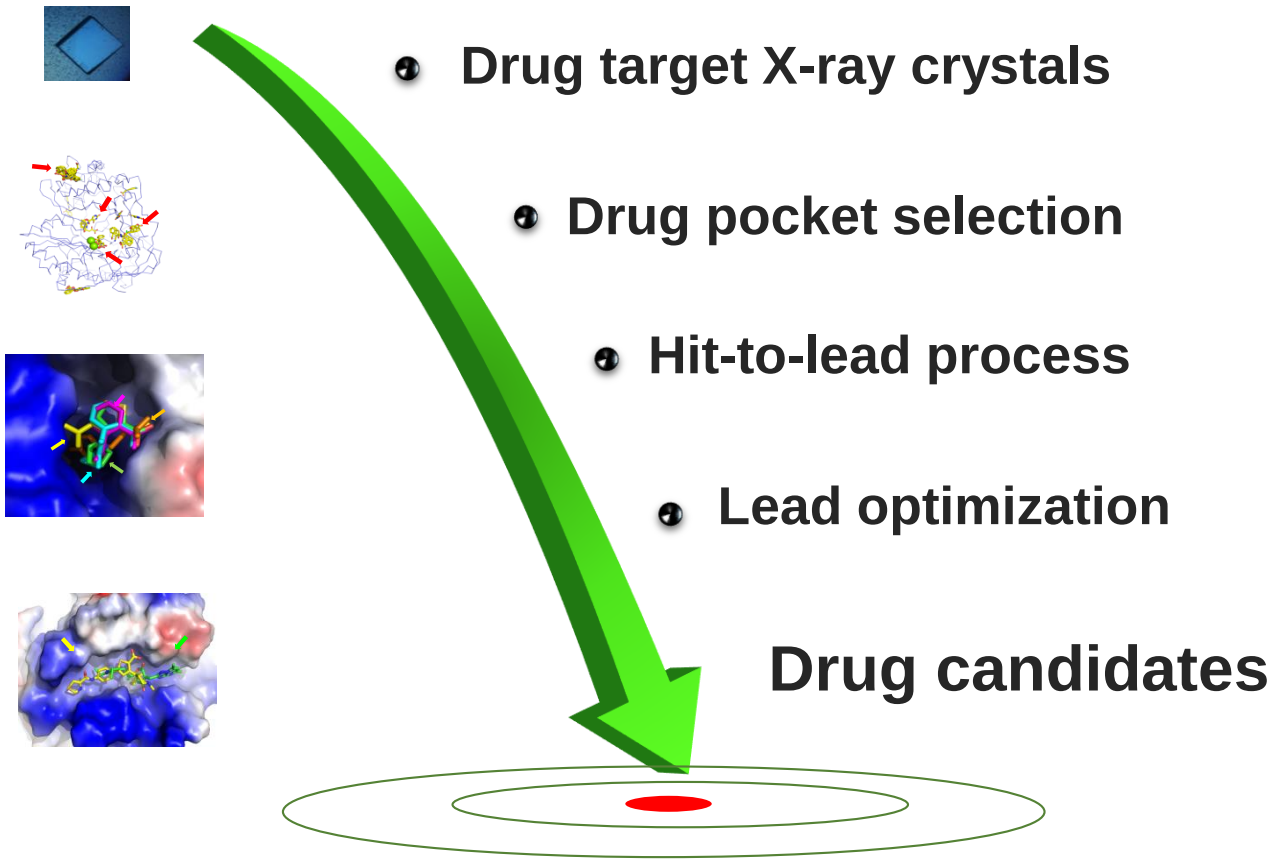
Opportunities

Significant unmet medical needs across a variety of viral infections

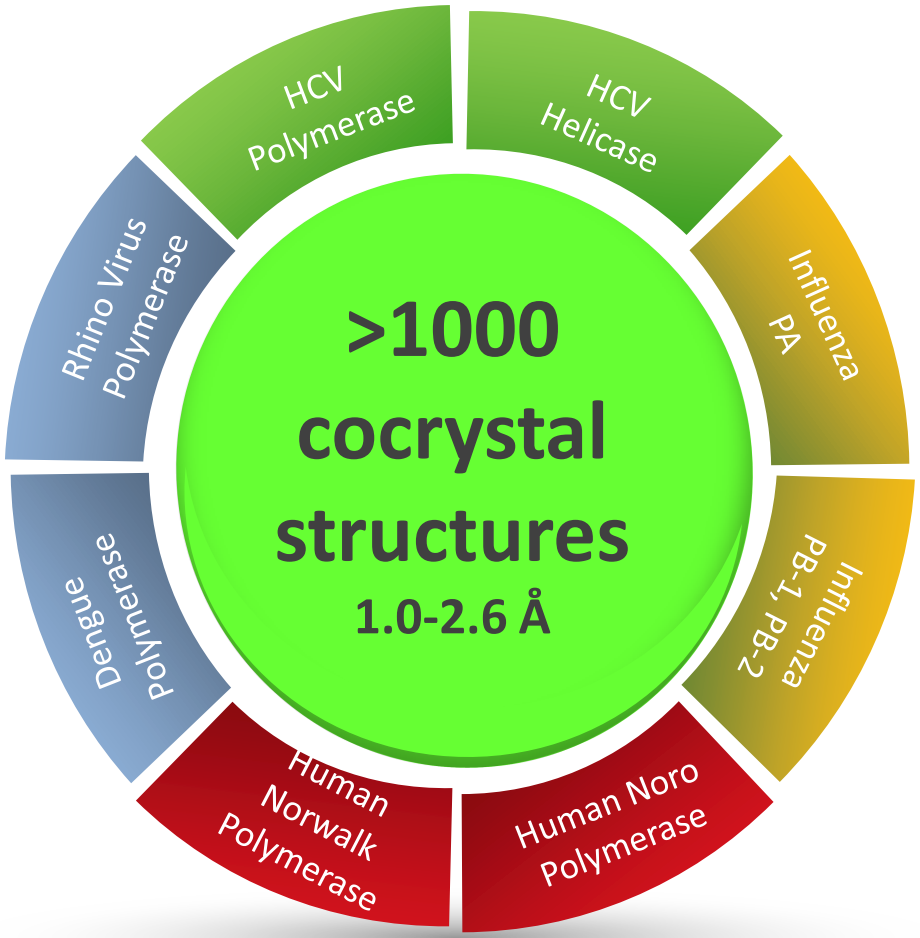
Influenza	Hepatitis	Norovirus
Seasonal and pandemic	Leading causes of liver failure and liver cancer	• Chronic (potentially orphan indication) • Acute gastroenteritis
3 - 5 million infections/year	Chronic infections > 71 million HCV	> 250 million acute cases/year
Estimated economic impact of seasonal flu in US: $50B to $150B	Opportunity for shorter combination therapy	No treatment available Economic cost in the US alone > $5 Billion

Reference: https://www.cdc.gov/flu, www.cdc.gov/hepatitis, www.cdc.gov/norovirus

Cocrystal Drug Discovery Platform Technology For Developing Broad Spectrum Antiviral Therapeutics



Technology Platform Focuses on Well Validated Drug Targets: Viral Replication Enzymes

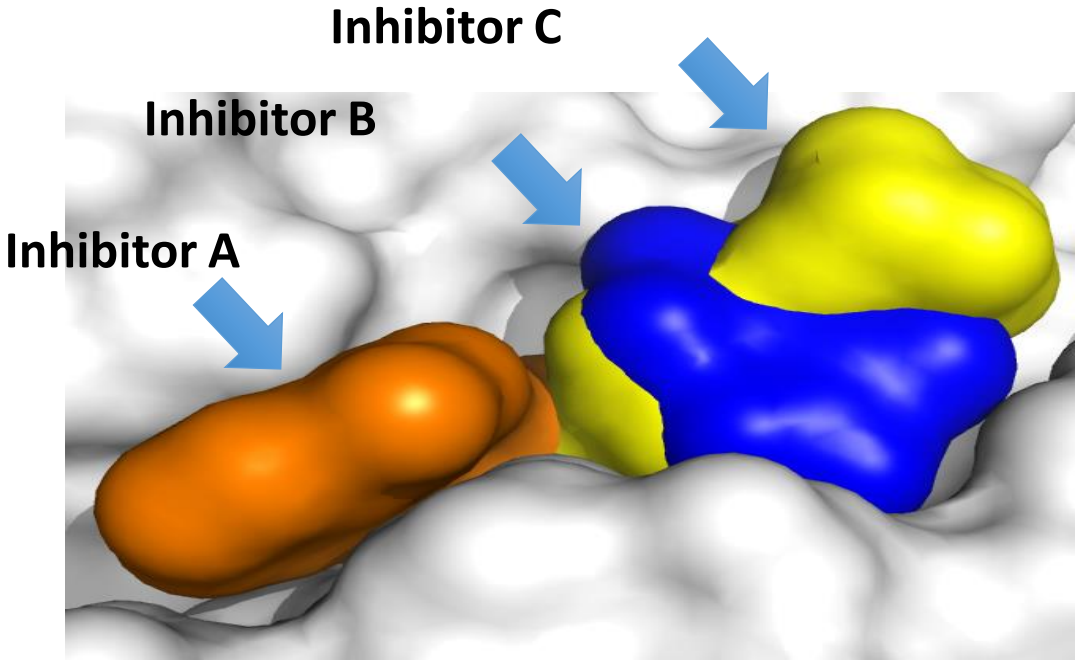


Cocrystal's Robust Development Pipeline

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

Structure-based Drug Discovery Technology

Example of HCV fragment hits



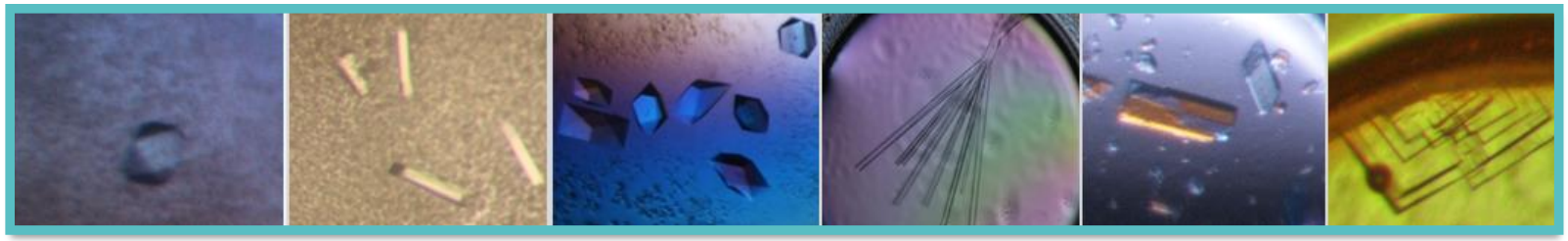
Advantages of the Cocrystal approach

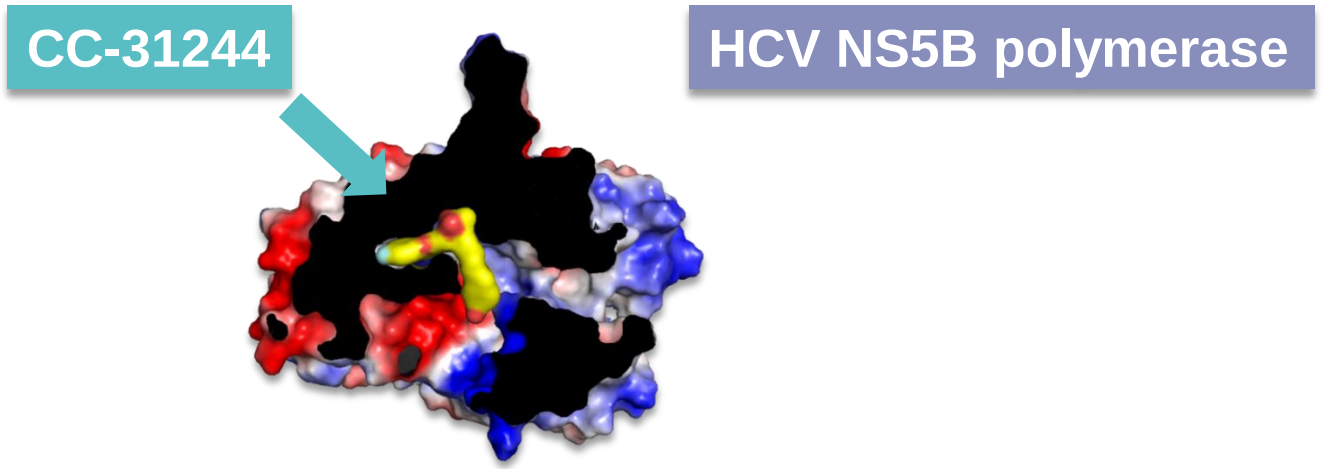
- Provides 3D structures of inhibitor protein complexes at near-atomic resolution with immediate insight to guide SAR
- Identifies attractive drug binding pockets
- Allows rapid turnaround of structural information through highly automated X-ray data processing and refinement

CC-31244: Broad Spectrum HCV NNI

Demonstration of Cocrystal's Enabling Technology

HCV GT1 – GT6 NS5B polymerase crystals





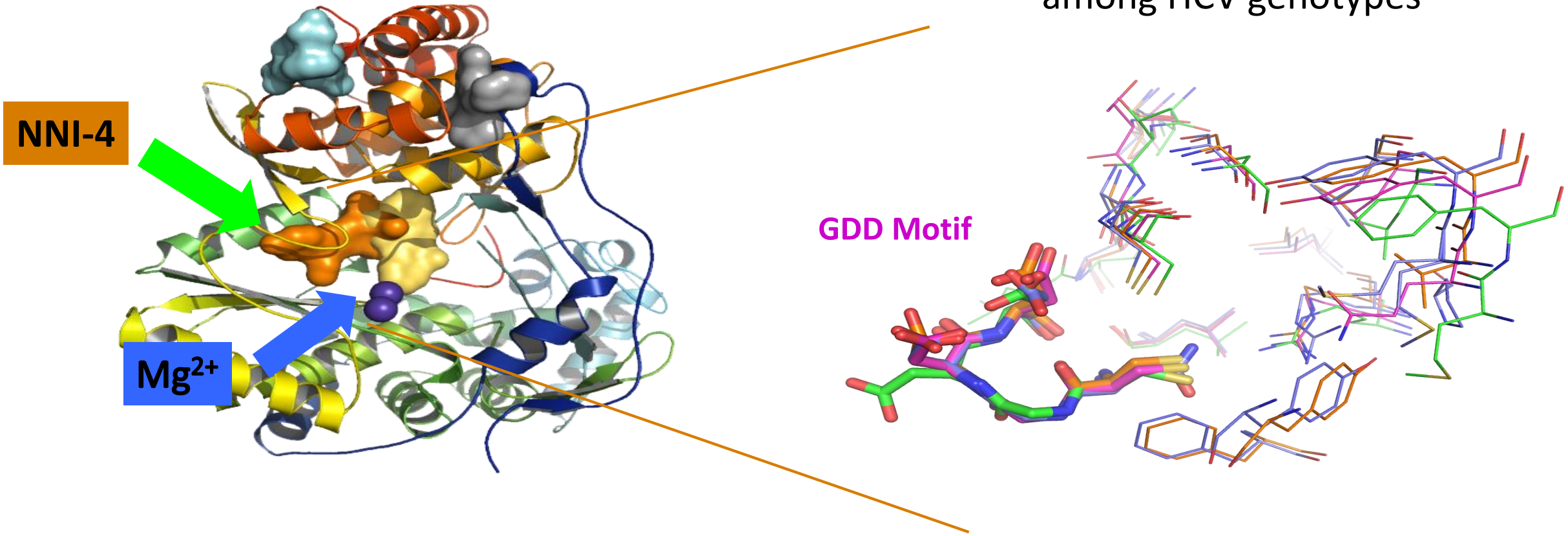
Novel HCV Non-nucleoside Inhibitor, CC-31244

Properties	Selection criteria
☑ **Pharmacological properties**	▪ Good antiviral activity (EC50, single digit nanomolar) ▪ High-affinity binding to a highly conserved drug binding site ▪ Broad spectrum against genotypes 1-6 ▪ High barrier to drug resistance ▪ Selective
☑ **Pharmacokinetics**	▪ Favorable PK properties ▪ Adequate half-time and biodistribution ▪ Potential for oral administration
☑ **Chemical properties**	▪ Stable molecule ▪ Suitable for API scale up and manufacturing
☑ **Safety and toxicity**	▪ Excellent profile for ADMET ▪ Absence of obvious cytotoxicity and cardiac toxicity ▪ Absence of obvious toxicity in animal studies

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

(A) HCV NS5B polymerase

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



CC-31244 Exhibits Broad Spectrum (Pan-genotypic) Antiviral Activity

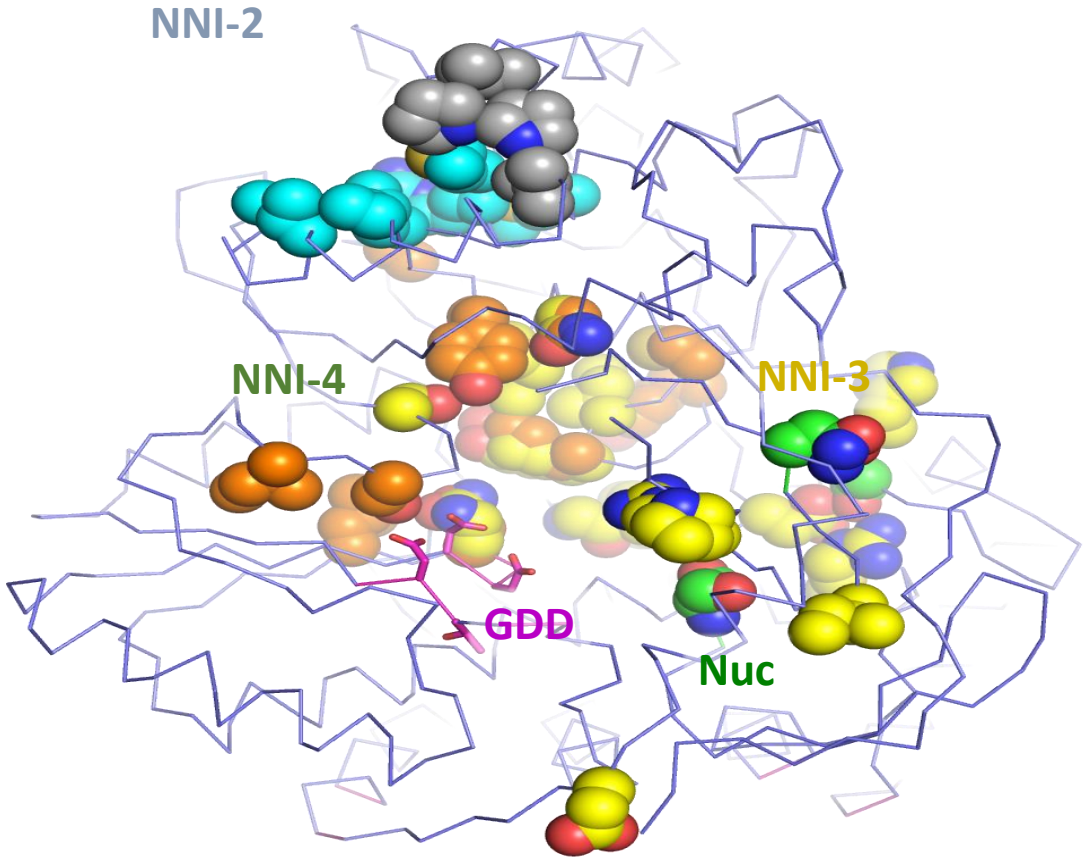
- **CC-31244 HCV replicon EC_{50} fold change, <6 fold**

HCV replicon/chimeric replicon EC_{50} results

Genotype	C-31244 EC_{50}, μM	EC_{50} Fold change	Sofosbuvir EC_{50}, μM	EC_{50} 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

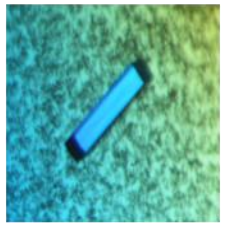
Drug Discovery Platform Enables Development of Antivirals with High Barrier to Drug Resistance

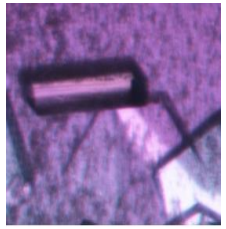
(A) Common NS5B drug resistant variants



(B) Cocrystal's NS5B drug resistant crystals

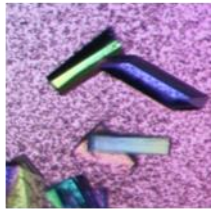

S365T


M423T


N316C


N316Y


L419M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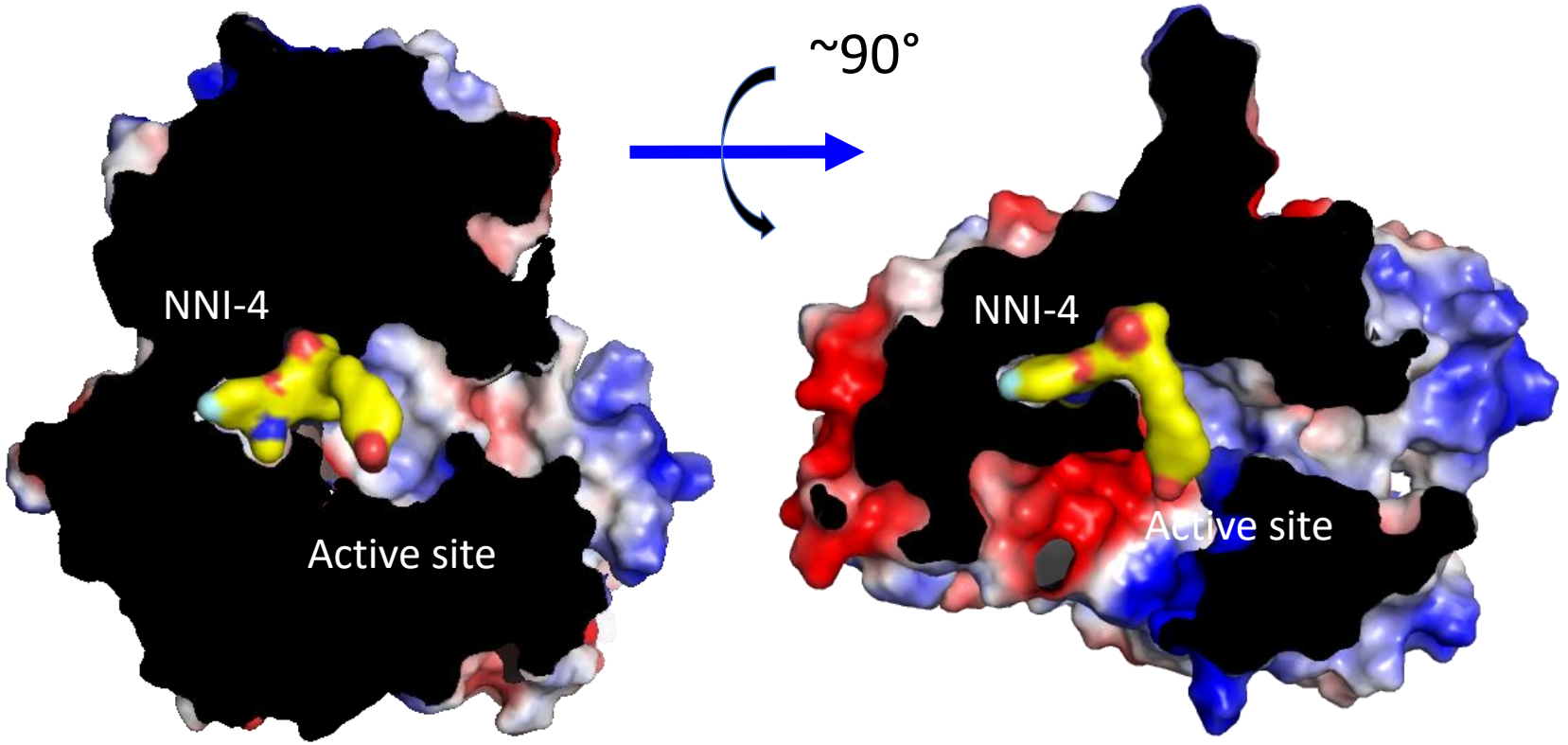
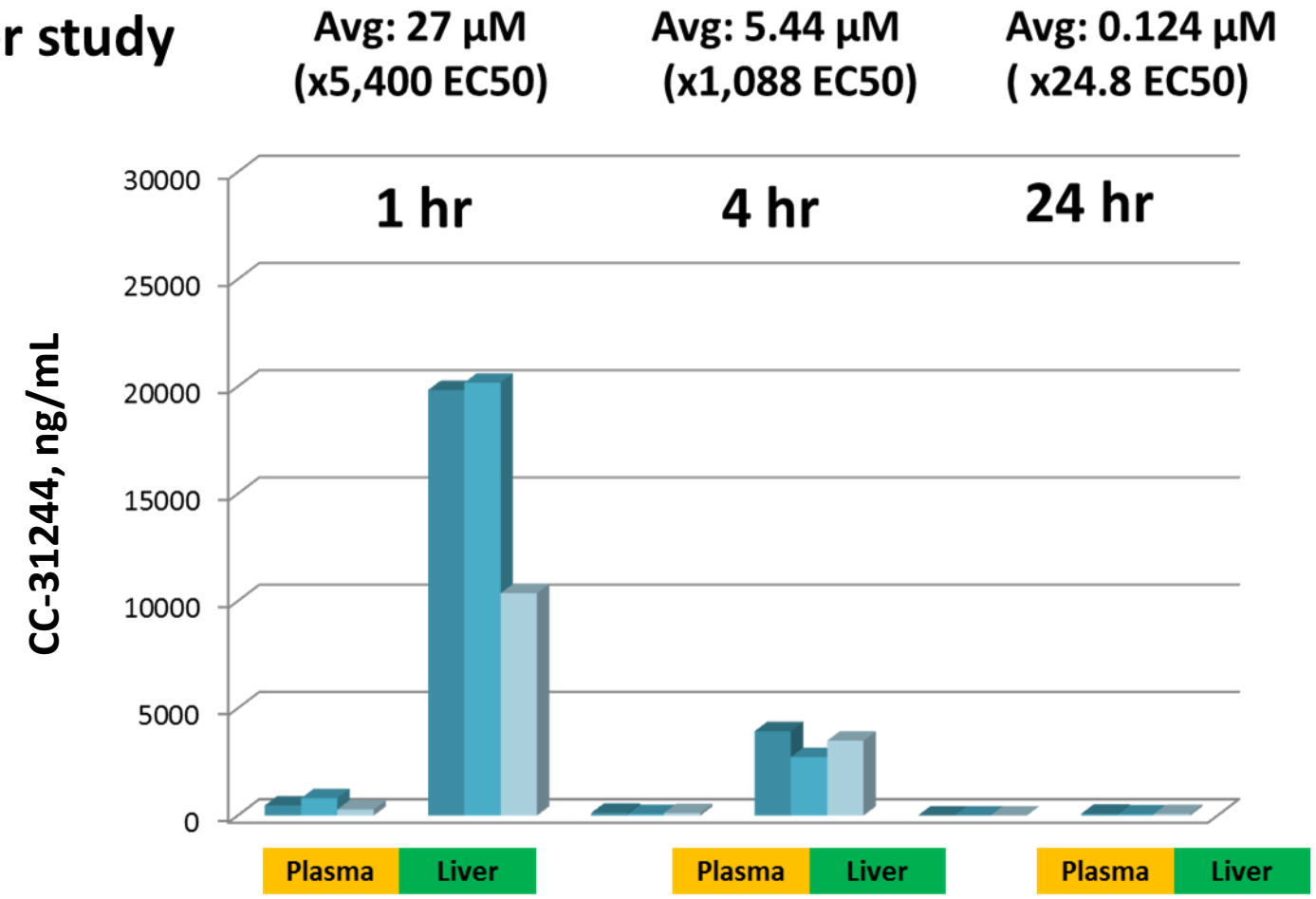
CC-31244 Extends From the Highly Conserved NNI-4 site To the Polymerase Active Site

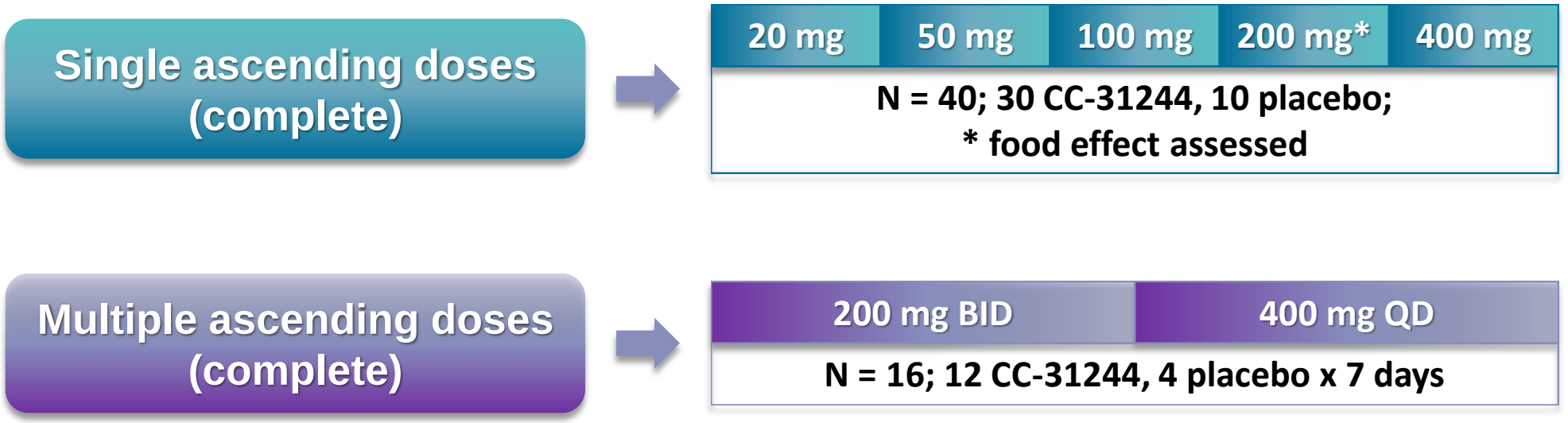


CC-31244 Exhibits Excellent Liver Targeting

Rat liver study



Phase 1a Study Completed



Endpoints

- Safety: adverse events (AEs) and laboratory abnormalities

Phase 1b Study Completed

HCV GT1
HCV RNA≥ 5 log_{10}IU/ml Naive

Single doses
QD or BID x 7 days

200 mg BID x 7 days	Status
N = 4; 3 CC-31244,1 placebo	Complete

400 mg QD x 7 days	Status
N = 5; 4 CC-31244, 1 placebo	Complete

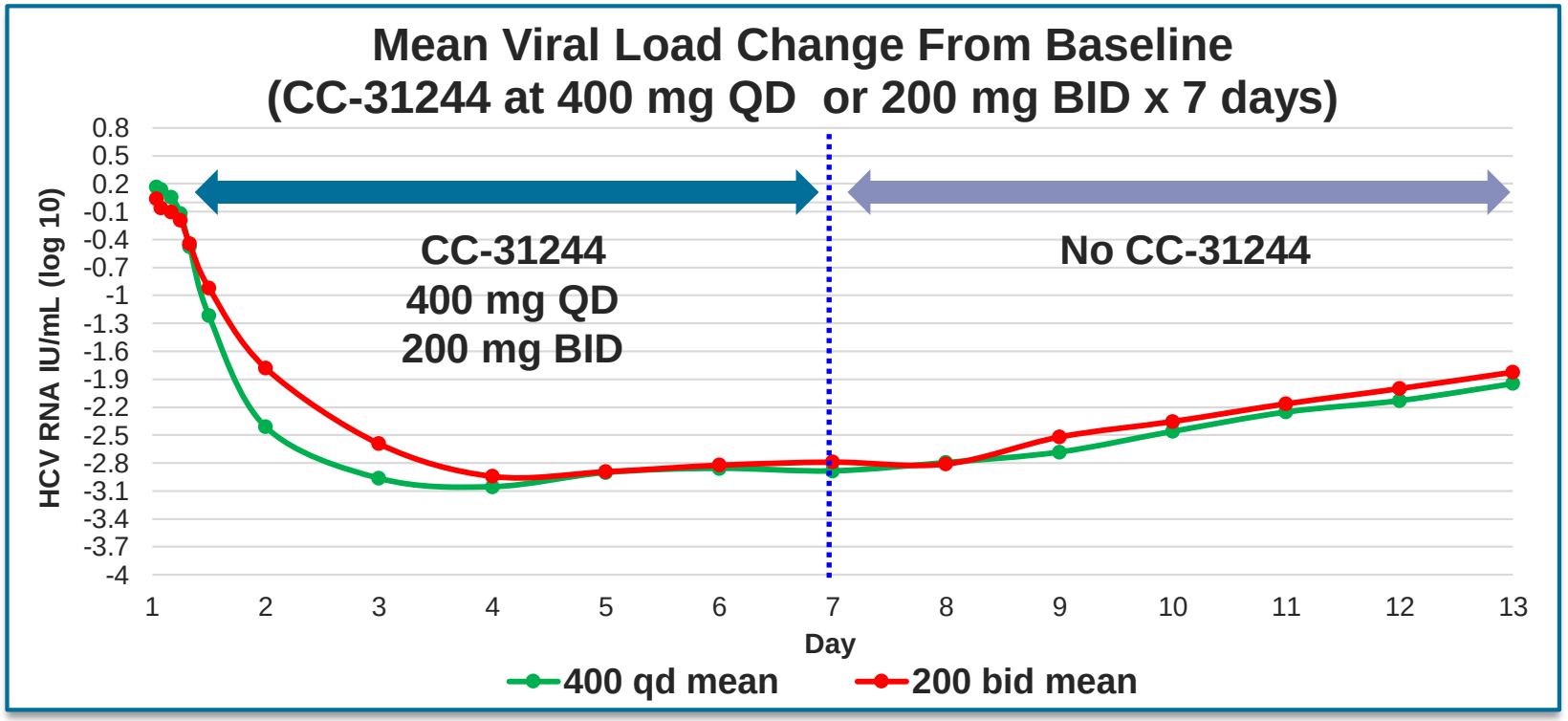
600 mg QD x 7 days	Status
N = 5; 4 CC-31244, 1 placebo	Complete

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



Cocrystal's HCV Strategy: Shorter Combination Therapy

Multiple opportunities in developing shorter combination therapy with approved HCV drugs

CC-31244 NS5B NNI

+

NS5A Inhibitor

NS5B Nuc

NS3 Protease Inhibitor

→

2 or 3 broad spectrum drugs for shorter therapy

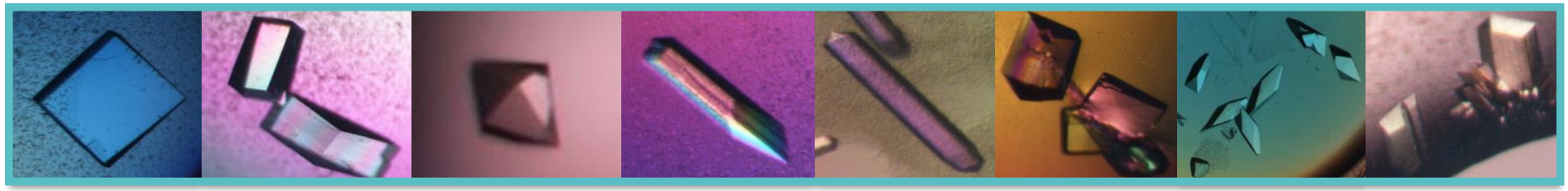
Best-in-Class Potential of Any NNI

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

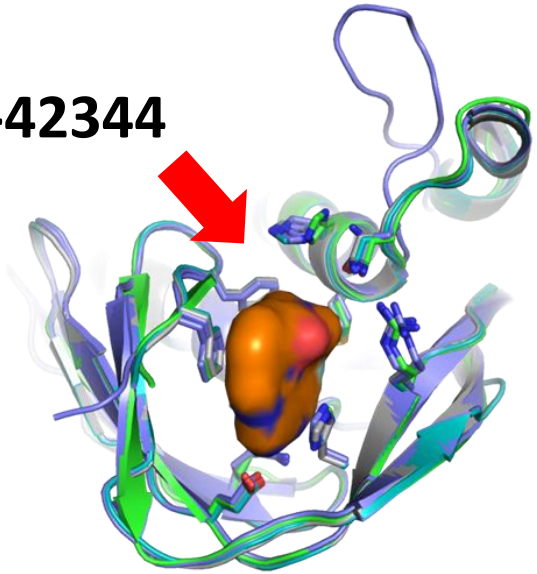
(* : approved DAA)

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

Summary and Conclusion

- Demonstrated value of Cocrystal's drug discovery platform for developing broad spectrum antivirals
- Demonstrated a favorable preclinical profile of Cocrystal's HCV lead, CC-31244
- Completed CC-31244 Phase 1a and 1b; demonstrated an acceptable safety profile in both healthy volunteers and HCV RNA viral load reduction of ~3 logs by 48 hours
- CC-31244 Phase 2a scheduled in Q2 2018
- Additional influenza and Noro IND filings scheduled in 2018/2019

COCRYSTAL PHARMA, INC.

Thank You!