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Cocrystal Pharma's Co-CEOs Highlight Pioneering Approach to Antiviral Drug Candidates Targeting Influenza and Coronaviruses as Fall Flu and COVID Season Begins

*The Company's antiviral candidate for seasonal and pandemic influenza shows*in vitro *activity against the avian influenza A PB2 protein, whereas current influenza vaccines offer no protection against pandemic avian influenza*

BOTHELL, Wash., Oct. 31, 2024 (GLOBE NEWSWIRE) -- As the fall seasonal influenza and COVID season gets underway in the Northern Hemisphere, Cocrystal Pharma, Inc. (Nasdaq: COCP) ("Cocrystal" or the "Company") highlights the ability of the Company's innovative structure-based drug discovery platform technology to discover and develop novel broad-spectrum antivirals therapeutics to treat a wide range of viral diseases, including newly emerging pandemic strains such as recent H5N1 avian influenza identified in the US.

"As our nation enters the fall flu and COVID season and learns of the emerging highly pathogenic avian H5N1 influenza A strain in dairy cattle and humans, the need for more effective antivirals is clear. Current flu vaccines are developed for seasonal influenza strains, not for pandemic avian influenza strains. Also, treatment-emergent resistance to approved antivirals and transmission of resistant viruses has been a challenging issue," said Sam Lee, PhD, President and co-CEO of Cocrystal. "For example, the widespread oseltamivir (Tamiflu®) resistance of the pandemic avian influenza strains could create a serous public health situation. Clearly, there continues to be an unmet need for therapeutics with a high barrier to resistance.

"We believe our approach makes it possible to develop highly effective therapeutics for noroviruses, coronaviruses and influenza A because we target the highly conserved, essential function of viral enzymes, regardless of whether the strain is seasonal or pandemic," he added. "We recently revealed the high-resolution cocrystal structure of the avian influenza PB2 protein complexed with CC-42344, further confirming that our PB2 inhibitor CC-42344 binds to its highly conserved PB2 region, indicating activity against this strain."

Cocrystal's platform utilizes Nobel Prize-winning technology to develop a new class of direct-acting antivirals that work against enzymes that are essential for viral replication. The Company is evaluating its oral CC-42344 in a Phase 2a study in healthy subjects infected with a seasonal influenza A strain. Topline safety and tolerability results from this trial are expected by the end of 2024, and preparations are underway for an Investigational New Drug (IND) application to conduct a late-stage clinical study with CC-42344 in the U.S.

The Company is also conducting a Phase 1 study with its oral protease inhibitor CDI-988, the first pan-viral drug candidate in clinical evaluation for both noroviruses and coronaviruses. Topline safety and tolerability results of the multiple-ascending cohorts are expected late this year or early next year. There is no approved vaccine or antiviral for norovirus. Norovirus is highly contagious and is the most common cause of acute gastroenteritis, which has gained notoriety for outbreaks in closed quarters such as on cruise ships and in nursing homes. According to the Centers for Disease Control and Prevention (CDC), an estimated 685 million cases and an estimated 200,000 deaths are attributed to norovirus each year worldwide, with an estimated societal cost of approximately $60 billion.

“We view the next viral pandemic as a question of timing as seasonal viruses like flu and COVID continue to evolve,” said James Martin, CFO and co-CEO of Cocrystal. “Our proprietary technology platform allows us to efficiently discover and develop potent, broad-spectrum, effective antiviral drug candidates for pandemic and seasonal outbreaks relatively quickly and far less costly than traditional approaches to drug development. As a small company, Cocrystal is highly efficient in utilizing our groundbreaking technology to develop differentiated antivirals for high-value indications with the goal of improving people’s lives.”

Avian Influenza

A multistate outbreak of highly pathogenic avian influenza in dairy cows was initially reported in March 2024. This is the first time that avian flu viruses were found in cows, with outbreaks now confirmed in herds in 14 states. In April 2024 the CDC confirmed an avian flu infection in a person exposed to dairy cows that were presumed to be infected with the virus. This is believed to be the first instance of likely mammal to human spread of this virus. In September 2024 the CDC reported the first human case of avian influenza without a known occupational exposure to sick or infected animals. As of October 30, 2024, the CDC has reported 36 human cases of this highly pathogenic avian influenza A in the U.S. during 2024.

The CDC analyzed blood collected from people of all ages in all 10 Health & Human Services regions during the 2022-2023 and 2021-2022 flu seasons. These samples were challenged with the avian flu subtype H5N1 virus to determine whether there was an antibody reaction. Data from this study suggest that there is extremely low to no population immunity to clade 2.3.4.4b A (H5N1) viruses in the U.S. Antibody levels remained low regardless of whether or not participants received a seasonal flu vaccination, meaning that seasonal flu vaccination did not produce antibodies to avian flu H5N1 viruses.

Antiviral Influenza Candidate CC-42344

CC-42344 is Cocrystal’s novel, broad-spectrum investigational antiviral candidate for the treatment of pandemic and seasonal influenza A. CC-42344 inhibits the first step in influenza A’s viral replication by binding to a highly conserved PB2 site of the influenza polymerase complex that is essential to replication and was discovered using Cocrystal’s proprietary structure-based drug discovery platform technology.

Cocrystal is evaluating safety, viral and clinical measures of oral CC-42344 in healthy volunteers who are challenged with influenza A in a Phase 2a human challenge study underway in the United Kingdom. CC-42344 was advanced into this study following favorable safety and tolerability results reported in a Phase 1 study in healthy volunteers conducted in Australia. *In vitro* testing showed CC-42344’s excellent antiviral activity against influenza A strains, including pandemic and seasonal strains, as well as against strains resistant to Tamiflu® and Xofluza®, while also demonstrating favorable pharmacokinetic and

safety profiles.

Cocrystal used its structure-based platform to determine the high resolution X-ray crystal structure of the recent avian influenza A (H5N1) PB2 protein, and confirmed activity of CC-42344 *in vitro* (NIH GeneBank ID:influenza A/Texas/37/2024(H5N1). The crystal structure of the avian influenza A (H5N1) PB2 protein showed new mutations located outside the PB2 active site. Subsequent studies showed that CC-42344 binds to the active site of the avian influenza A (H5N1) PB2 protein as previously demonstrated with the pandemic and seasonal influenza A PB2.

Structure-Based Platform Technology
Cocrystal's proprietary structural biology, along with its expertise in enzymology and medicinal chemistry, enable its development of novel antiviral agents. The Company's platform provides a three-dimensional structure of inhibitor complexes at near-atomic resolution, providing immediate insight to guide Structure Activity Relationships. This helps to identify novel binding sites and allows for a rapid turnaround of structural information through highly automated X-ray data processing and refinement. The goal of this technology is to facilitate the development of best-in-class antiviral therapies that have fast onset of action and/or shortened treatment time, are safe, well tolerated and easy to administer, are effective against all viral subtypes that cause disease and have a high barrier to viral resistance.

About Cocrystal Pharma, Inc.
Cocrystal Pharma, Inc. is a clinical-stage biotechnology company discovering and developing novel antiviral therapeutics that target the replication process of influenza viruses, coronaviruses (including SARS-CoV-2), noroviruses, and hepatitis C viruses. Cocrystal employs unique structure-based technologies and Nobel Prize-winning expertise to create first- and best-in-class antiviral drugs. For further information about Cocrystal, please visit www.cocrystalpharma.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the potential efficacy of Cocrystal's product candidates against certain viruses, ongoing research and development efforts including the expected timing of clinical studies and topline results for such product candidates, and the potential market for such product candidates. The words "believe," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "could," "target," "potential," "is likely," "will," "expect" and similar expressions, as they relate to us, are intended to identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events. Some or all of the events anticipated by these forward-looking statements may not occur. Important factors that could cause actual results to differ from those in the forward-looking statements include, but are not limited to, risks relating to our ability to obtain regulatory authority for and proceed with clinical trials including the recruiting of volunteers for such studies by our clinical research organizations and vendors, the results of such studies, our collaboration partners' technology and software performing as expected, general risks arising from clinical studies, receipt of regulatory approvals, regulatory changes, and potential development of effective treatments and/or vaccines by competitors, including as part of the programs financed by the U.S. government, and potential mutations in a virus we are targeting that

may result in variants that are resistant to a product candidate we develop. Further information on our risk factors is contained in our filings with the SEC, including our Annual Report on Form 10-K for the year ended December 31, 2023. Any forward-looking statement made by us herein 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.

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