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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): November 13, 2018**

**Cocrystal Pharma, Inc.**

(Exact name of registrant as specified in its charter)

Delaware	001-38418	35-2528215
(State or other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

19805 N. Creek Parkway Bothell, WA	98011
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (786)-459-1831

Former name or former address, if changed since last report: 1860 Montreal Road, Tucker GA 30084

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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## Item 7.01 Regulation FD Disclosure

On November 13, 2018, Dr. Sam Lee, President of Cocrystal Pharma, Inc. (the “Company”), delivered a presentation on the preclinical characterization of CC-42344, a broad spectrum, influenza A PB2 inhibitor, at the 6<sup>th</sup> ISRV AVG Conference in Washington, DC. A copy of the presentation is being furnished as Exhibit 99.1 hereto and is hereby incorporated by reference.

The information in this Current Report on Form 8-K (including exhibits hereto) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”) or otherwise subject to the liabilities under such section, and shall not be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, or the Exchange Act.

## Item 9.01 Financial Statements and Exhibits

### (d) Exhibits.

Exhibit	Description
99.1	<a href="#"><u>ISRV AVG Conference Presentation by Dr. Sam Lee, dated November 13, 2018</u></a>

## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**Cocrystal Pharma, Inc.**

Date: November 13, 2018

By: /s/ James Martin

Name: James Martin

Title: Chief Financial Officer

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## 6<sup>TH</sup> ISRV AVG CONFERENCE

Preclinical characterization of CC-42344, a broad spectrum,  
potent influenza A PB2 inhibitor for potential triple route  
(oral, inhalation, IV) treatment

*Sam Lee*

*November 13, 2018*

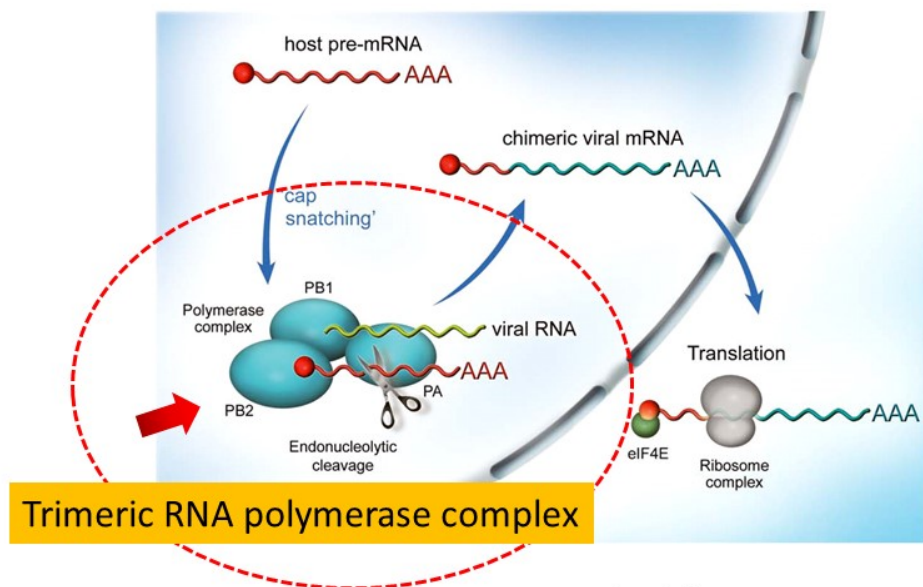
**CRYSTAL**  
PHARMA, INC.

## Forward Looking Statements

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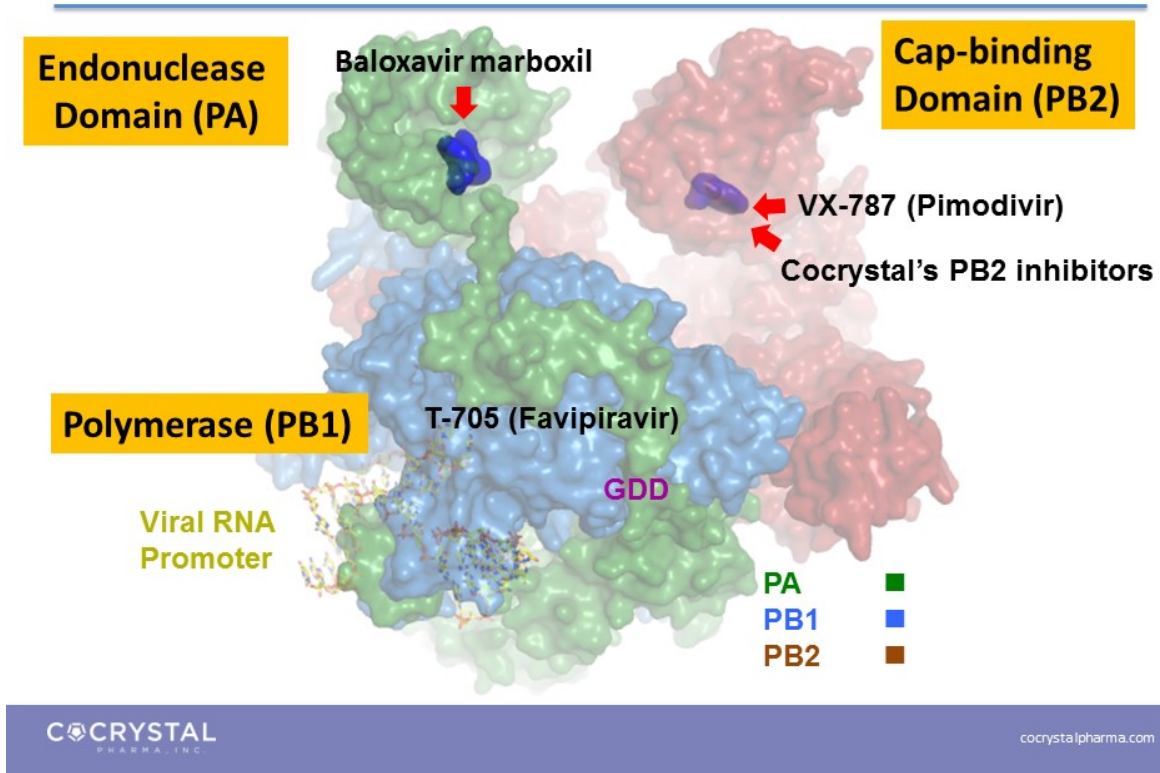
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are prefaced by words such as "expect," "plan," "intend," "anticipate," and similar words. Forward-looking statements are based on our current expectations 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. 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.

## Cap Binding (PB2), Endonuclease (PA), and Polymerase (PB1) Are Essential For Influenza Viral Replication



Boivin S et al. *J. Biol. Chem.* 2010;285:28411-28417

## Influenza Replication Inhibitors

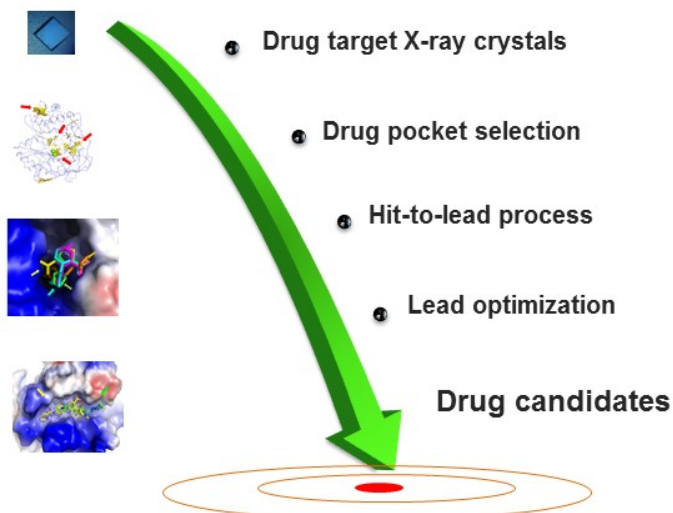




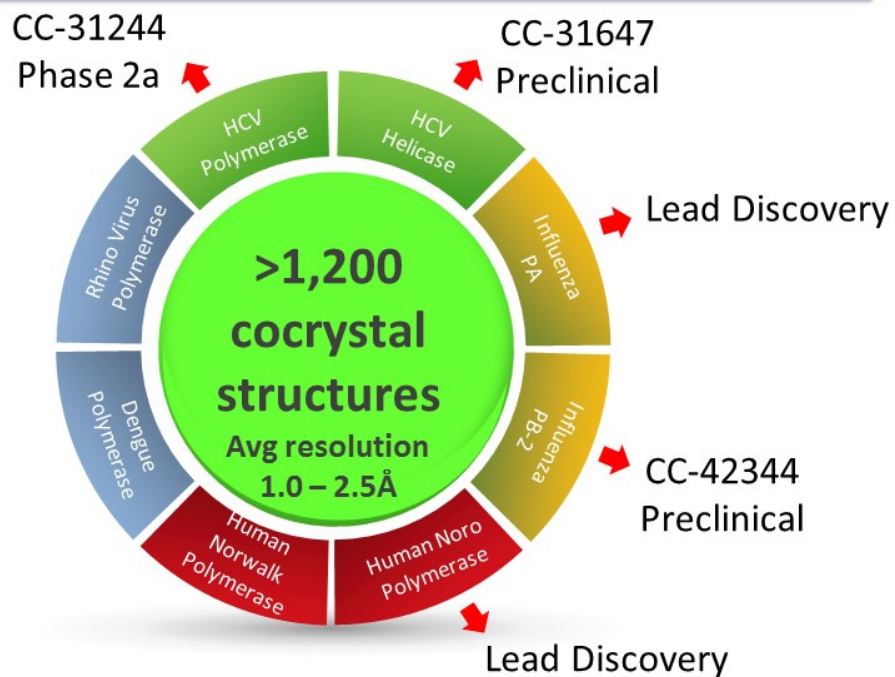
## Cocrystal Drug Discovery Platform Technology For Developing Broad Spectrum Antiviral Therapeutics



Influenza PB2 crystals

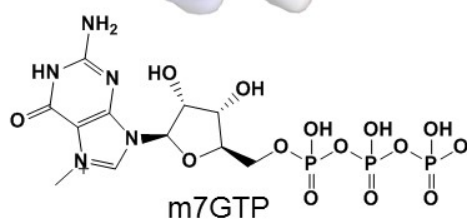
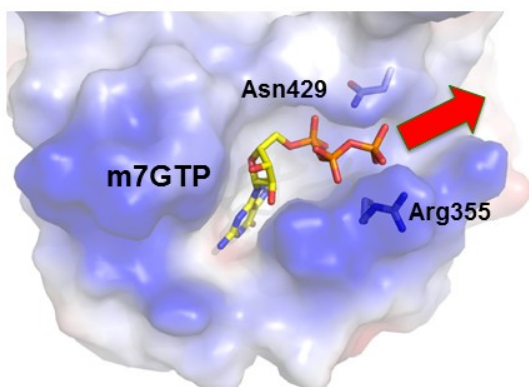


## Cocrystal Technology Platform Focuses on Well Validated Drug Targets: Viral Replication Enzymes

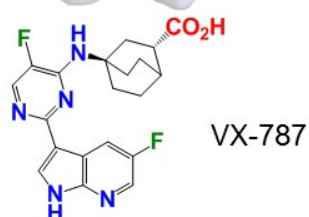
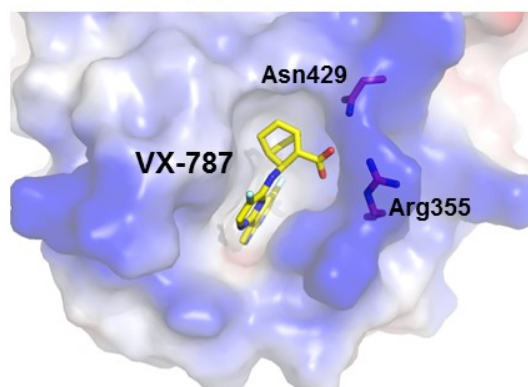


# m7GTP Binds To Influenza Cap-Binding Domain

(A) m7GTP

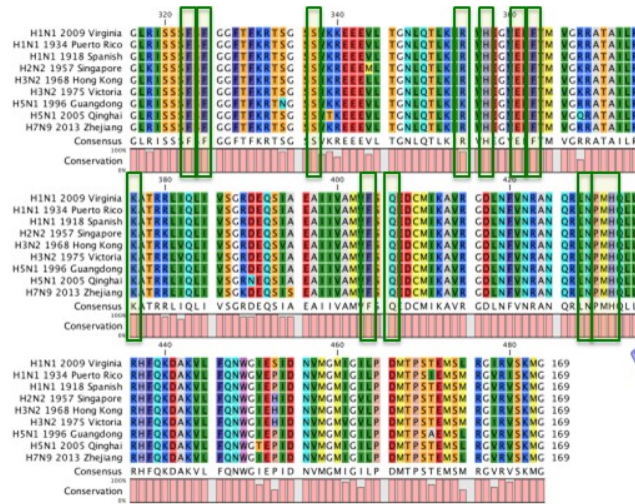


(B) VX-787

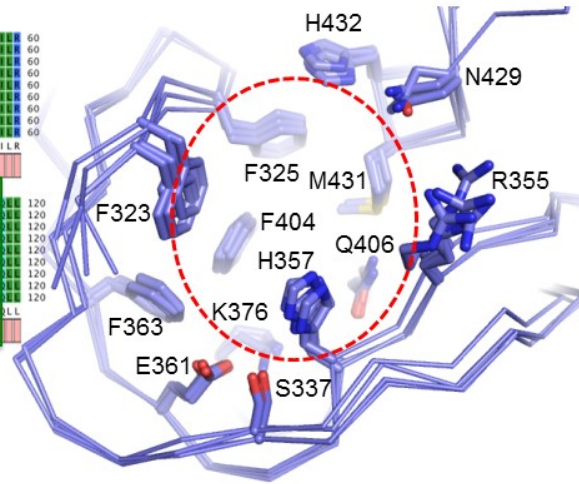


## PB2 m7GTP Binding Site is Highly Conserved

(A) PB2 sequence comparison



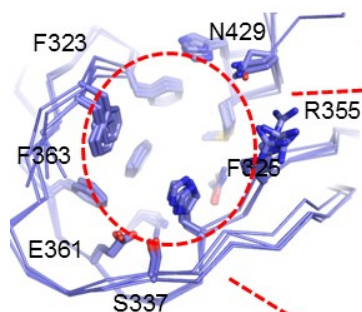
(B) m7GTP binding pocket



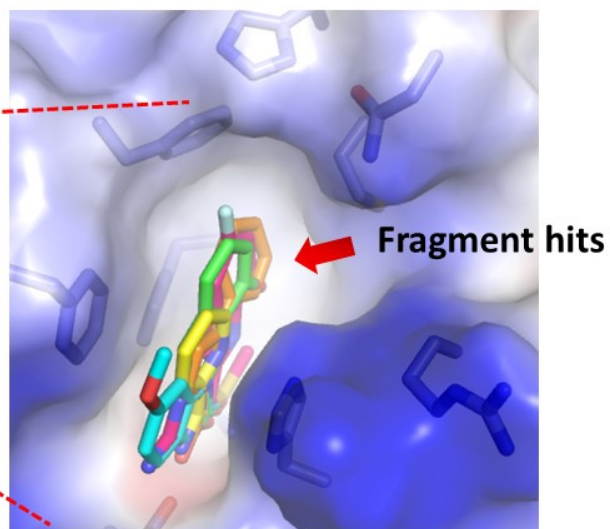
## m7GTP Binding Pocket is a Fragment Hot Spot

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(A) m7GTP binding pocket

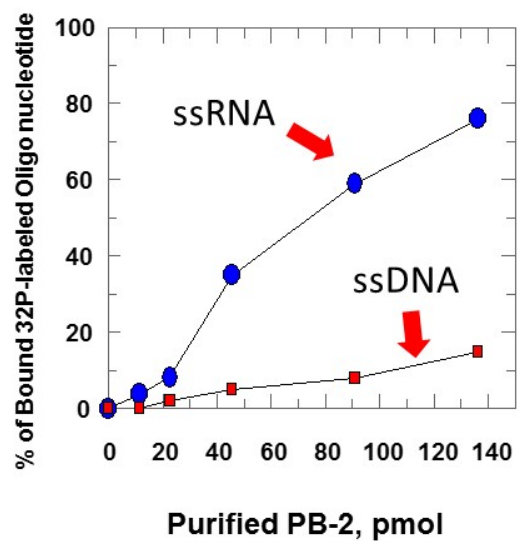


(B) Fragment hits

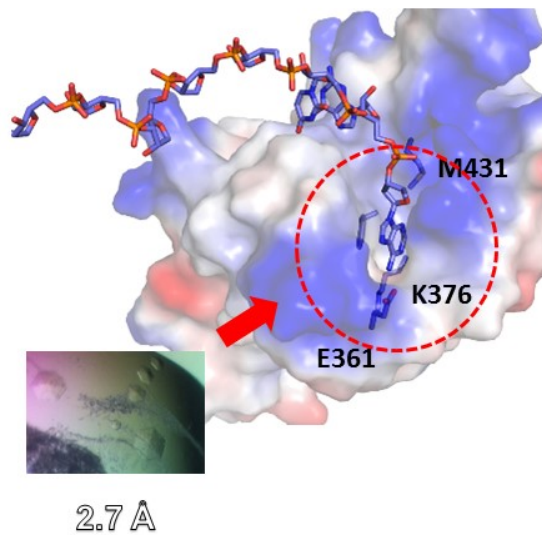


## Crystal Structure of PB2-ssRNA Complex Determined

(1) ssRNA binding activity of PB2



(2) ssRNA binding activity of PB2



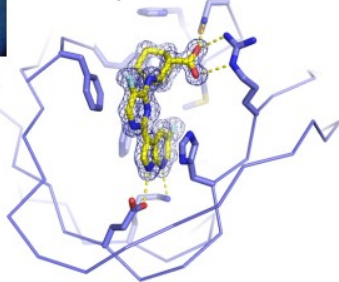


## Highly Conserved Binding Modes of PB2 Inhibitors



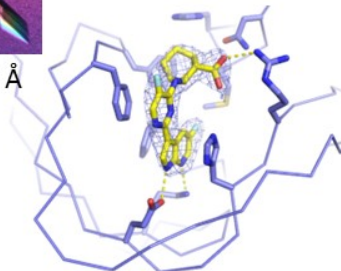
H1N1 Spanish 1918

1.25 Å



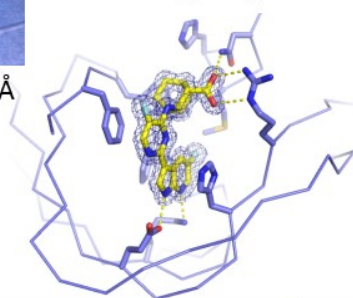
H3N2 Victoria 1975

1.6 Å



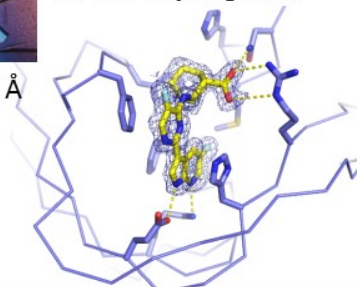
H5N1 Guangdong 1996

2.0 Å





H7N9 Zhejiang 2013

1.5 Å



## Cocrystal's PB2 Leads

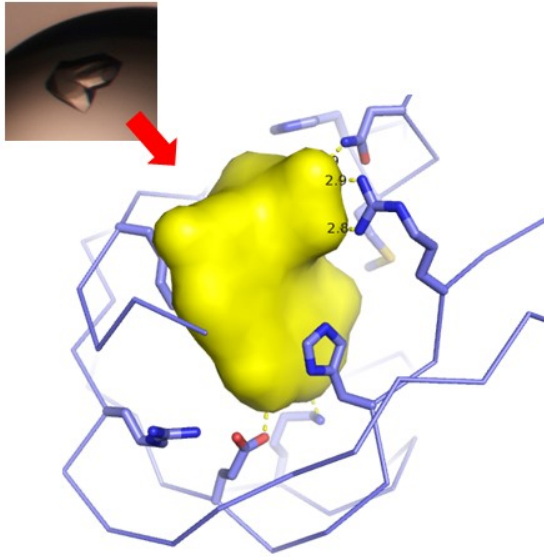
Influenza strain	Cocrystal Preclinical Lead		Cocrystal's backup PB2 inhibitors			
	VX-787 EC50 nM	42344 EC50 nM	42343 EC50 nM	42487 EC50 nM	42500 EC50 nM	42530 EC50 nM
 <b>Pandemic H1N1</b> Influenza A/CA/07/2009	2.4	 0.12	5	0.9	2.7	ND
H1N1 Influenza PR/8/34	1	1	1.2	1.2	2	0.5
<b>Pandemic H5N1</b> Influenza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



# Influenza A Lead CC-42344 Properties

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## CC-42344 cocrystals



- Binds to the highly conserved m7GTP binding pocket of PB2
- Exhibits broad spectrum activity against seasonal and pandemic influenza strains,  $EC_{50}$  0.12-9 nM
- Favorable preclinical safety profile and pharmacokinetic properties

Cocrystal structure of CC-42344 (1.47 Å)

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

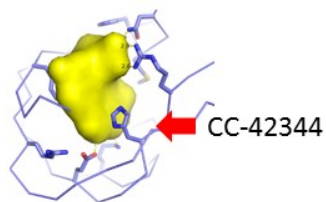
Influenza serotype	Strain	CC-42344, EC <sub>50</sub> nM
H1N1	A/PR/8/34	1
H1N1	A1/Denver/1/57	3
H1N1	A/Fort Monmouth/1/47	2
H1N1	A/NY/18/09	5
H3N2	A/AICHI/2/68	0.2
H5N1	Duck/MN/1524/81	<3.2
H5N1	Hong Kong/213/2003	4.5
H5N1	Thailand/16/2004	<3.2
H7N7	Netherlands/219/2013	5.6
H7N9	Anhui/1/2013	<3.2
H1N1- Tamiflu resistant	A/HK/2369/09 H274Y	9
H3N2-Tamiflu resistant	A/Wuhan/395/95	0.5
H5N1- Amantadine resistant	Duck/MN/1524/81	8.6

## CC-42344: Pharmacological, Safety, Toxicity, and PK Evaluations Completed To Date

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- ☒ In vitro antiviral profiling against seasonal and pandemic influenza A strains
- ☒ Cytotoxicity including larger screen: HepG2/high content analysis and 13 cell lines
- ☒ Caco-2 bidirectional permeability
- ☒ CYP inhibition (HLM): inhibition (2D6, 3A, 1A, 2B6, 2C8, 2C9, 2C19) & time dependent inhibition (2D6, 3A4)
- ☒ Thermodynamic/aqueous solubility
- ☒ pION solubility determination (at pH 7.4)
- ☒ Metabolic stability in rat and human microsomes (intrinsic clearance)
- ☒ Plasma protein binding (human)
- ☒ Plasma stability/half-life determination (human, rat)
- ☒ Pharmacokinetics: in rats (IV/PO), mouse (IV/PO) and dogs (IV/PO)
- ☒ In silico genotoxicity/carcinogenicity
- ☒ Off-target: kinase/receptor profiling; safety screen (CEREP)
- ☒ Mitochondrial toxicity (GLU/GAL)
- ☒ Mini Ames (genotox) screen
- ☒ Mini hERG (in vitro pharmacology) screen
- ☒ Exploratory 7-day mouse tox study (up to 500 mg/kg/day)

## In Vitro and In Vivo Assessment of CC-42344

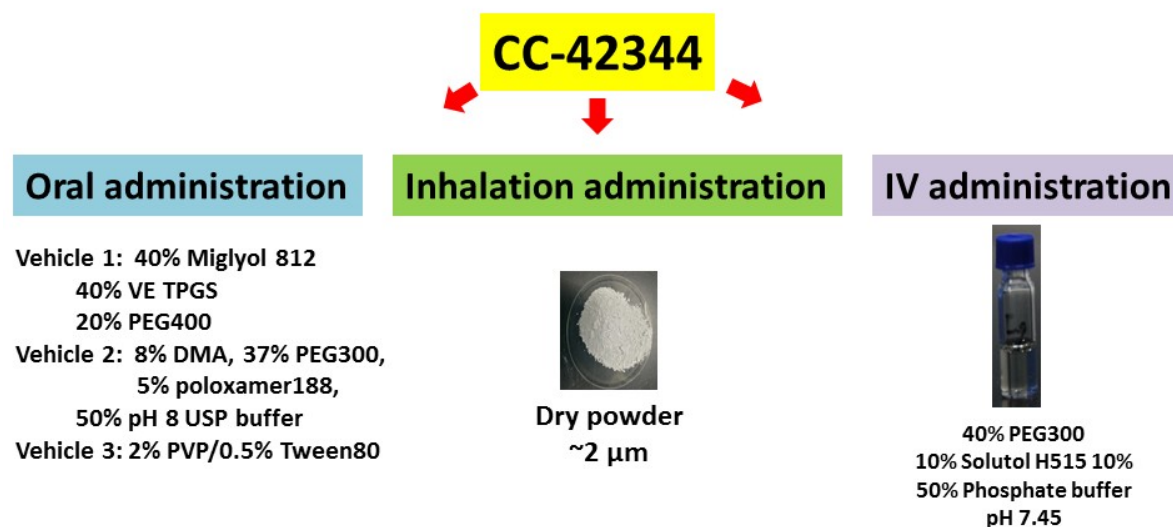


H1N1 EC50, nM	1
H1N1 EC90, nm.	2
Cytotoxicity (HepG2) at 10 $\mu$ M	No
Cytotoxicity (13 cell lines) at 10 $\mu$ M	No
Mitochondria toxicity at 10 $\mu$ M	No
Off-target inhibition at 10 $\mu$ M	No
Solubility in PBS, $\mu$ M	90.8
Caco2 A-B, $10^{-6}$ cm/s	20
Caco2 B-A, $10^{-6}$ cm/s	2.5

Dose (Rat & Mouse, single dose)	PO 5mg/kg IV 1mg/kg
Oral bioavailability, %F	45% (rat); 57% (mouse)
Cl (ml/min/kg)	40 (rat); 27 (mouse)
Vd (L/kg)	18 (rat); 1.77 (mouse)
t <sub>1/2</sub> (h)	5.24 (rat); 0.75 (mouse)
C <sub>max</sub> (nM)	1,600 (rat), 1,600 x EC50; 9,544 (mouse), 9,544 x EC50
C <sub>min</sub> (nM)	34 (rat); 148 (mouse)
hERG IC50	>10 $\mu$ M
Metabolic stability (liver microsomes)	rat, >60 min; Human, >60 min
CYP1A2, 2C19, 2C9, 2D6 & 3A4 IC50s	>10 $\mu$ M
Time-dependent CYP3A	No inhibition at 10 $\mu$ M
Time-dependent CYP2D	

## Multiple Routes of Administration (Oral, Inhalation, IV) Explored

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## In Vivo Assessment of CC-42344

Comparative maximum formulation single PO dose exposures in rat

Test formulation	PO Dose (mg/kg)	Fed or fasted	T <sub>1/2</sub> (hours)	Plasma C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hours)	Plasma AUC <sub>0-∞</sub> (ng.h/mL)
40% miglyol/40% VE TPGS/20% PEG400	300	Fed	3.82	2,333 (5.3 μM)	0.83	7,857
2% PVP/0.5% Tween80	500	Fed	2.15	30,633 (70 μM)	1.17	95,913
	800		1.96	65,300 (148 μM)	6.00	600,000
8% DMA/37%PEG300/5% poloxamer188/50% USP buffer, pH 8	200	Fed	1.78	39,067 (89 μM)	1.00	292,854

Comparative single dose IV pharmacokinetics

Animal species	Dose (mg/kg)	T <sub>1/2</sub> (hours)	V <sub>d</sub> (L/kg)	Cl (mL/min/kg)	AUC <sub>0-last</sub> (ng h/mL)
Female BALB/C mouse	2.5	2.02	1.79	37.8	1097
Male Sprague-Dawley rat	1	5.24	17.9	39.9	385

## In Vivo Assessment of CC-42344



- Single dose inhalation pharmacokinetics in the female Balb/c mouse

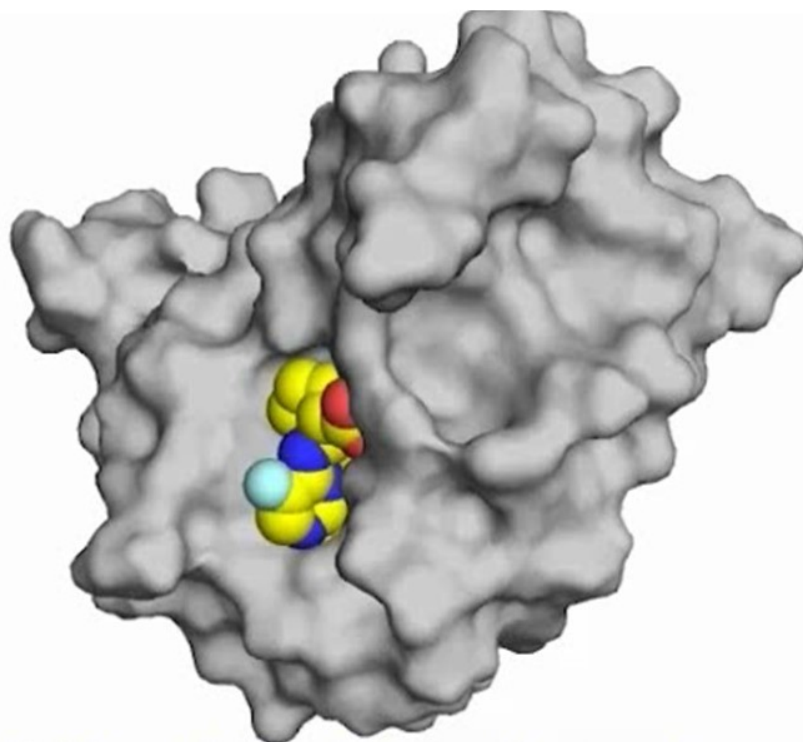
☐ Dry power formulation developed

☐ Dose 0.8-1.2 mg of dry power (~200 ug of CC-42344)



Dry powder  
~2  $\mu\text{m}$

Time course	CC-42344 concentration	CC-42344 concentration
	Lung	Plasma
1 hr	984 $\mu\text{M}$ 	5.6 $\mu\text{M}$ 
24 hr	218 $\mu\text{M}$	0.081 $\mu\text{M}$
48 hr	8.6 $\mu\text{M}$	0.052 $\mu\text{M}$
72 hr	0.63 $\mu\text{M}$	0
96 hr	0.35 $\mu\text{M}$	0

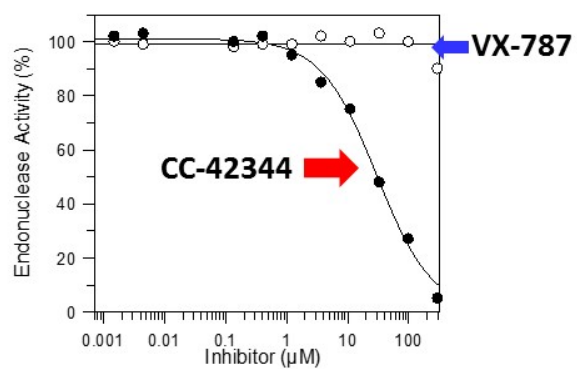


## PB2 Cap binding domain

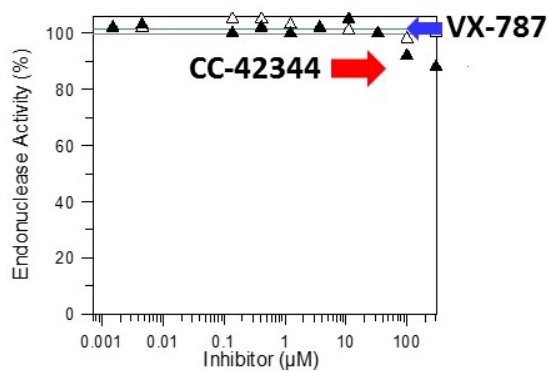


## CC-42344 Inhibits The Endonuclease Activity of Influenza A Trimeric Complex (PA:PB1:PB2)

(A) PA:PB1:PB2 trimeric complex

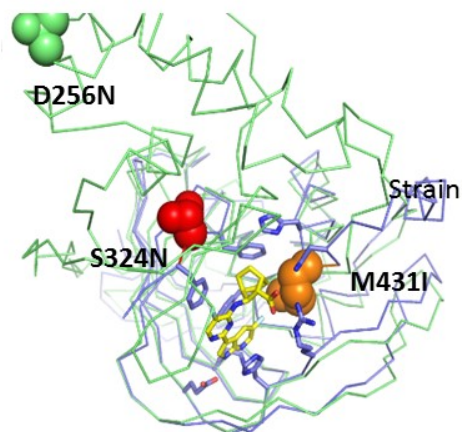


(B) PA endonuclease



## Drug Resistant Profile of Cocrystal PB2 Lead, CC-42344

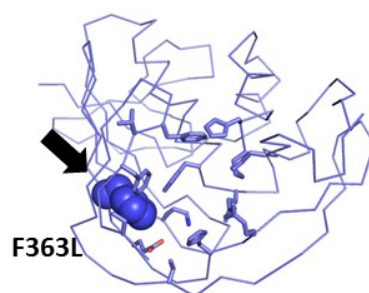
(A) VX-787: 3 resistant H1N1 viruses  
**D265N, S324N, M431I**



3 mutations identified after  
treatment with VX-787

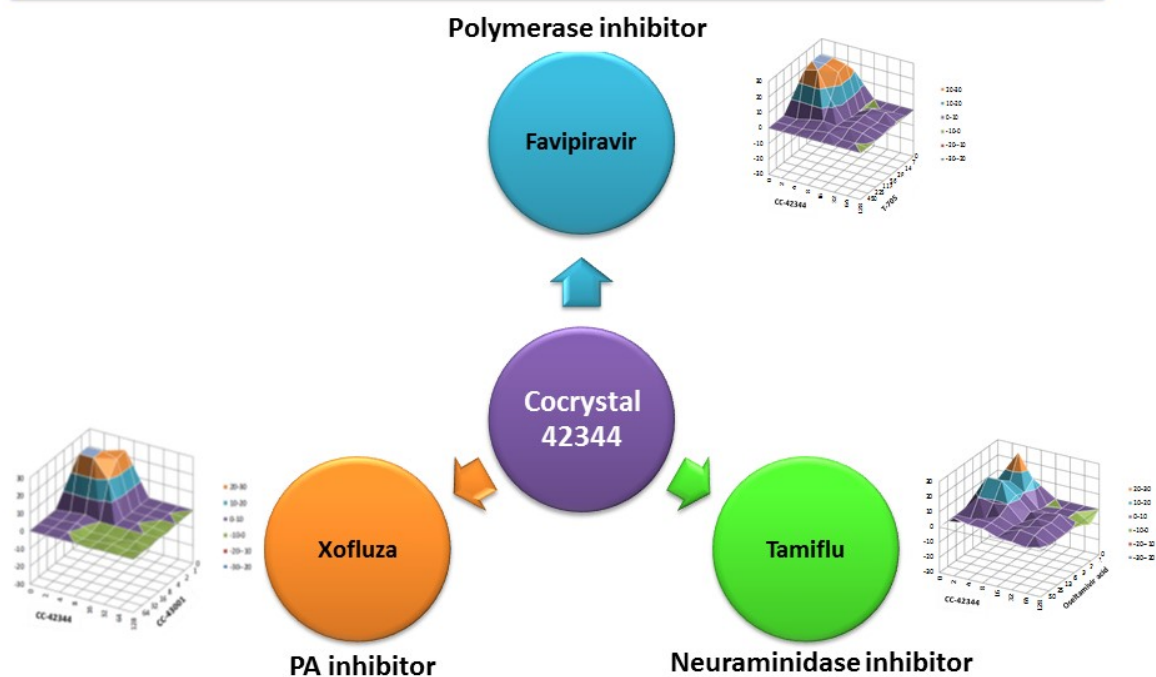
Cocrystal PB2 lead

(B) CC-42344: **1** resistant H1N1 virus  
**F363L**



1 mutation identified after  
treatment with CC-42344

## CC-42344 Shows Strong Synergistic Effects With Approved Influenza Antivirals



# Summary

Property	Cocrystal CC-42344	Pimodivir (VX-787)
Antiviral activity against seasonal and pandemic influenza	Single digit nanomolar, Broad spectrum	Single digit nanomolar, Broad spectrum
Drug resistance profile	One mutation F363L	Three mutations D256N, S324N, M432I
Route of Administration	Inhalation, IV, and oral routes Currently explored	Oral, BID
Chemical stability (>24 months)	Yes	Data not available
Synergistic Effects with replication inhibitors	Yes	Data not available

