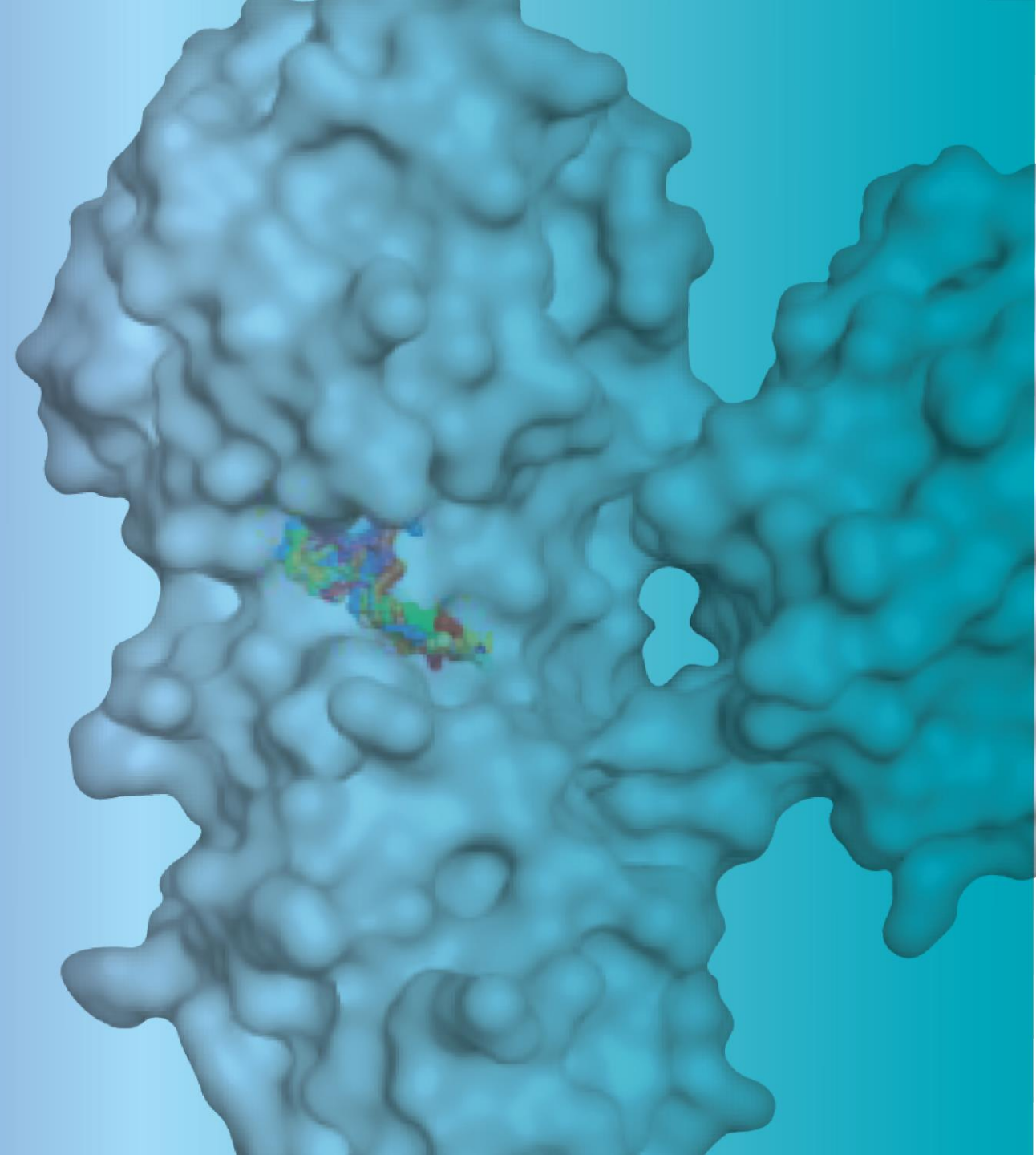




Potent antivirals to combat  
some of the most serious  
diseases facing humanity

February 2022

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



# 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; expected results of our collaboration with Merck Sharp & Dohme Corp. ("Merck"), the potential future payments and royalties in connection with the collaboration; with the expected future characteristics and progress in developing a compound for the effective treatment and prevention of COVID-19 infections and the anticipated timing of achieving the value-driving milestones, including planned initiation of two COVID-19 Phase 1 trials in 2022 for two product candidates; the expected progress of our Influenza A program including Phase 1 subject enrollment in the first quarter of 2022; the expected progress of our norovirus program and the anticipated timing of achieving the value-driving milestones, including preclinical lead selection planned for 2022-2023; 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 the COVID-19 pandemic 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, possible delays resulting from lockdowns in Australia, 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, 2020. 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.

*Applying powerful, proprietary drug discovery platform technology to develop first- and best-in-class broad-spectrum antiviral drugs*

## **Advancing programs in high-value antiviral drug targets**

- Pandemic SARS-CoV-2, SARS-CoV-2 variants, and coronaviruses
- Pandemic and seasonal influenza A
- Norovirus gastroenteritis

## **Drug candidates with clinically validated mechanisms of action**

- Effectively cure viral diseases
- Broad-spectrum and potent antiviral activity
- Designed to be effective for emerging variants and existing drug resistant viruses

## **Proprietary drug discovery platform technology**


- Unique drug discovery platform technology developed with Nobel Prize-winning technology

*Focused on advancing a robust product pipeline toward commercialization*

# Investment Highlights

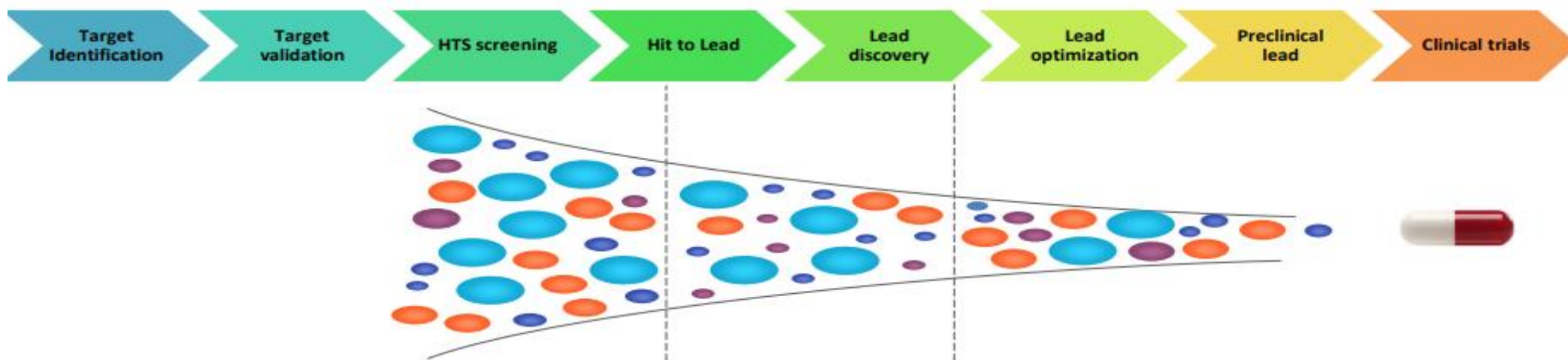
- Targeting large, global markets for the treatment of acute and pandemic viral diseases
- Proprietary drug discovery platform technology
- Advancing COVID-19 and influenza programs
  - COVID-19 oral protease inhibitor – Planned Phase 1 trial initiation in 2022
  - COVID-19 CDI-45205 lead molecule selected – Planned Phase 1 trial initiation in 2022
  - Influenza A CC-42344 (oral administration) – Initiation of Phase 1 subject enrollment expected in 1Q22
- Merck collaboration for influenza A/B therapeutic validates Cocrystal's drug discovery platform technology with potential for up to \$156 million in milestone payments + royalties
- Seasoned leadership includes experienced management, senior scientists and two Nobel laureates
- Cost-efficient operations and clean capital structure; cash sufficient to fund planned operations

# Robust Therapeutic Pipeline Addressing Unmet Medical Needs

Program		Discovery	Preclinical	Phase 1	Phase 2	Phase 3
COVID-19	Oral Protease Inhibitors	Planned Phase 1 trial initiation in 2022				
COVID-19 (Licensed)	CDI-45205 Protease Inhibitor	Planned Phase 1 trial initiation in 2022				
COVID-19	Replication Inhibitors	Discovery ongoing				
Influenza A	CC-42344 PB2 Inhibitor	Phase 1 trial enrollment expected to begin in 1Q22				
Influenza A/B	Influenza A/B Inhibitor	In collaboration with  MERCK				
Hepatitis C (HCV)	CC-31244 Pan-genotypic NS5B NNI	Available for partnering				
Norovirus Gastroenteritis	Replication and Protease Inhibitors	Preclinical lead selection planned for 2022-2023				

# Platform Provides Rapid, Efficient Drug Discovery and Development

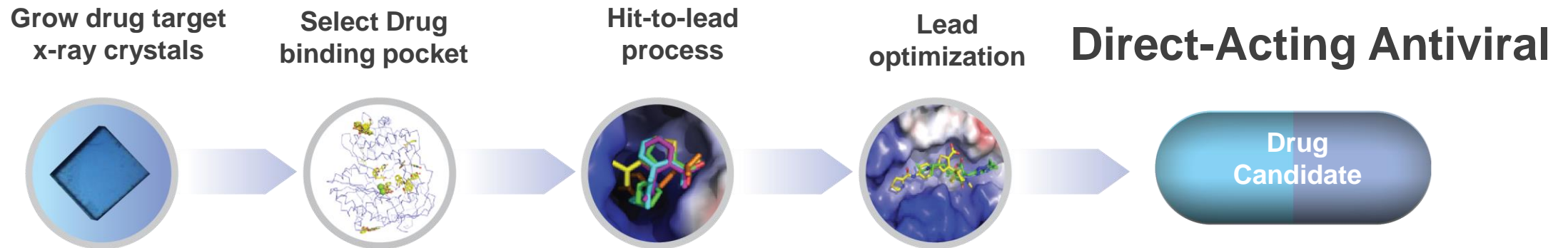
Traditional antiviral drug discovery and development can be long, costly and risky, with high rates of attrition



Cocrystal's technology platform provides potential for viable drug candidates at reduced costs and with shorter discovery and development timelines

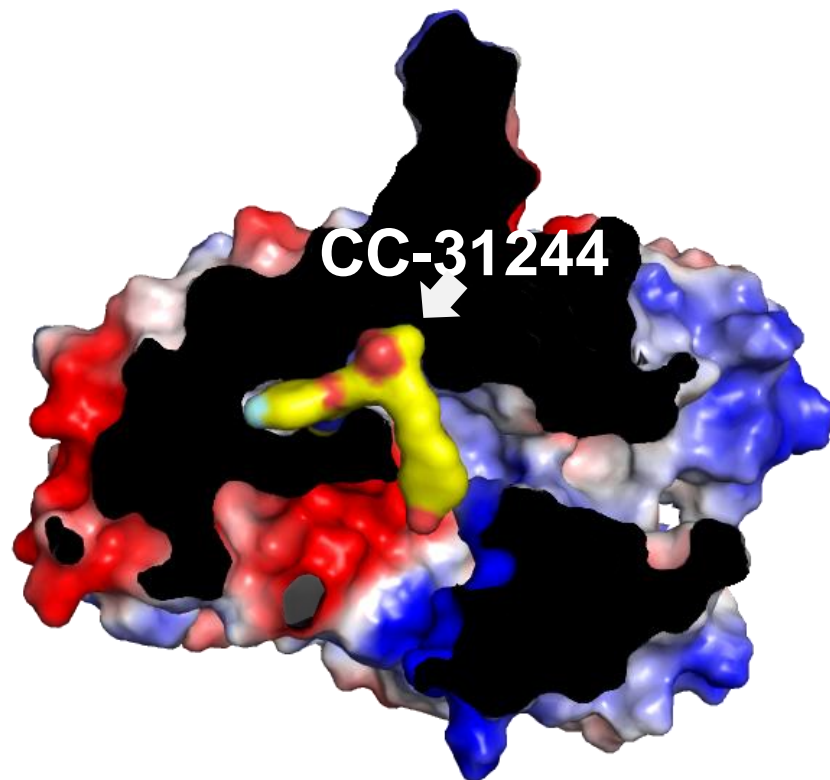
# Proprietary Drug Discovery Platform Technology for Direct-Acting Antivirals

Cocrystal's technology platform provides potential for novel drug candidates at reduced development timelines and costs



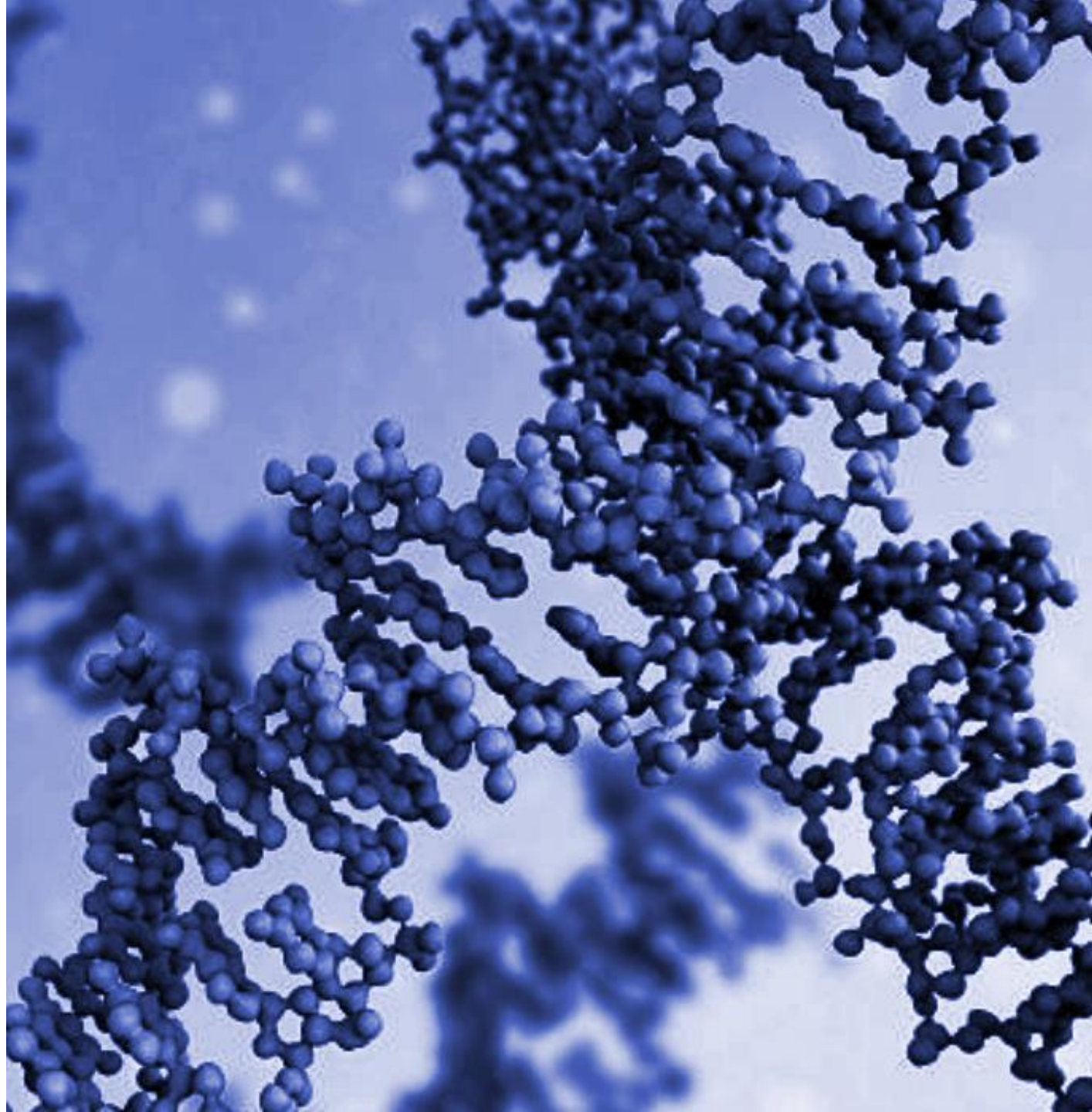
Provide high resolution 3D structures of drug target complexed with inhibitor at atomic level

# Robust Antiviral Drug Discovery Founded by Proprietary Technology



- Provide 3D structures of inhibitor protein complexes at near-atomic resolution with immediate insight to guide chemistry
- Identify novel drug binding pockets
- Design and develop broad-spectrum inhibitors with high barrier to drug resistance

# SARS-CoV-2 and SARS-CoV-2 Variants, and other Coronaviruses



# Significant Need for Antivirals to Combat Coronavirus Infections

- There is no approved COVID-19 antiviral prophylactic treatment
- Merck's molnupiravir and Pfizer's paxlovid (nirmatrevir plus ritonavir) received FDA emergency use authorization
- Coronaviruses constantly change through mutation<sup>1</sup>
- Multiple variants of COVID-19 have emerged<sup>1</sup>
- The original variant that caused the initial COVID-19 cases in January 2020 is no longer circulating as newer variants have increased<sup>2</sup>

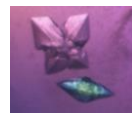
<sup>1</sup><https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html>

<sup>2</sup><https://www.cdc.gov/coronavirus/2019-ncov/variants/understanding-variants.html>

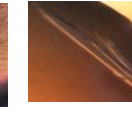
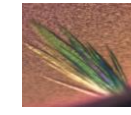
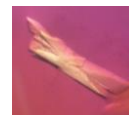
# Novel COVID-19 Preclinical Leads



SARS-CoV-2 main protease (1.8 Å)

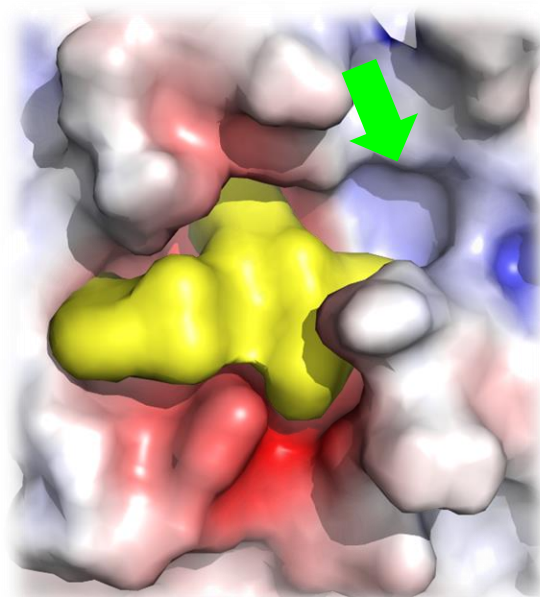


SARS-CoV-1 main protease (1.56 Å)



MERS-CoV main protease (1.9 Å)

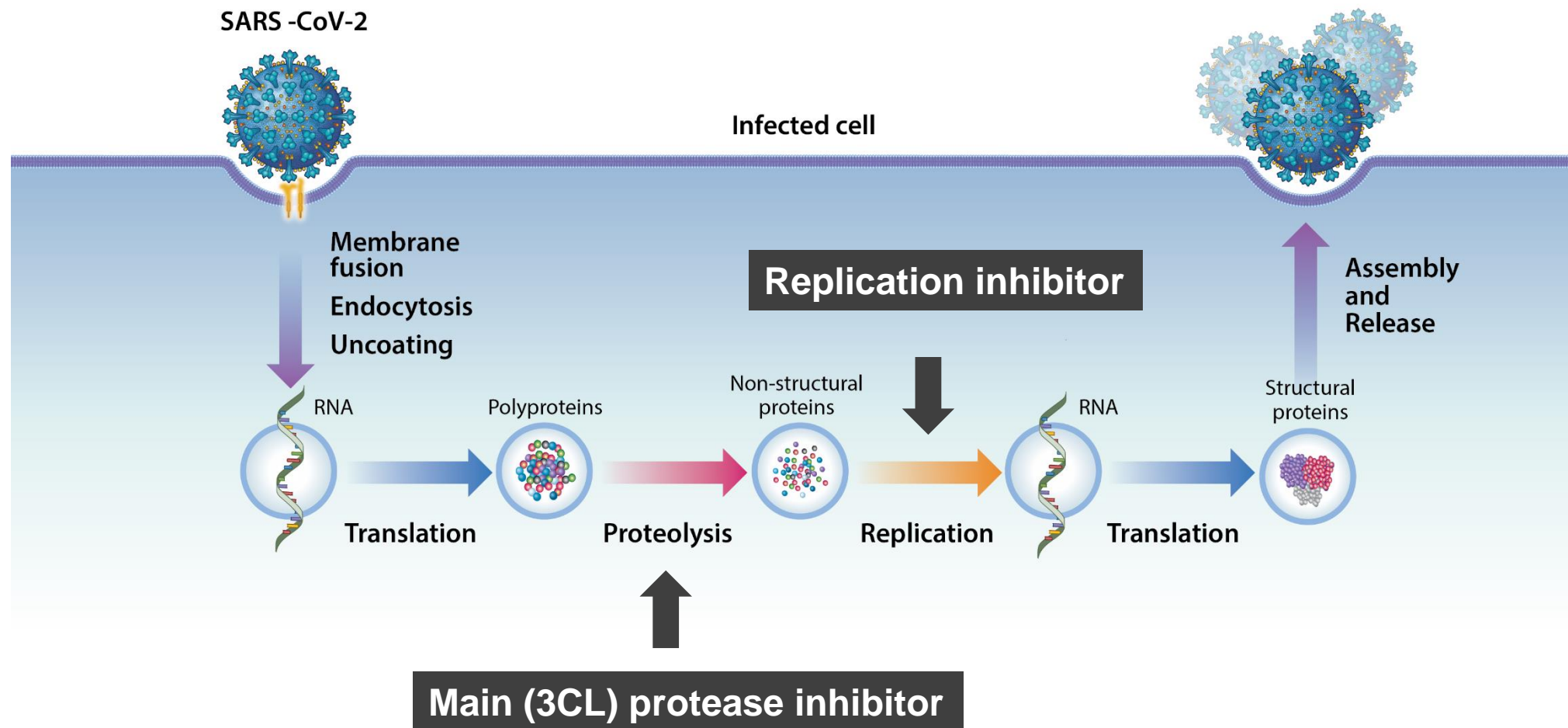
## Main (3CL) protease inhibitor



Cocrystal structure of SARS-CoV-2  
Main (3CL) protease

- Binds to a highly conserved, essential residue (Cys145) of SARS-CoV-2 main (3CL) protease and other coronavirus main (3CL) proteases
- Exhibits broad-spectrum activity against SARS-CoV-2 and its variants including Delta and Omicron variants
- Shows favorable ADMET and PK properties and *in vivo* efficacy in MERS-CoV infected mouse model

# COVID-19: How Cocystal Protease Inhibitor Will Work



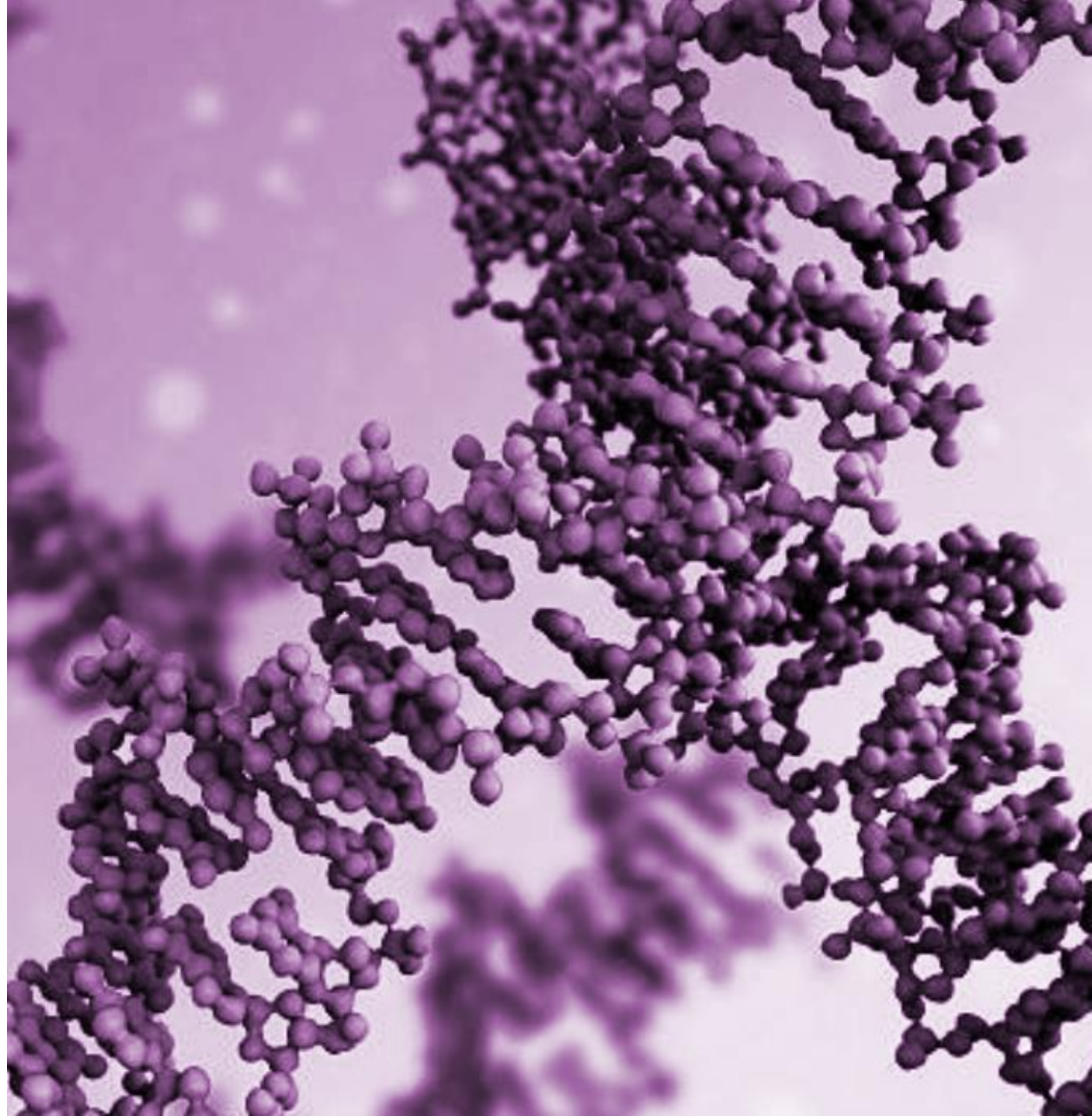
# COVID-19 Program Status

- Oral broad-spectrum protease inhibitor
  - Selected preclinical leads
  - Initiated scale-up synthesis
  - Planned clinical trial initiation in 2022
- Oral broad-spectrum replication inhibitors
  - Lead discovery ongoing
- Intranasal broad-spectrum protease inhibitor, CDI-45205
  - Licensed from Kansas State University Research Foundation (KSURF)
  - Completed exploratory toxicology study
  - Initiated scale-up synthesis and process chemistry development
  - Pre-IND briefing package submitted
  - Planned clinical trial initiation in 2022

# Clinical Trial Design for COVID-19 Protease Inhibitors

- Planned Phase 1 trial design for intranasal/pulmonary CDI-45205 and oral SARS-CoV-2 inhibitors
  - Randomized, placebo-controlled, double-blind, single-ascending-dose/multiple-ascending-dose trial
  - Healthy volunteers
  - Evaluate safety, tolerability, pharmacokinetics and the effect of food
- Planned Phase 2 trial design for intranasal CDI-45205 and oral SARS-CoV-2 inhibitors
  - Randomized, double-blind, placebo-controlled trial
  - Non-hospitalized patients with mild or moderate COVID-19
  - Change in viral load as primary outcome measure

# Influenza A Program



# Influenza: A Major Global Health Concern

- Worldwide: 1 billion cases<sup>1</sup>, 3-5 million severe illnesses<sup>2</sup> and up to 650,000 deaths<sup>1</sup> annually
- Not well managed with currently approved vaccines having only 10-60% efficacy<sup>1</sup>
- Current antivirals are burdened by significant viral resistance
  - Tamiflu® has long history of drug resistance<sup>3</sup>
  - Xofluza™ has shown emergence of drug resistant mutations<sup>4</sup>

<sup>1</sup>ResearchAndMarkets.com, *Transformative Influenza Vaccines, 2020*

<https://www.researchandmarkets.com/reports/5187584/transformative-influenza-vaccines-2020>

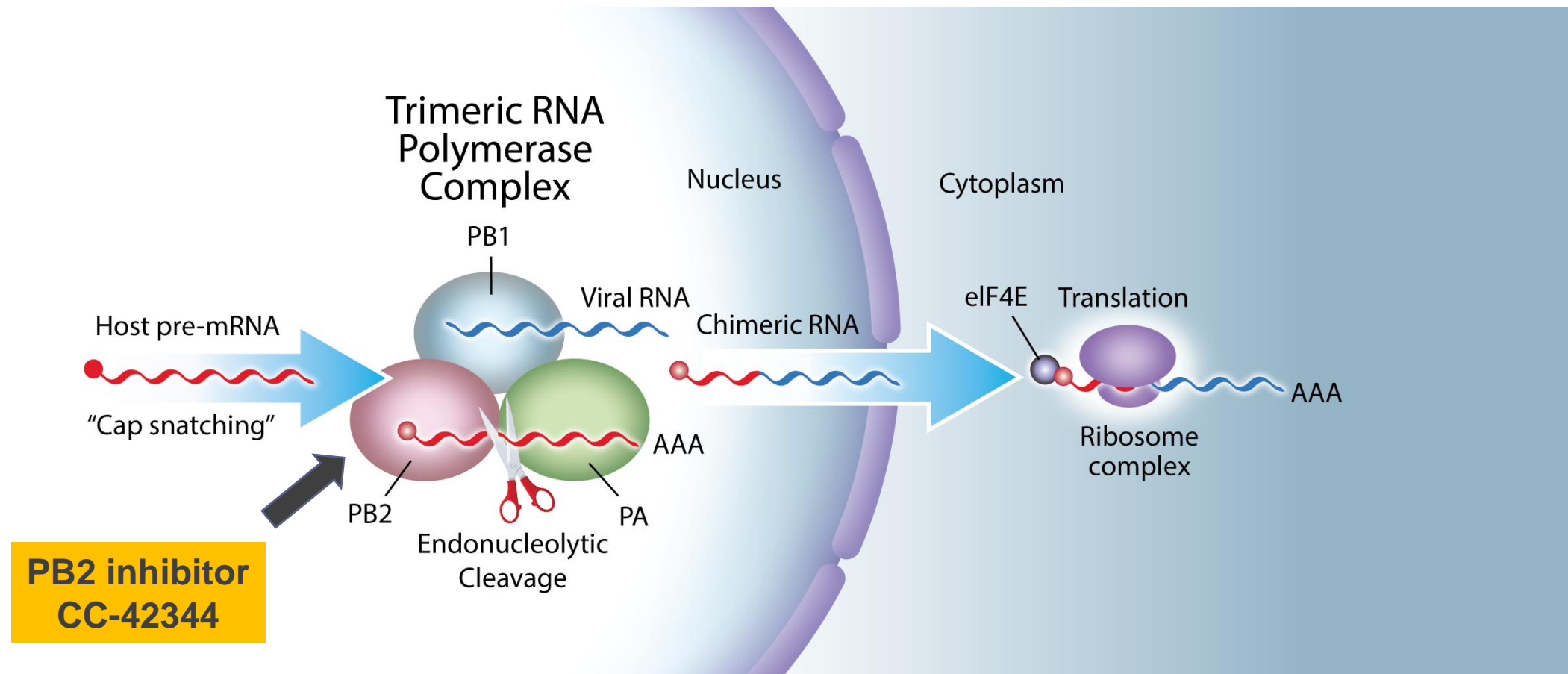
<sup>2</sup>World Health Organization (WHO): <https://www.medscape.com/answers/219557-3459/what-is-the-global-incidence-of-influenza>

<sup>3</sup>ScienceDaily (March 2014) Tamiflu-resistant influenza related to mutations in genome

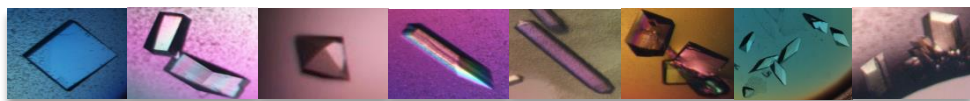
<sup>4</sup>NEJM Journal Watch (September 2018) A Promising Drug for Influenza?

# PB2 Inhibitor CC-42344 Blocks Influenza Viral Replication

Cap Binding (PB2), Endonuclease (PA), and Polymerase (PB1) are Essential for Influenza Viral Replication

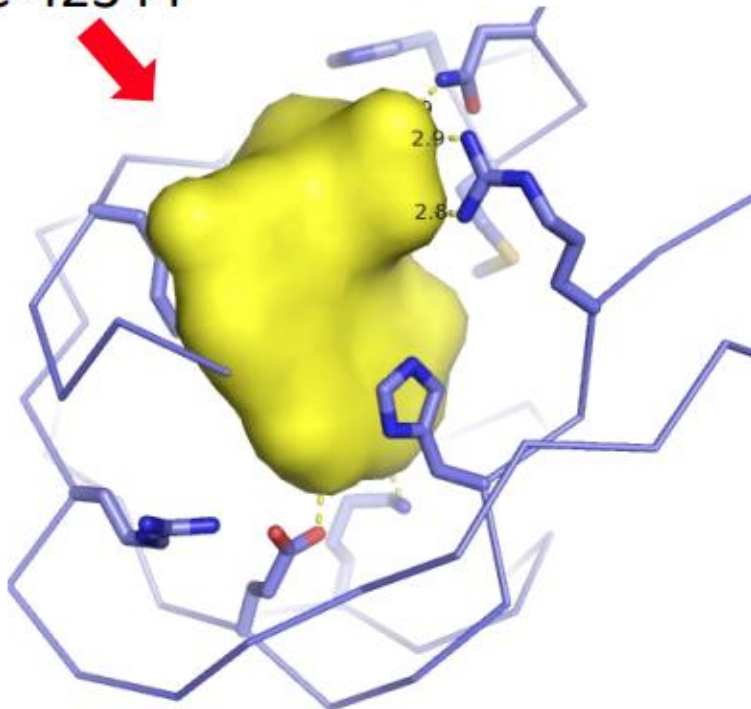


# CC-43244: Pandemic and Seasonal Influenza A Therapeutic



Pandemic and seasonal influenza A PB2 crystals

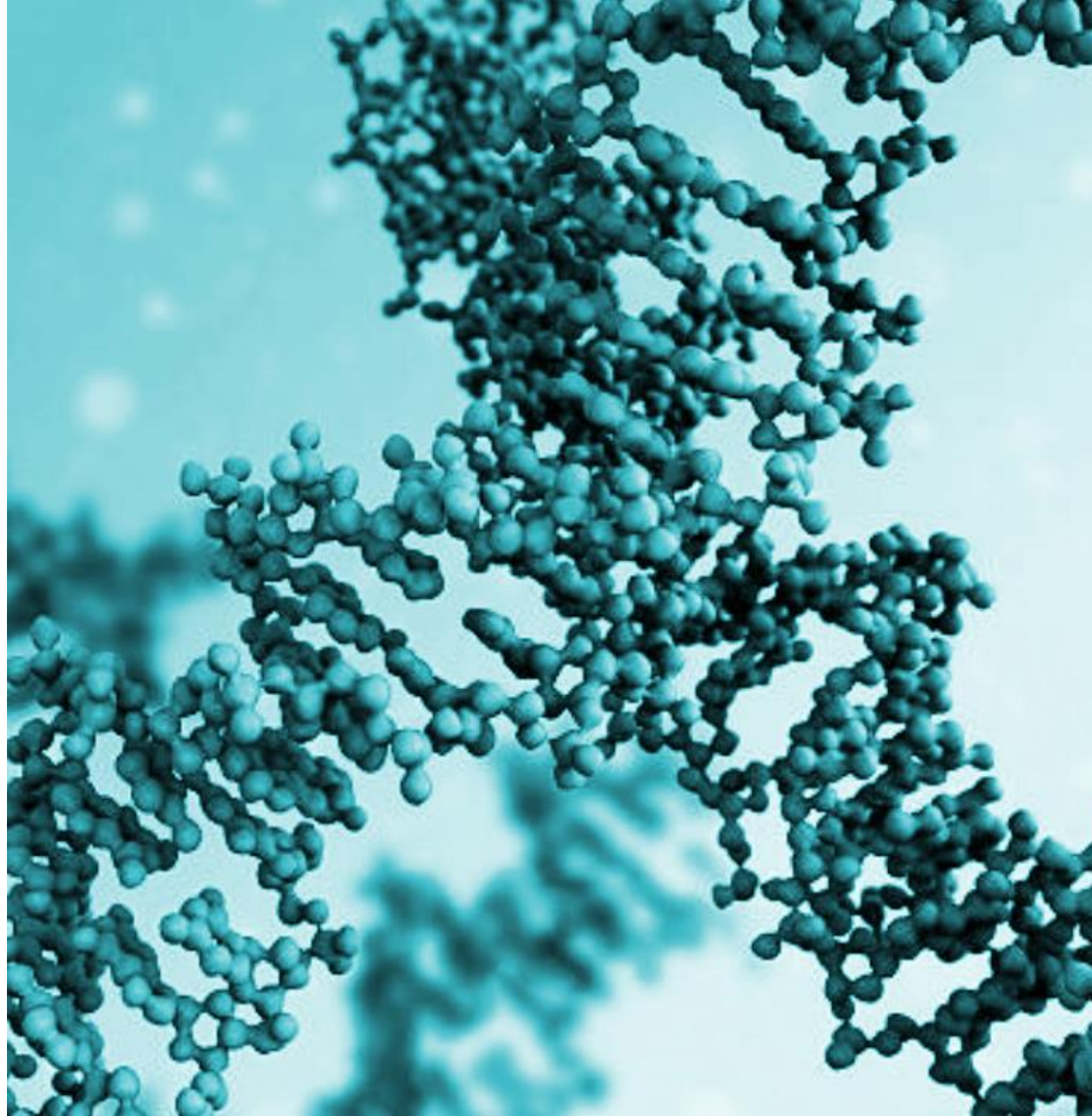
CC-42344



Cocrystal structure of CC-42344 (1.47 Å)

- PB2 inhibitor binds to highly conserved pocket on replication enzyme
- Exhibits excellent broad-spectrum activity against pandemic and seasonal strains, and activity against known resistant strains
  - Pandemic H1N1 and H1N1 Xofluza resistant, H3N2 and H3N2-oseltamivir resistant, H5N1 (avian flu), H7N7
- Has favorable pharmacokinetic and drug-resistance profiles
- Demonstrated strong *in vitro* synergistic effects in combination studies with Xofluza, Tamiflu and Favipiravir
- IND-enabling studies completed
- Received Australian regulatory approval to initiate Phase 1 study
- Enrollment expected to begin in 1Q22

# Influenza A/B Program with



# Collaboration Validates Technology with Potential for Lucrative Returns

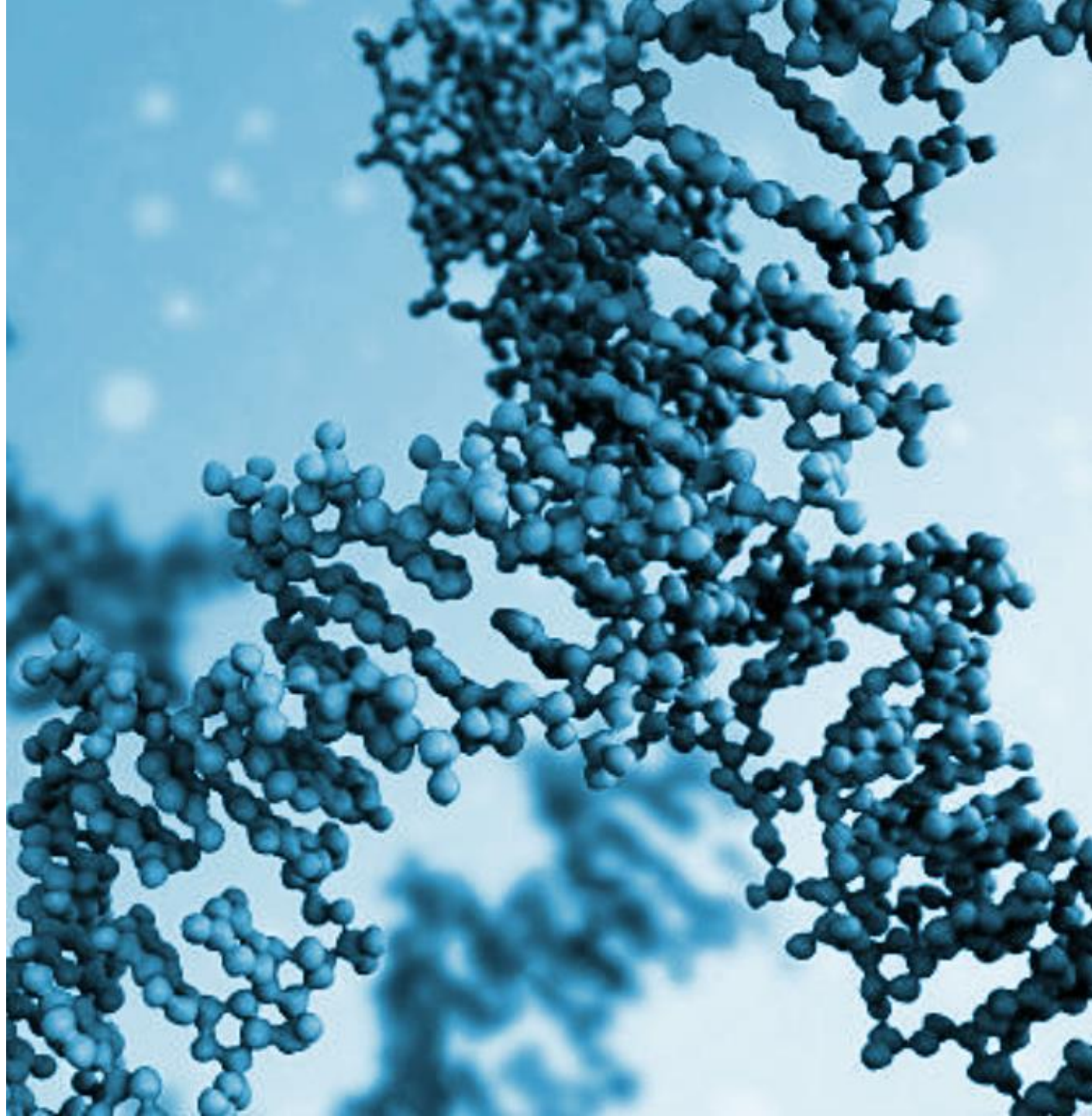
- Broad-spectrum, potent candidates developed to be active against seasonal, pandemic and existing drug-resistant influenza A and B strains
- Announced exclusive worldwide license and collaboration with Merck in January 2019

**Cocrystal eligible to receive up to \$156 million in milestone payments  
+ royalties on product sales**

- Agreement structure for first 2 years:
  - Cocrystal received \$4 million upfront and reimbursed R&D expenses
  - Jointly developed potent influenza A/B inhibitors
  - Cocrystal met all research collaboration agreement obligations
- Merck's responsibilities under current phase of agreement:
  - R&D, including clinical development and funding
  - Worldwide commercialization of product(s) derived from collaboration



# Norovirus Gastroenteritis Program



# Norovirus: Large Market with No Approved Treatments

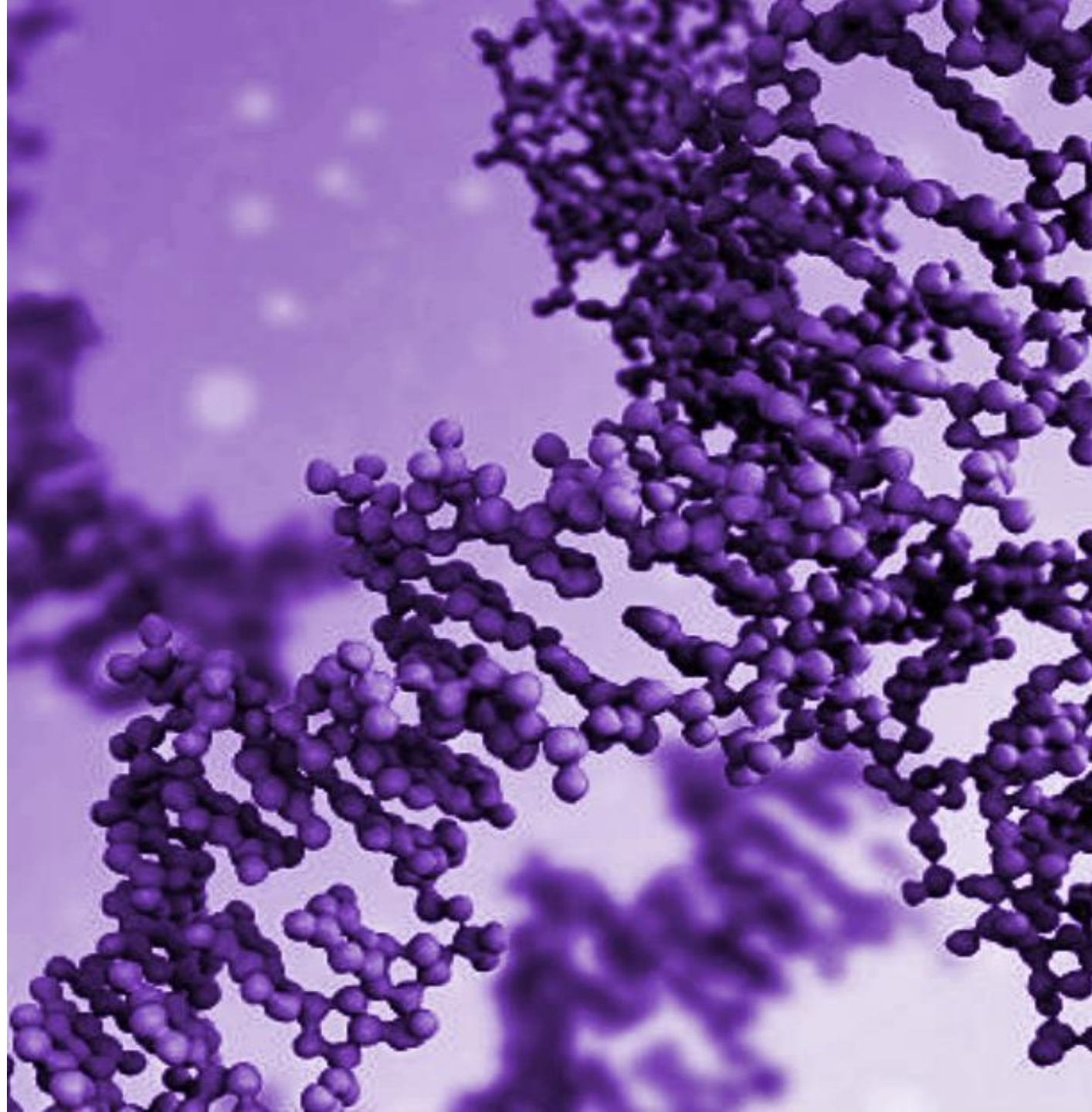
- Highly contagious virus that causes symptoms of acute gastroenteritis including nausea, vomiting, stomach pain and diarrhea
- Major cause of gastrointestinal illness in closed and crowded environments including hospitals, nursing homes, childcare facilities and cruise ships
- Responsible for approximately 685 million infections annually worldwide and nearly 90% of all epidemic, non-bacterial outbreaks of gastroenteritis<sup>1</sup>
- Estimated annual cost of \$60 billion worldwide due to direct healthcare costs and lost productivity<sup>1</sup>
- Between 19 million and 21 million cases and 109,000 hospitalizations annually in the U.S.<sup>1</sup>

<sup>1</sup>CDC, Norovirus Disease in the United States, 2020

# Developing Broad-Spectrum Norovirus Protease and Replication Inhibitors

- Broad-spectrum norovirus protease and replication inhibitors are being developed
- Ongoing drug discovery efforts
  - Oral protease inhibitor discovery using its proprietary drug discovery platform technology
  - Preclinical evaluation of KSURF licensed norovirus protease inhibitors
  - Proof-of-concept animal model studies with selected inhibitors
- Preclinical lead selection planned for 2022-2023

# Hepatitis C Program



# Hepatitis C: Increase in Rate of New Infections

- An estimated 58 million people worldwide have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year<sup>1</sup>
- An estimated 290,000 deaths occurred in 2019 worldwide due to hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer)<sup>1</sup>
- Rate of new hepatitis C infections in U.S. reported to CDC in 2018 was four times as high as 2010<sup>2</sup>
- Need for shorter duration of therapy with novel direct-acting antivirals

<sup>1</sup> WHO statistics: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>

<sup>2</sup> U.S. Health and Human Services statistics <https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/data-and-trends/index.html>

# CC-31244: HCV NNI Next-Generation Combination Cocktail Therapy

- Potential best-in-class HCV non-nucleoside inhibitor (NNI) with a strong profile
- Broad-spectrum, potent NS5B polymerase inhibitor with high barrier to resistance
- Effective against known NNI drug-resistant variants
- Once-a-day orally administered; liver targeting
- Phase 2a combination trial with favorable results<sup>1</sup>

*Seeking partner for clinical advancement of CC-31244 as a combination therapy*

<sup>1</sup>Trial design: first 2 weeks of CC-31244 + Epclusa, then additional 4 weeks of Epclusa only, for total of 6 weeks of treatment

# Seasoned Leadership

## Management

### Sam Lee, Ph.D.

*Interim Co-Chief Executive Officer & President*

25+ years of anti-infective drug discovery research experience, including HCV and influenza antivirals; played key role in early development of phosphoinositide 3-kinase (PI3K) delta inhibitor, Zydelig

**icòs**<sup>®</sup>

**Zydelig**

### James J. Martin, MBA, CPA

*Interim Co-Chief Executive Officer & Chief Financial Officer*

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

**VBI VACCINES**

**MOTUS**<sup>GI</sup>



**nims**

## Scientific Advisory Board

### Roger Kornberg, Ph.D.

*Chairman of the Board, Chairman of the Scientific Advisory Board*

- Professor  
Stanford University School of Medicine
- Nobel Laureate

### Michael Levitt, Ph.D.

*Member*

- Professor  
Stanford University School of Medicine
- Nobel Laureate

### Baek Kim, Ph.D.

*Member*

- Director of Center for Drug Discovery  
Emory University

### Bob Lehman, Ph.D.

*Member*

- Professor (Emeritus)  
Stanford University School of Medicine

### Gary Schoolnik, M.D.

*Member*

- Professor (Emeritus)  
Stanford University School of Medicine

### Roland Strong, Ph.D.

*Member*

- Professor  
Fred Hutchinson Cancer Research Center

### Christophe Verlinde, Ph.D.

*Member*

- Professor (Emeritus)  
University of Washington

# Expanding Intellectual Property Portfolio

## Coronavirus

- Issued patents in U.S. and major countries
- Pending U.S. provisional applications

## Pandemic Influenza A

- PB2 (influenza A inhibitor)
  - Pending applications in PCT and Taiwan
  - Pending U.S. provisional applications

## Influenza A/B

- Influenza A/B inhibitor
- Pending applications in U.S. and worldwide

## Norovirus

- Issued patents in U.S. and major countries
- Pending U.S. provisional applications

## HCV

### NS5B (NNI)

- Issued patents in U.S.
- Pending applications in U.S. and worldwide
- Pending U.S. provisional application

# Financial Snapshot

**~\$52 Million**  
Market cap

**759,000**  
Average 3 month  
daily share volume<sup>1</sup>

**\$61.6 Million**  
Cash/equivalents as of  
September 30, 2021

**97.5 Million**  
Common shares outstanding

**97.7 Million**  
Fully diluted shares

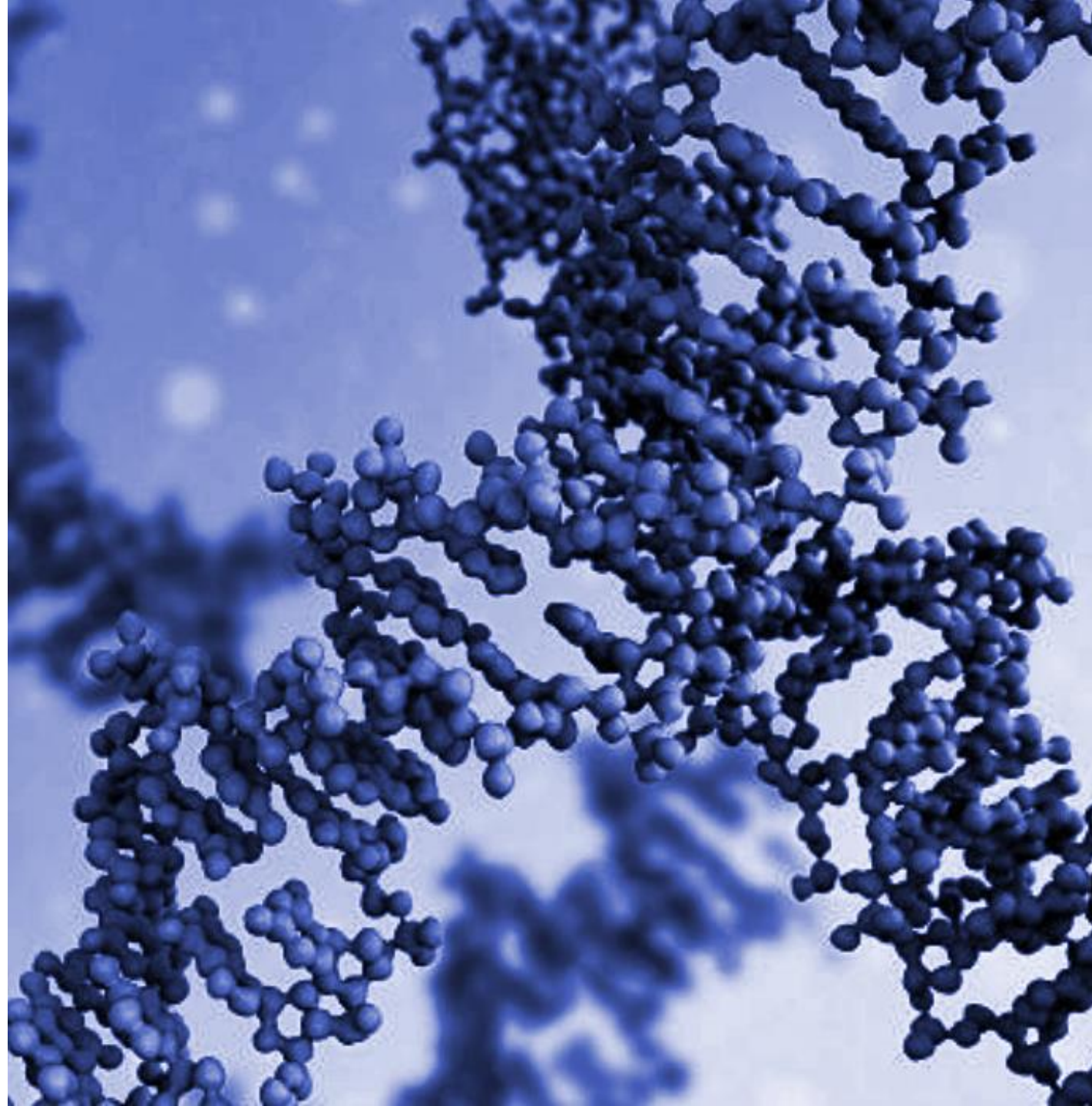
- Clean balance sheet
  - No preferred shares
  - No debt
- Only 243,000 warrants
- Cash sufficient to fund planned operations

<sup>1</sup> Yahoo Finance (Nov. 29, 2021)

# Summary

- Targeting large, global markets for the treatment of acute and pandemic viral diseases
- Proprietary drug discovery platform technology
- Advancing COVID-19 and influenza programs:
  - COVID-19 oral protease inhibitor – Planned Phase 1 trial in 2022
  - COVID-19 CDI-45205 lead molecule selected – Planned Phase 1 trial in 2022
  - Influenza A CC-42344, Phase 1 (oral administration) enrollment expected to begin in 1Q22
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- Cost-efficient operations and clean capital structure; cash sufficient to fund planned operations

# Appendix



# CC-31244: HCV NNI Next-Generation Combination Cocktail Therapy

- Potential best-in-class HCV non-nucleoside inhibitor (NNI) with a strong profile
- Broad-spectrum, potent NS5B polymerase inhibitor
- Effective against known NNI drug-resistant variants
- Orally administered; liver targeting

## **Favorable HCV Phase 2a trial results**

- 6 weeks of Epclusa® therapy including 2 weeks of CC-31244
- Treatment was well tolerated with no study discontinuations due to adverse events
- 8 of 12 subjects (67%) achieved both SVR12 and SVR24 (considered virologic cure)
- 4 patients had virologic relapse at Week 10, 4 weeks after completion of treatment
- 8 patients who achieved SVR had significantly higher frequency of CD8+ T cells compared with the 4 who relapsed, providing opportunities for personalized medicine