



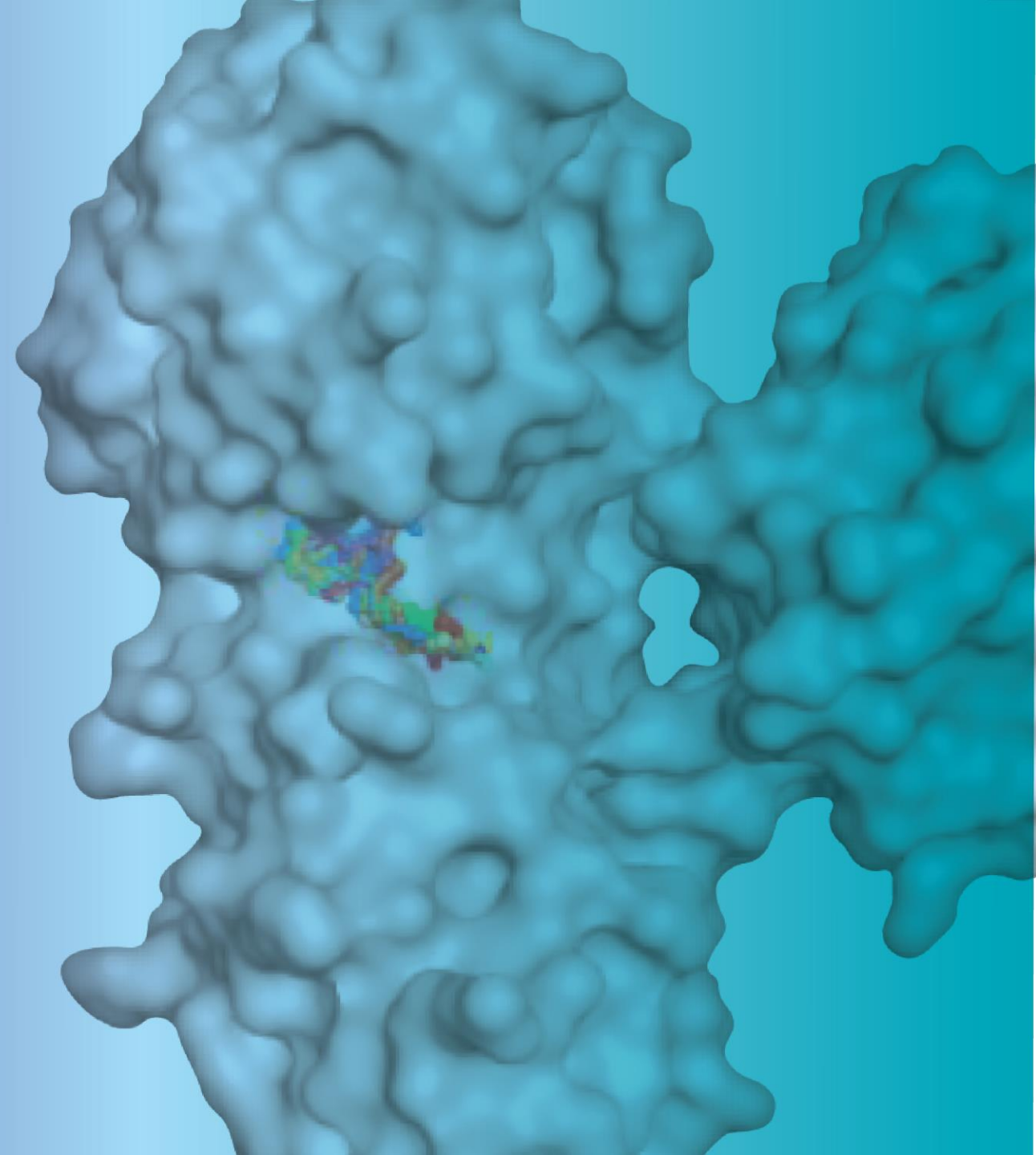
**First-in-Human Study of CC-42344,  
A Novel Broad-Spectrum Influenza A  
Polymerase PB2 Inhibitor**

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7<sup>th</sup> ISIRV-AVG CONFERENCE

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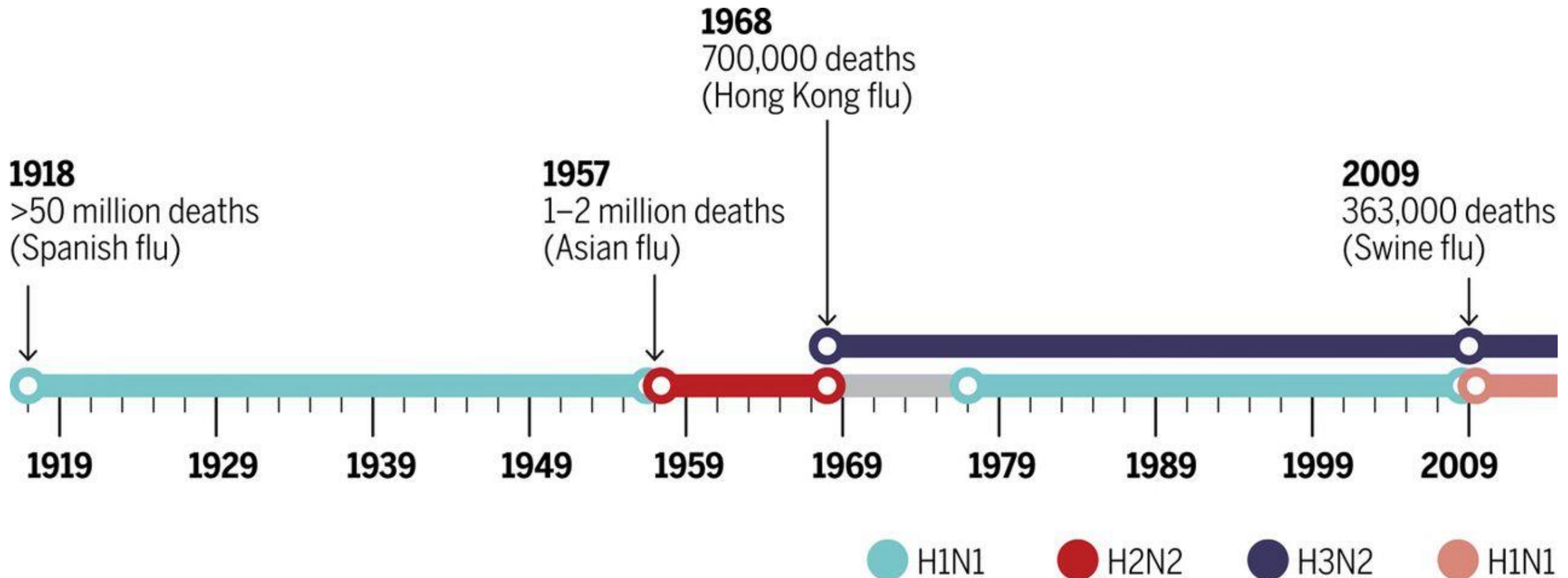
# Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the market opportunities for the treatment of acute and chronic viral diseases which are the focus of our programs; the development pipeline; our technology platform's ability to produce viable drug candidates at reduced development timelines and costs; the potential future payments and royalties in connection with the collaboration with Merck Sharp & Dohme Corp. ("Merck"); the expected future characteristics and progress in our clinical programs, including anticipated initiation of a Phase 1 study for oral influenza PB2 inhibitor, CC-42344, in H2 2023, a Phase 1 study for the COVID-19 CDI-988 oral protease inhibitor in H1 2023, and a Phase 1 study for Oral influenza PB2 inhibitor, CC-42344 in H1 2024; our exploration of other collaboration opportunities, and our expectations regarding future liquidity.

Forward-looking statements are prefaced by words such as "anticipate," "expect," "plan," "could," "may," "will," "should," "would," "intend," "seem," "potential," "appear," "continue," "future," "believe," "estimate," "forecast," "project," 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. We caution you, therefore, against relying on any of these forward-looking statements. Our actual results may differ materially from those contemplated by the forward-looking statements for a variety of reasons, including, without limitation, the risks arising from the impact of COVID-19 and its current spread in China and the potential spreading to the United States and other places where clinical trial for our studies are conducted, the Ukraine war, inflation and interest rate increases on the national and global economy, on our collaboration partners, clinical research organizations ("CROs"), Contract Manufacturing Organizations, and on our Company, including raw material and test animal shortages and other supply chain disruptions or labor shortages, the ability of our CROs to recruit volunteers for, and to proceed with, clinical trials, our and our collaboration partners' technology and software performing as expected, the results of future preclinical and clinical trials, general risks arising from clinical trials, receipt of regulatory approvals, regulatory changes, development of effective treatments and/or vaccines by competitors, including as part of the programs financed by the U.S. government, potential mutations in the virus which may result in variants that are resistant to a product candidate we develop, and our reliance on Merck for further development in the influenza A/B program under the license and collaboration agreement. Further information on the risk factors that could cause actual results to differ materially from those expressed or implied by forward-looking statements, is contained in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2022. Any forward-looking statement made by us in this presentation speaks only as of the date on which it is made. Factors or events that could cause our actual results to differ may emerge from time to time, and it is not possible for us to predict all of them. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future developments or otherwise, except as may be required by law.

# Influenza A Is Responsible For Pandemic and Seasonal infections

The influenza pandemic 100 years: >53 million deaths



Taubenberger JK et al. *Sci. Transl. Med.* 2019; 11, eaau5485



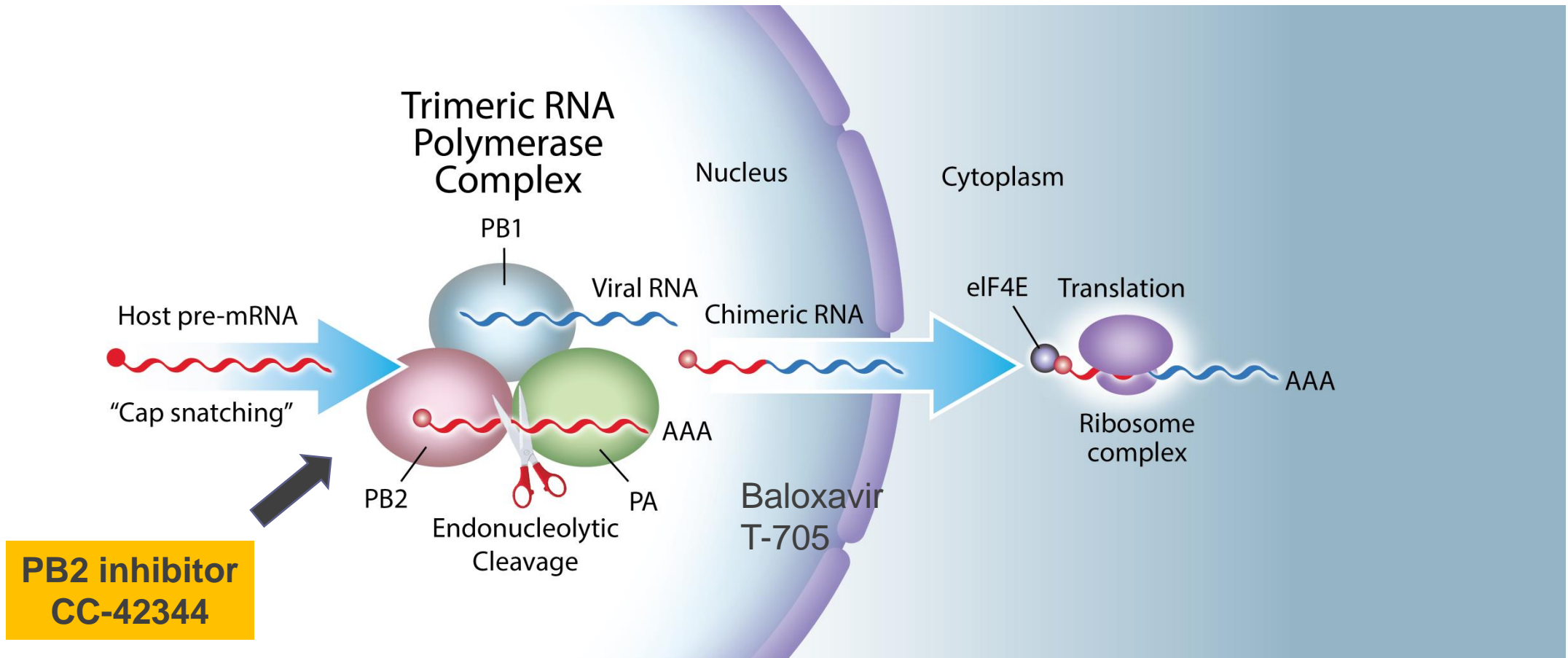
## Avian Influenza PB2 Acquires Mutations Before Human Pandemic



### Influenza PB2 protein

- Essential for viral replication
- Human adaptation PB2 mutations including 1918 Spain E627K increase
  - ↑ Polymerase activity
  - ↑ Viral replication
  - ↑ Pathogenicity
  - ↑ Transmission

# Cocrystal's PB2 Inhibitor CC-42344 Blocks The First Step of Influenza A Viral Replication

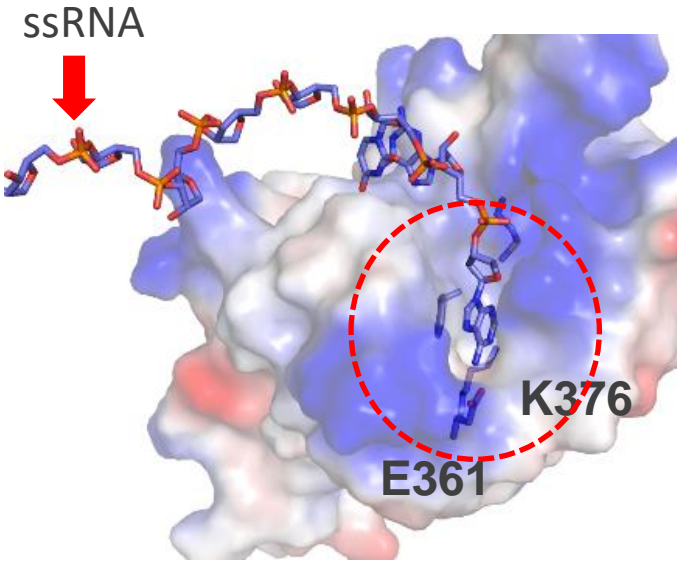




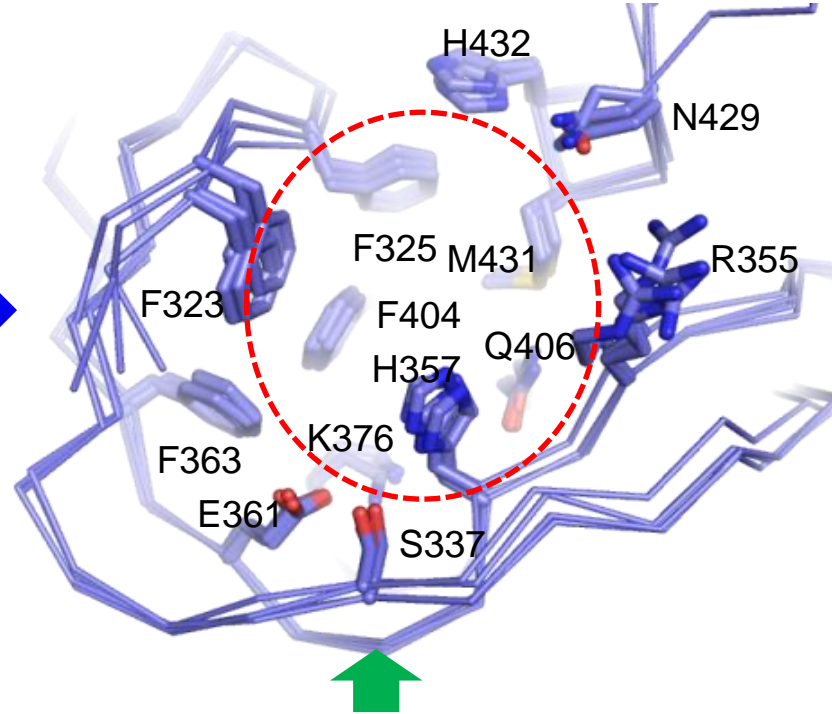
# CC-42344 is a Broad-Spectrum Antiviral with High Barrier to Resistance: Targeting a Highly Conserved Active Site of PB2

## Structure-based drug discovery platform technology was applied for CC-42344 development

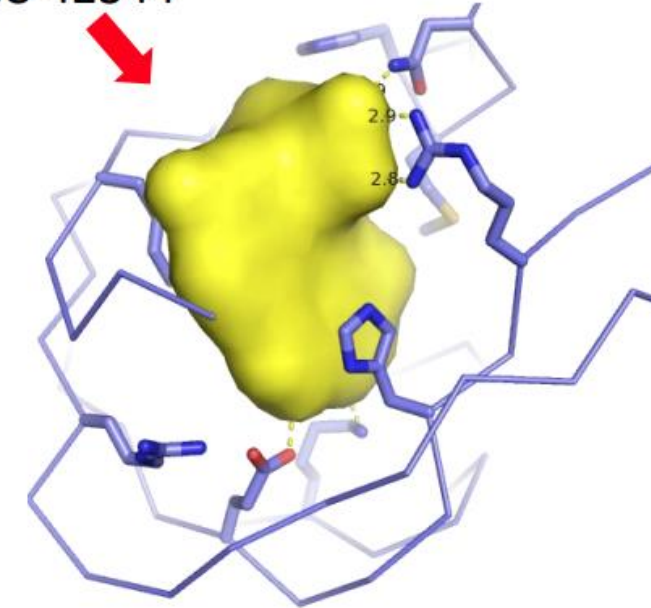
(A) PB2:ssRNA complex



(B) Highly conserved binding pocket

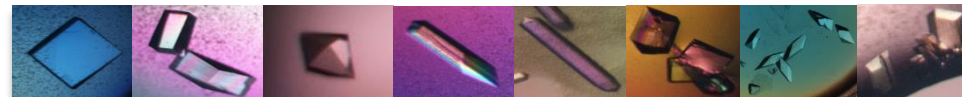


(C) PB2:CC-42344 structure  
CC-42344



Single digit nanomolar EC50  
against baloxavir- and  
oseltamivir- resistant strains

H1N1 H2N2 H3N2 H5N1 H7N9 PB2 crystals



# CC-42344 vs Pimodivir (VX-787): Key Differences

Property	Pimodivir (VX-787)	Cocrystal CC-42344
<b>Broad-spectrum activity</b>	Single digit nanomolar EC50 Seasonal and pandemic influenza A strains	<b>Single digit nanomolar EC50</b> Seasonal and pandemic influenza A strains
<b>Drug resistance</b>	<b>Six major resistance variants on PB2</b> <b>Q306H, S324I, S324N, S324R, F404Y, N510T*</b> (EC <sub>50</sub> fold shift, 63-257)	<b>No resistance variant</b> (one mutation, <b>F363L</b> , detected by deep sequencing from resistance screening)
<b>Mechanism of inhibition</b>	<b>Single MOI</b> Targets m7GTP pocket of free PB2	<b>Multiple MOIs</b> Targets free PB2, pre-mRNA bound PB2, and trimeric polymerase complex (PB2:PA:PB1)
<b>Route of Administration</b>	Oral	<b>(1) Oral</b> <b>(2) Inhalation</b> <b>(3) Injectable</b>
<b>Status of clinical trials</b>	<b>Phase 3 halted</b>	<b>Oral Phase 1, Complete</b> <b>Inhalation Phase 1, planned in 2024</b>

7 \*Byrn RA, et al. *Antimicrob Agents Chemother* 2015; 59, 1569-1582



# CC-42344 Shows Highly Favorable Safety and Excellent Antiviral Activity in H1N1-Infected Human Bronchial Epithelia

Normal human respiratory epithelia



No  
treatment

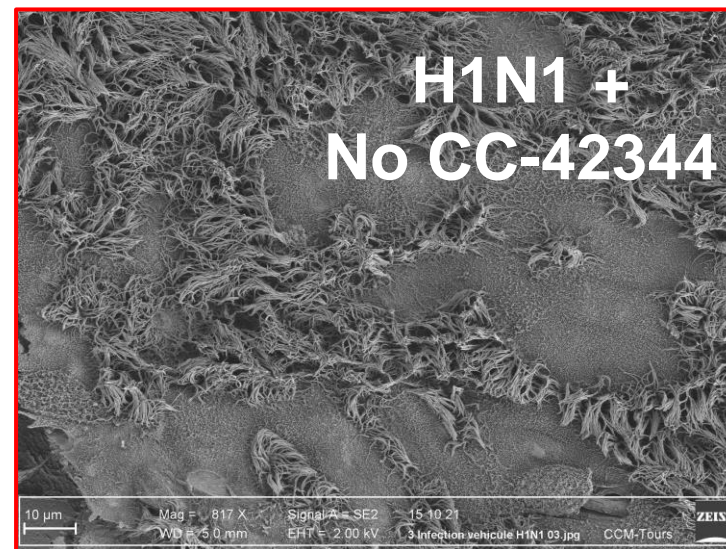


+ H1N1  
infection



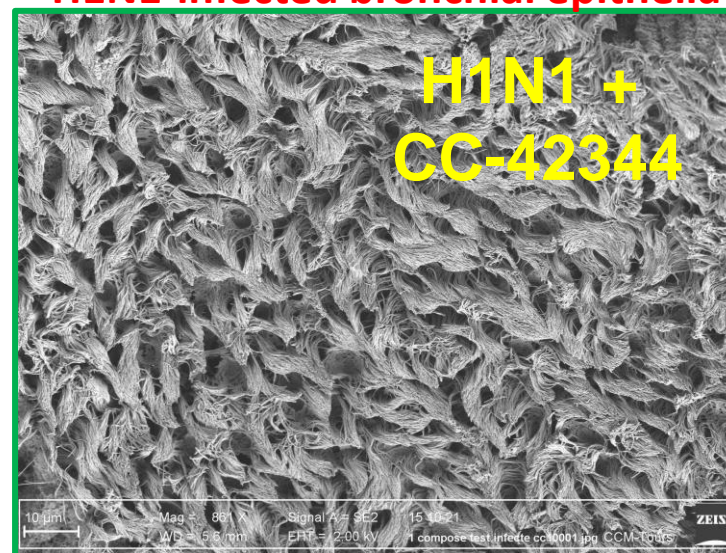
With  
CC-42344

H1N1 +  
No CC-42344




H1N1-infected bronchial epithelia

H1N1 +  
CC-42344







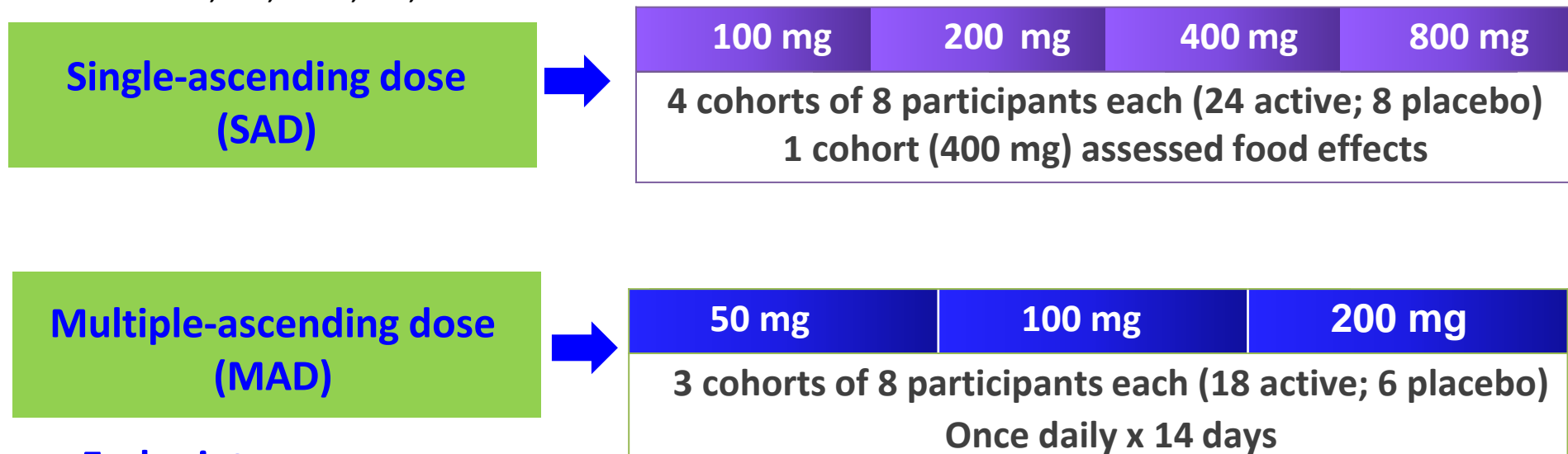
A Phase 1 Study in Healthy Participants to Evaluate the  
Safety, Tolerability, and PK of the Oral Influenza A  
PB2 Inhibitor CC-42344

# Phase 1 Study Complete

Phase 1 trial site: Linear Clinical Research-Harry Perkins Research Institute, Perth, Australia

## Participants:

- Single-center, randomized, double-blind, placebo-controlled
- Single-ascending dose, multiple-ascending dose; 7-day nontreatment follow-up period
- Healthy adult volunteers
- Each cohort comprised of 8 subjects; 6, CC-42344 and 2, placebo
- N = 56; 32, SAD; 24, MAD



## Endpoints

- Adverse events (AEs), physical exam, viral signs, ECGs, and lab indices
- Food effect

# Key Entry Criteria

- Healthy males and females  $\geq 18$  and  $\leq 55$  years
- Body weight  $\geq 50$  kg
- Body mass index  $\geq 18$  and  $\leq 32$  kg/m<sup>2</sup>
- Non-pregnant, non-lactating
- Must abstain from alcohol or caffeine from 48 hours before study confinement through study
- Must not have taken prescribed medication in 14 days before dosing, or OTC drugs and herbal remedies within 7 days before dosing (except vitamins, minerals, paracetamol, HRT)
- Other routine screening criteria to include exclusion concurrent illness and clinical laboratory values or history



# Demographics of SAD and MAD cohorts

	SAD (N=32)	MAD (N=24)
<b>Age (Years)</b>		
Mean	33.0 ± 11.1	25.8 ± 5.7
Median	30.0	24.0
Range	18-54	19-39
<b>Male, n (%)</b>	18 (56%)	18 (75%)
<b>Ethnicity, n (%)</b>		
Hispanic or Latino	5 (16%)	2 (8%)
Not Hispanic or Latino	27 (84%)	22 (92%)
<b>Race, n (%)</b>		
American Indian or Alaska Native	0	0
Native Hawaiian or Other Pacific Islander	0	2 (8%)
White	22 (69%)	15 (63%)
Black or African American	0	1 (4%)
Asian	5 (16%)	5 (21%)
Multiple	5 (16%)	1 (4%)

# SAD: Summary of Treatment-Emergent Adverse Events

System Organ Class (SOC) Preferred Term (PT)	CC-42344 Fasted (N=24) n (%) E	Placebo Fasted (N=8) n (%) E	All Subjects (N=32) n (%) E
<b>Subjects with at Least One TEAE</b>	10 (42%) 14	4 (50%) 6	17 (53%) 23
<b>Nervous system disorders, n (%)</b>	5 (21%) 5	4 (50%) 4	9 (28%) 9
Headache	3 (13%) 3	3 (38%) 3	6 (19%) 6
Dizziness	1 (4%) 1	0	1 (3%) 1
Muscle contractions involuntary	0	1 (13%) 1	1 (3%) 1
Sensory disturbance	1 (4%) 1	0	1 (3%) 1
<b>Musculoskeletal and connective tissue disorders, n (%)</b>	2 (8%) 2	1 (13%) 1	3 (9%) 3
Limb discomfort	1 (4%) 1	0	1 (3%) 1
Muscular weakness	0	1 (13%) 1	1 (3%) 1
Musculoskeletal stiffness	1 (4%) 1	0	1 (3%) 1
<b>Gastrointestinal disorders, n (%)</b>	2 (8%) 2	0	2 (6%) 2
Gastroesophageal reflux disease	1 (4%) 1	0	1 (3%) 1
Vomiting	1 (4%) 1	0	1 (3%) 1

n: Number of subjects, E: Number of adverse events

# MAD: Summary of Treatment-Emergent Adverse Events

System Organ Class (SOC) Preferred Term (PT)	CC-42344	Placebo	All
	Fed (N=18) n (%) E	Fed (N=6) n (%) E	Subjects (N=24) n (%) E
<b>Subjects with at Least One TEAE</b>	12 (67%) 27	4 (67%) 11	16 (67%) 38
<b>Injury, poisoning and procedural complications</b>	5 (28%) 7	1 (17%) 1	6 (25%) 8
Vascular access site dermatitis	1 (6%) 2	0	1 (4%) 2
Palate injury	1 (6%) 1	0	1 (4%) 1
Scratch	1 (6%) 1	0	1 (4%) 1
Sunburn	0	1 (17%) 1	1 (4%) 1
Vascular access site bruising	1 (6%) 1	0	1 (4%) 1
Vascular access site pain	1 (6%) 1	0	1 (4%) 1
Vascular access site swelling	1 (6%) 1	0	1 (4%) 1
<b>Nervous system disorders</b>	5 (28%) 6	1 (17%) 2	6 (25%) 8
Headache	4 (22%) 5	1 (17%) 2	5 (21%) 7
Presyncope	1 (6%) 1	0	1 (4%) 1
<b>General disorders and administration site conditions</b>	4 (22%) 6	1 (17%) 1	5 (21%) 7
Fatigue	2 (11%) 2	1 (17%) 1	3 (13%) 3
Catheter site pain	2 (11%) 2	0	2 (8%) 2
Vessel puncture site bruise	2 (11%) 2	0	2 (8%) 2

n: Number of subjects, E: Number of adverse events



# Topline Safety Data Summary

SAD cohorts	MAD cohorts
<b>Overall treatment-emergent AE (TEAE) rate</b> <ul style="list-style-type: none"><li>42% (10/24) in CC-42344 cohorts</li><li>50% (4/8) in placebo subjects</li></ul>	<b>Overall treatment-emergent (TEAE) rate</b> <ul style="list-style-type: none"><li>67% (12/18) in CC-42344 cohorts</li><li>67% (4/6) in placebo subjects</li></ul>
<b>Headache was the most frequently reported TEAE</b> <ul style="list-style-type: none"><li>3/24 or 13% in CC-42344 cohorts</li><li>3/8 or 38% in placebo subjects</li></ul>	<b>Headache was the most frequently reported TEAE</b> <ul style="list-style-type: none"><li>4/18 or 22% in CC-42344 cohorts</li><li>1/6 or 17% in placebo subjects</li></ul>

# CC-42344 Oral PB2 Inhibitor Shows a Highly Favorable Safety and Tolerability Profile with Oral administration to healthy volunteers

## Phase 1 SAD and MAD summary and next steps

- Phase 1 study healthy volunteer study completed:
  - **No serious or grade 3 AEs reported**
  - **No treatment discontinuations**
  - **No clinically significant observations noted in laboratory assessments, vital signs, physical exam findings, or ECGs**
  - **PK results pending**
- Phase 2a human challenge study planned in 2H of 2023
  - CRO: hVIVO, Queen Mary's Bioenterprise Centre, London, UK
  - Study design: randomized, double-blind, placebo-controlled in healthy volunteers treated after inoculation with an influenza strain

# CC-42344: Potential to Be Best-in-Class Influenza A PB2 Inhibitor

✓	<b>Broad-spectrum activity</b>	<b>Activity against pandemic and seasonal influenza A strains and drug resistant strains</b>
✓	<b>Potency and resistance</b>	<b>Single digit nanomolar potency with high barrier to resistance</b>
✓	<b>Mechanism of Action</b>	<b>Novel inhibition mechanism</b>
✓	<b>Combination regimen</b>	<b>Strong synergistic effects with approved influenza antivirals and no DDI issues</b>
✓	<b>Safety profile</b>	<b>Phase 1 – SAD and MAD completed Highly favorable safety and tolerability profile with Oral administration to healthy volunteers</b>





# Influenza A Oral Inhibitor CC-42344

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

