



05 JUN 2025

# Antiviral Development Landscape for COVID-19 & Influenza

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ON BEHALF OF THE INTREPID ALLIANCE SCIENTIFIC WORKING GROUP

## **Disclaimer**

The INTREPID Alliance is a not-for-profit consortium of innovative biopharmaceutical companies committed to accelerating antiviral research, aiming to ensure that we have a stronger pipeline and are better prepared for future pandemics.

As part of our efforts, the INTREPID Alliance maintains and publishes a centralized list of promising investigational candidate compounds, with the purpose of knowledge-sharing and to support better pandemic preparedness. These compounds have been selected based on objective, scientific criteria, using publicly available sources, and at arm's length from commercial influence of our member companies. See criteria listed in the report "Antiviral Clinical Development Landscape and Promising Clinical Compounds." The designation of certain compounds as promising is based upon currently available information, and exclusively upon an assessment against these criteria. "Promising" is not a promotional claim. Candidate compounds have not been assessed by regulatory authorities to be safe and efficacious for the treatment of disease in humans. Our content is designed to be factual, informative, and non-commercial. It is not designed or intended to advertise or promote any pharmaceutical product or therapy or to advance the commercial interests of any company.



# Mission of INTREPID Alliance: Founded March 2022

The INTREPID Alliance is a non-profit consortium of eight pharmaceutical companies and affiliate organizations dedicated to accelerating the development of new treatments for emerging/future pandemic threats.



intrepidalliance.org



linkedin.com/company/intrepid-alliance



https://www.intrepidalliance.org/antiviral-pipeline/

## The INTREPID Alliance augments the antiviral R&D ecosystem by:

- Providing a landscape and listing\* of preclinical and clinical phase antivirals
- Generating publications on topics such as target compound profiles, animal/assay models, and "Deep Dives" on viral families
- Piloting an advisory program for biotechs and academia
- Advocating for the importance of antivirals as part of pandemic preparedness and will help catalyzed funding for antiviral R&D









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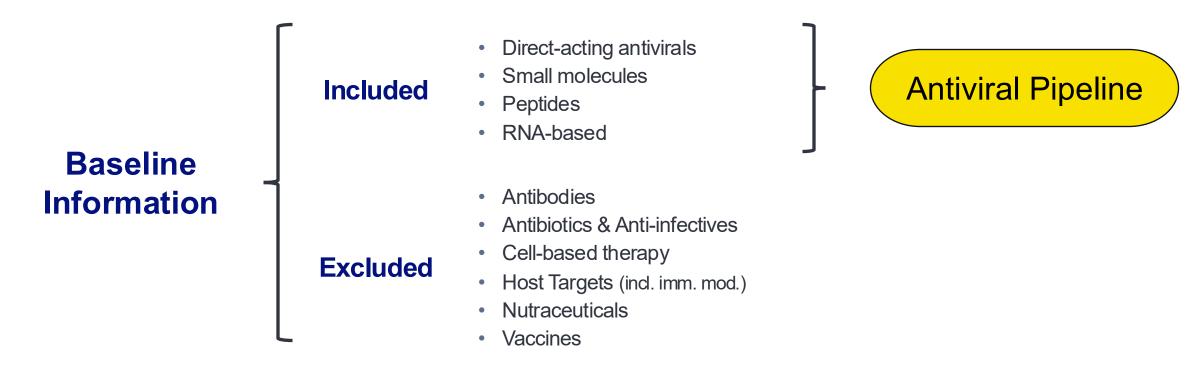






# INTREPID Alliance Landscape Analysis Components\*

- Airfinity monitors 13 viral families that pose the greatest risk of pandemic potential.
  - With thanks to Airfinity for its contributions to the presentation.



- ► Emerging information is reviewed on a semi-annual basis.
- Antiviral Landscape updated on the INTREPID Alliance website on a semi-annual basis.



<sup>\*</sup>Now 13 viral families to align with updated World Health Organization (WHO) Pathogens Prioritization report from June 2024.

# Intrepid Alliance Antiviral Landscape: Overview of 13 Priority Viral Families\*

As of December 18, 2024, for the 13 Viral Families with Greatest Risk of Pandemic Potential, Clinical Phase & Approved Antiviral Compounds Fall Into 9 of 13 and Preclinical Into 7 of 13

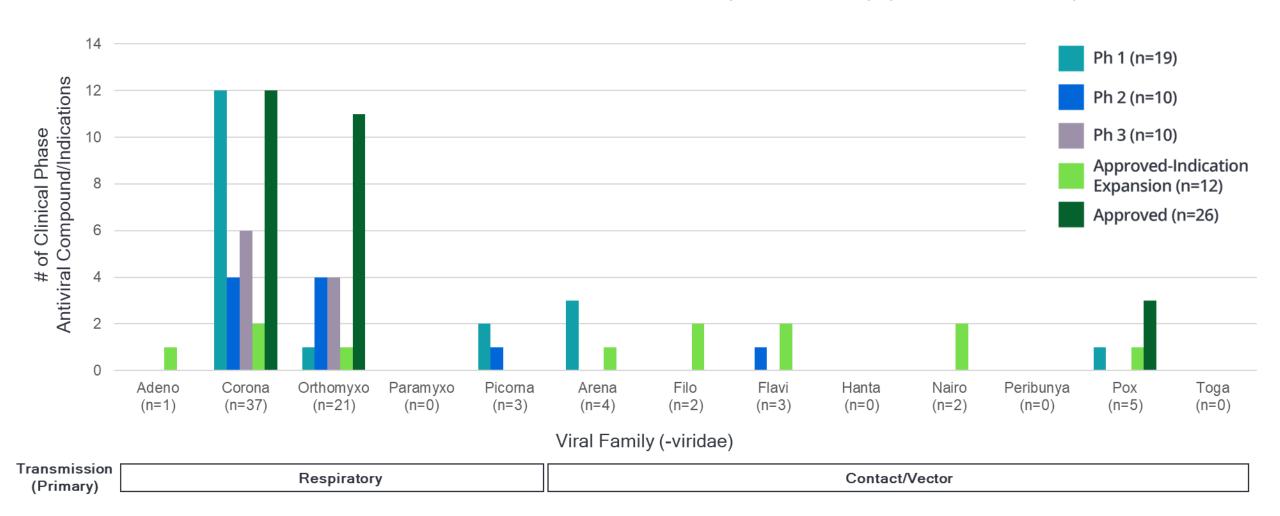
| Primarily Respiratory Transmission |   |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|
|                                    | Disease I   | Disease Indication (n)**                           |  |  |  |  |  |
| Pillar                             | Preclinical (103)   | Clinical (39)                                      |  |  |  |  |  |
| Adenoviridae                       | X   | <ul> <li>HuAdeno A-G (1)</li> </ul>                |  |  |  |  |  |
| Coronaviridae                      | <ul> <li>COVID-19 (74)</li> <li>MERS-CoV (5)</li> <li>SARS-CoV-1 (5)</li> <li>Seasonal CoV (1)</li> </ul> | • COVID-19 (25)                                    |  |  |  |  |  |
| Orthomyxoviridae                   | <ul> <li>Influenza (12)</li> </ul>  | <ul><li>Influenza (10)</li></ul>                   |  |  |  |  |  |
| Paramyxoviridae                    | <ul><li>Hendra virus (1)</li><li>Measles (1)</li><li>Nipah virus (3)</li><li>Parainfluenza (1)</li></ul>  | X  |  |  |  |  |  |
| Picornaviridae                     | X   | <ul><li>Polio (2)</li><li>Rhinovirus (1)</li></ul> |  |  |  |  |  |

| Primarily Contact/Vector-Mediated Transmission |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|
|  | Disease  | Disease Indication (n)**   |  |  |  |  |  |  |
| Pillar   | Preclinical (22)   | Clinical (13)  |  |  |  |  |  |  |
| Arenaviridae                                   | <ul><li>Junin virus (1)</li><li>Lassa fever (1)</li></ul>                                    | <ul><li>Lassa fever (3)</li><li>Chapare hem. fever (1)</li></ul> |  |  |  |  |  |  |
| Filoviridae                                    | X  | • Ebola (2)  |  |  |  |  |  |  |
| Flaviviridae                                   | <ul><li>Dengue (5)</li><li>West Nile (1)</li><li>Yellow fever (1)</li><li>Zika (2)</li></ul> | • Dengue (3)   |  |  |  |  |  |  |
| Hantaviridae                                   | X  | X  |  |  |  |  |  |  |
| Nairoviridae                                   | X  | Crimean Congo hem. fever (2)                                     |  |  |  |  |  |  |
| Peribunyaviridae                               | X  | X  |  |  |  |  |  |  |
| Poxviridae                                     | • Mpox (8)   | • Mpox (2)   |  |  |  |  |  |  |
| Togaviridae                                    | • Chikungunya (3)  | X  |  |  |  |  |  |  |

**X** = absence of preclinical or clinical phase antivirals

# The Majority of Clinical Phase Antiviral Compound/Indications Are Targeting Coronaviruses and Orthomyxoviruses\*

# Clinical Phase Antiviral Compound/Indications by Virus Family (4th Edition, N=78)

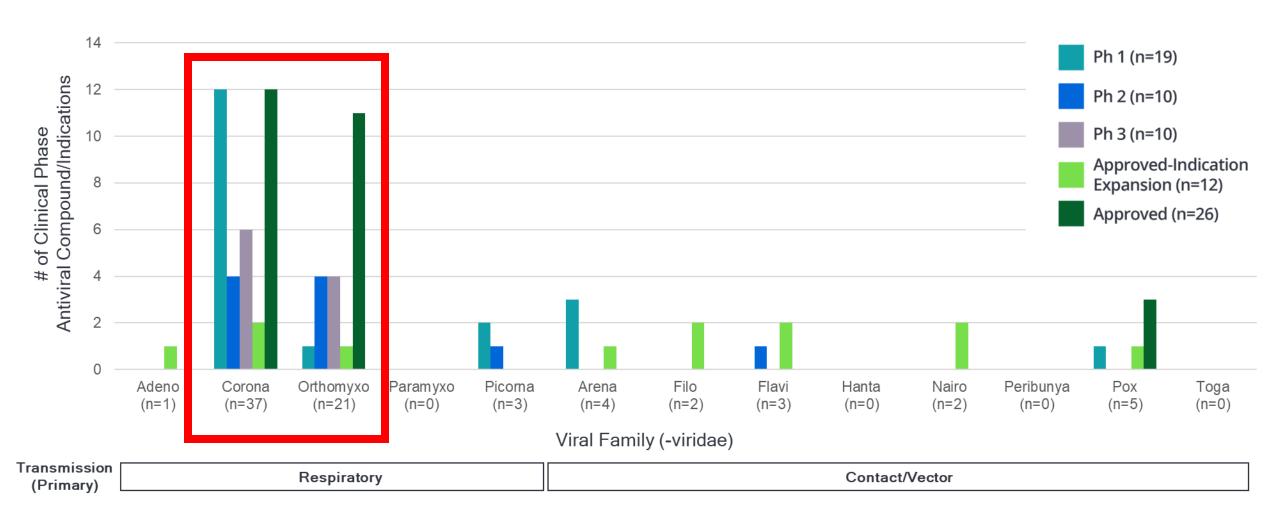


<sup>\*</sup>As of December 18, 2024. Adenoviridae has 1 clinical phase program listed in Archived.



# The Majority of Clinical Phase Antiviral Compound/Indications Are Targeting Coronaviruses and Orthomyxoviruses\*

# Clinical Phase Antiviral Compound/Indications by Virus Family (4th Edition, N=78)

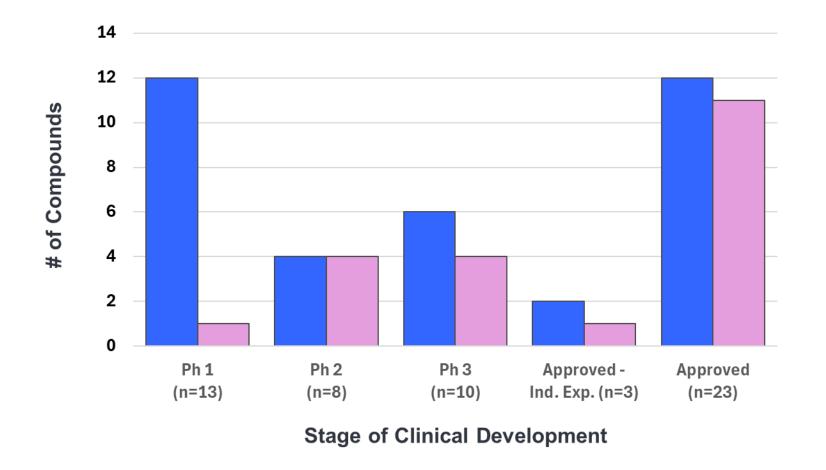


<sup>\*</sup>As of December 18, 2024. Adenoviridae has 1 clinical phase program listed in Archived.



## Antiviral Compounds for COVID-19 and Influenza Span the Stages of Clinical Development\*

Comparable numbers of late stage and approved compounds identified for COVID-19 and Influenza Early development (Phase 1) has more activity for COVID-19



COVID-19 (n=36)

- > 12 Approved compounds
- Ongoing Indication Expansion evaluations with 2 compounds already approved only for Influenza
  - Amantadine, Oseltamivir
- 10 compounds in Phase 2/3
- > 12 compounds in Phase 1

#### Influenza (n=21)

- > 11 Approved compounds
- Ongoing Indication Expansion evaluation with 1 compound currently approved only for COVID-19
  - Molnupiravir
- > 8 compounds in Phase 2/3
- 1 compounds in Phase 1



<sup>\*</sup>As of December 18, 2024; Number of compounds in ongoing development; Approved – Ind. Exp.= ongoing Indication Expansion evaluation with an antiviral approved for a different virus disease indication.

#### Protease Inhibitors Predominate the Antiviral Mechanisms of Action in Clinical Development for COVID-19\*

Compounds approved for COVID-19 are primarily protease or replication inhibitors. 68% (15/22) compounds in clinical development are SARS-CoV-2 main protease inhibitors. There are no active programs identified for compounds targeting assembly-release.

| Stage of    |               |        | ANTIVIRAL M              | ECHANISM OF AC          | TION                   |                       |                          |
|-------------|---------------|--------|--------------------------|-------------------------|------------------------|-----------------------|--------------------------|
| Development | EN7<br>(n = 1 |        | PROTEASE<br>(n = 4 + 15) |                         | REPLICATION<br>(n=7+1) |                       | ASSEMBLY-RELEASE (n = 0) |
| Approved    | Umifenovir    |        | Ensitrelvir              |                         | Molnupiravir           | Azvudine              |                          |
| (n=12)      |               |        | Nirmatrelvir/rtv         |                         | Remdesivir             | Enisamium (VR17-04)   |                          |
|             |               |        | Leritrelvir (RAY1216)    |                         | Favipiravir            | Triazavirin           |                          |
|             |               |        | Simnotrelvir/rtv         |                         |                        | Mindeudesivir (VV116) |                          |
| Phase 3     | YKYY017       |        | GST-HG171                | FB2001                  |                        |                       |                          |
| (n=6)       |               |        | QLS1128                  | WPV01                   |                        |                       |                          |
|             |               |        | STI-1558                 |                         |                        |                       |                          |
| Phase 2     |               |        | EDP-235                  |                         | SHEN26                 |                       |                          |
| (n=4)       |               |        | Ibuzatrelvir             |                         |                        | _                     |                          |
|             |               |        | HS 10517/Ritonavir       |                         |                        |                       |                          |
| Phase 1     | Delcetravir   | NV-387 | ALG-097558               | ISM3312                 |                        |                       |                          |
| (n=12)      | HY3000        | RQ-01  | ASC11/Ritonavir          | Limnetrelvir (ABBV 903) |                        |                       |                          |
|             | IPD-52520     |        | CDI-988                  | S-892216                |                        |                       |                          |
|             |               |        | GS-00202                 |                         |                        |                       |                          |



# Replication Inhibitors Predominate the Antiviral Mechanisms of Action in Clinical Development for Influenza\*

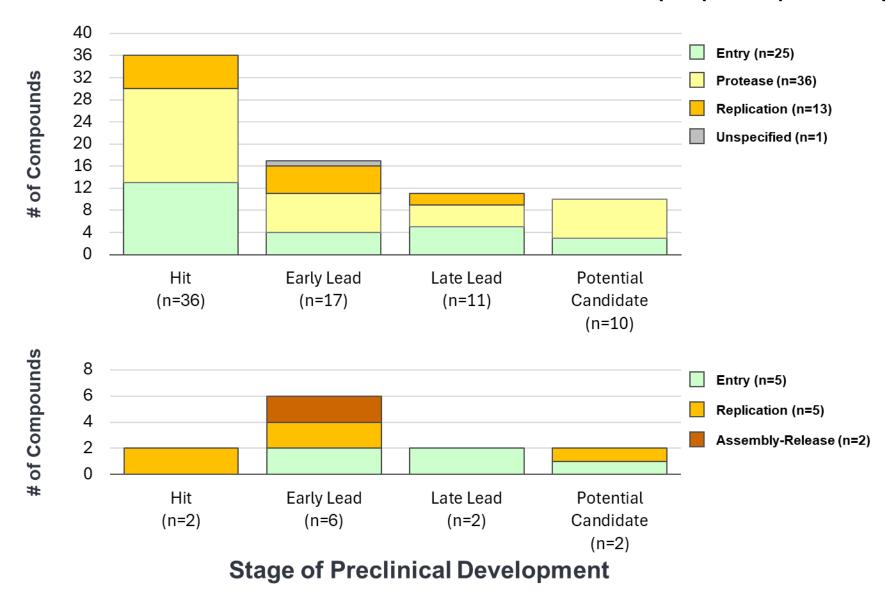
| Stage of         | ANTIVIRAL MECHANISM OF ACTION** |                        |                             |  |  |  |
|------------------|---------------------------------|------------------------|-----------------------------|--|--|--|
| Development      | ENTRY<br>(n=3+1)                | REPLICATION<br>(n=4+6) | ASSEMBLY-RELEASE<br>(n=4+2) |  |  |  |
| Approved         | Amantadine                      | Baloxavir Marboxil     | Laninamivir                 |  |  |  |
| (n=11)           | Rimantadine                     | Favipiravir            | Oseltamivir                 |  |  |  |
|                  | Umifenovir                      | Triazavirin            | Peramivir                   |  |  |  |
|                  |                                 | Enisamium (VR17-04)    | Zanamivir                   |  |  |  |
| Phase 3          |                                 | GP681                  |                             |  |  |  |
| (n=4)            |                                 | SHEN26                 |                             |  |  |  |
|                  |                                 | TG-1000                |                             |  |  |  |
|                  |                                 | ZX-7101A               |                             |  |  |  |
| Phase 2          | CD388                           | CC-42344               | HNC042                      |  |  |  |
| (n=4)            |                                 |                        | AV5080                      |  |  |  |
| Phase 1<br>(n=1) |                                 | TRX100 (AV5124)        |                             |  |  |  |

- ➤ Similar numbers of approved compounds for Influenza across antiviral mechanisms of action.
- ➤ In clinical development, replication inhibitors are the most common.
  - Primarily targeting viral polymerase or endonuclease



<sup>\*</sup>As of December 18, 2024; \*\* Host proteases mediate viral protein cleavage.

# The Majority of Active Preclinical Antiviral Programs Include Compounds for COVID-19 and Influenza Disease Indications (75 (59.5%) and 12 (9.5%) of 12, respectively)\*



#### COVID-19 (n=75)

- Protease inhibitors (36/75, 48%) and entry inhibitors (25/75, 33%) are distributed across the stages of preclinical development.
- The majority of protease inhibitors target the main protease (Mpro) whereas the entry inhibitors are evaluating different entry-related targets.

#### Influenza (n=12)

- ➤ 12 compounds of all the 51 Non-COVID-19 compounds (23.5%) across the entire preclinical landscape
- Entry inhibitors have the most representation in later stage preclinical



# Summary of INTREPID Alliance Preclinical and Clinical Development Landscape for COVID-19 and Influenza (4<sup>th</sup> Edition)\*

- Compounds targeting SARS-CoV-2 or influenza antiviral mechanisms of action predominate the preclinical and clinical antiviral landscape across 13 viral families with pandemic potential
- 20 distinct direct-acting antiviral compounds have regulatory approvals for COVID-19 or Influenza
  - 9 for COVID-19; 8 for Influenza; 3 for both COVID-19 and Influenza
- The majority of compounds with on-going preclinical and clinical activity are targeting:
  - COVID-19: the SARS-CoV-2 main protease
  - Influenza: the influenza viral proteins associated with replication
- Robust clinical evaluation and a viable regulatory strategy are needed to demonstrate:
  - The potential clinical benefit (e.g., safety and efficacy) addressing unmet medical need(s).
  - The potential utility for treating circulating viral variants resistant to current approved treatments
  - The barrier to development of resistance for each compound and compound class
  - The potential use of combination treatment strategies





# Interested in engaging with us?

We welcome all feedback through our online portal. As with previous listings, developers are invited to submit non-confidential information on their compound candidates. All reports are updated quarterly.

For more information, please feel free to email me at jim@intrepidalliance.org.

- intrepidalliance.org
- in linkedin.com/company/intrepid-alliance



# **Supplemental Information**



# Mission of INTREPID Alliance: Founded March 2022



The INTREPID Alliance is a consortium of eight pharmaceutical companies and affiliate organizations dedicated to accelerating the development of new treatments for emerging/future pandemic threats

The IA is supportive of and contributing to the 100 Days Mission (100 Days Mission June 2021) and the International Pandemic Preparedness Secretariat (IPPS) Science and Technology Group (STEG)



#### The INTREPID Alliance will generate a landscape and listing\* of antivirals that are:

- Phase 2-ready that can be quickly deployed into Phase 2/3 clinical trials following the identification of an emerging pandemic (i.e., as proposed by the 100-Days Mission)
- Preclinical stage compounds that may have utility against thirteen viral families identified by INTREPID Alliance as having potential to result in a pandemic
- The Alliance will help create efficiencies in antiviral R&D through publications such as target compound profiles; animal/assay other model landscaping; and by piloting an advisory program for biotechs and academia
- The Alliance will advocate the importance of antivirals as part of pandemic preparedness and will help catalyzed funding for antiviral R&D









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# INTREPID Alliance Antiviral Landscape: Our Approach

#### INTREPID Alliance Landscaping Activities

- Highlight strengths and weaknesses of the antiviral drug development pipeline for potential pandemic viral pathogens
- Support the 100 Days Mission (100DM) which seeks to identify two 'Phase 2 ready' therapeutic candidates against each of the identified viral pathogen families of greatest pandemic potential

#### Landscape Analysis

- A living analysis of the antiviral landscape that will be updated based on emerging data
- Derived from Airfinity database information on diverse compounds against 13 viral families (see slide 7)
- Focused on direct-acting small molecule antivirals

#### Timing and Publication on Website

- 1st Edition: Initial triage and selection of clinical compounds with favorable properties and antiviral mechanism of action January 2024
- 2nd Edition: Detailed review and identification of most Promising Clinical and Approved-Indication Expansion Compounds April 2024
- 3<sup>rd</sup> Edition: Quarterly update for Clinical Development Landscape; initial Antiviral Preclinical Development Landscape release; Mpox Clinical and Preclinical Landscape October 2024
- 4th Edition: Quarterly update for Clinical and Preclinical Antiviral Landscape April 2025
- Semi-Annual Updates Ongoing



## Landscape Analysis Components\*

Airfinity monitors 13 viral families that pose the greatest risk of pandemic potential. With thanks to Airfinity for its contributions to the presentation.

#### Baseline Information Identified:

- Diverse Compound/Indications by Viral Family and Disease
- Phase of Development (e.g., Preclinical through Phase 4, Approved)
- MOA/Target
- Route of Administration
- Developer or Sponsor (Type, Location)
- Clinical Trials (Links, Status, Trial Site Locations)

#### **Inclusion Criteria:**

- Preclinical & Clinical
  - Known antiviral MOA
  - In vitro/In vivo activity
  - Small molecules
  - Peptides
  - RNA-based
- Clinical
  - SAD/MAD data ongoing or completed
  - FIH ongoing or completed
  - No major safety signals

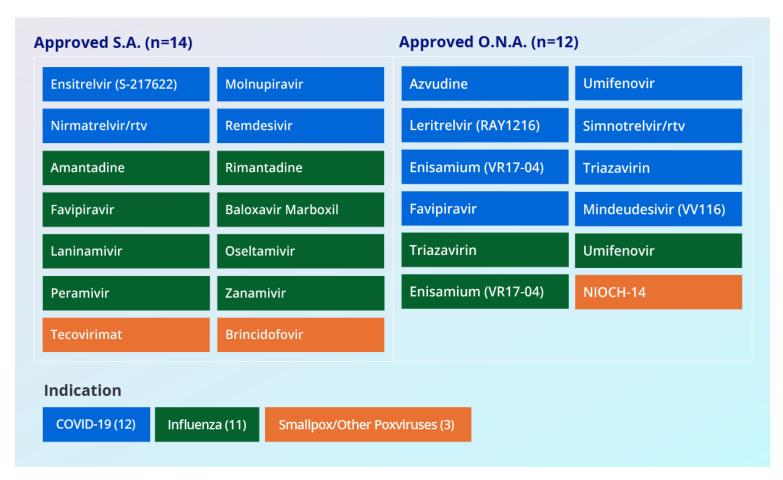
#### Figures & Tables:

- 13 Viral Families of Interest for Pandemic **Preparedness**
- Total Pipeline by Viral Family
- Promising Clinical and Indication-**Expansion Compounds**
- Compounds by Viral Family and Phase of Development
- Compounds by MOA/Target and Viral Family
- Phase of development vs viral disease for each MOA
- Developer or Sponsor
- Preclinical compounds
- Emerging information is reviewed on a semi-annual basis.
- Antiviral Landscape updated on the INTREPID Alliance website on a semi-annual basis.



<sup>\*</sup>Now 13 viral families to align with updated World Health Organization (WHO) Pathogens Prioritization report from June 2024. MOA: mechanism of action; SAD/MAD: Single Ascending Dose/Multiple Ascending Dose; FIH: first-in-human.

# Approved Antivirals: COVID-19, Influenza, Smallpox/Other Poxviruses\*



- 22 distinct antiviral compounds have received regulatory approval for COVID-19, Influenza, or Smallpox/Other Poxviruses
- 4 compounds are approved for COVID-19 and Influenza (favipiravir, triazavirin, umifenovir, and enisamium)
- 3 compounds have regulatory authorization by Animal Rule Development or similar mechanism
  - Tecoviramat is approved for Smallpox in U.S.
     & EU, and Cowpox and Mpox in EU only
  - Brincidofovir for Smallpox in U.S.
  - NIOCH-14 for Smallpox in Russia

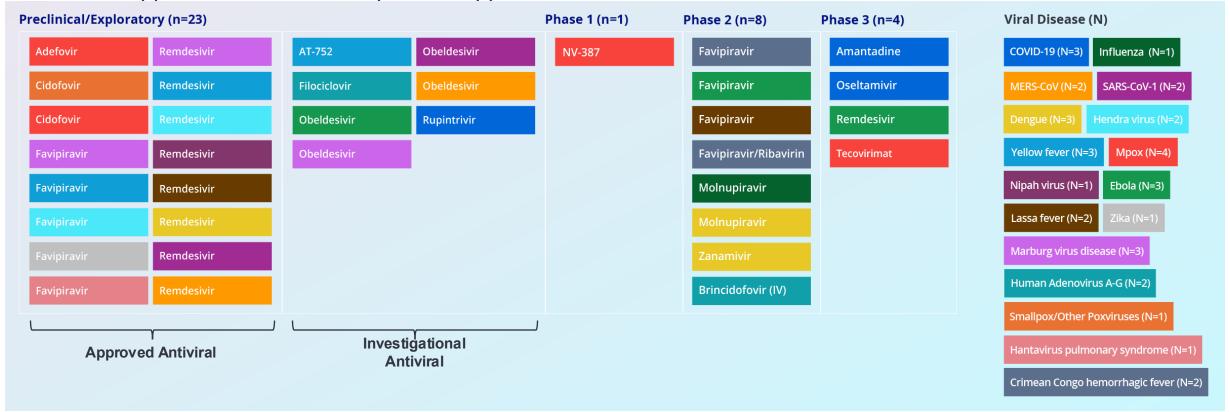


<sup>\*</sup>As of December 18, 2024; WHO defined Other National Authority (https://www.who.int/publications/m/item/list-of-transitional-wlas).

# Antiviral-Indication Expansions: Preclinical & Clinical Compound/Indications (N=36)

Investigational: Antiviral compounds in clinical phase development for a different virus disease indication.

Approved: Antiviral compounds approved for treatment of a different virus disease indication.



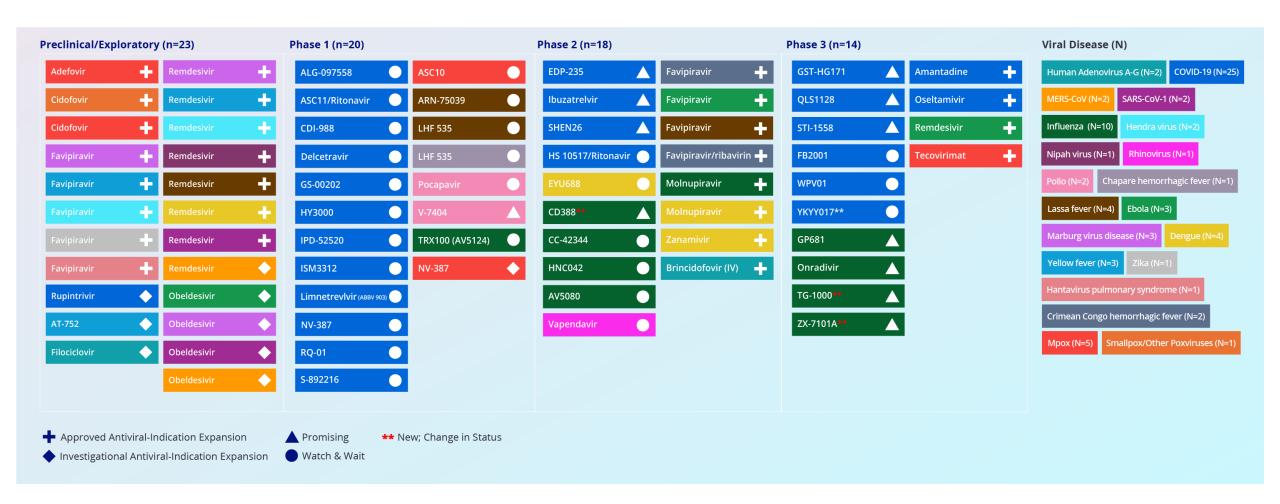
- ▶ 6 of these antivirals (favipiravir, remdesivir, molnupiravir, amantadine, oseltamivir, & zanamivir) are approved for treatment of COVID-19 and/or Influenza.
  - ▶ Adefovir is approved for treating Hepatitis B virus disease and cidofovir is approved for treating CMV disease.
  - ► Tecovirimat is approved for treating smallpox.
- Favipiravir and remdesivir have the most indication expansions under evaluation (9 each).



<sup>\*</sup>As of December 18, 2024; Clinical phase Investigational (Unapproved) and Approved antivirals being explored for expanded indications.

## All Clinical Phase & Approved Antivirals (N=75)

INTREPID Alliance Analysis (4th Edition)\*

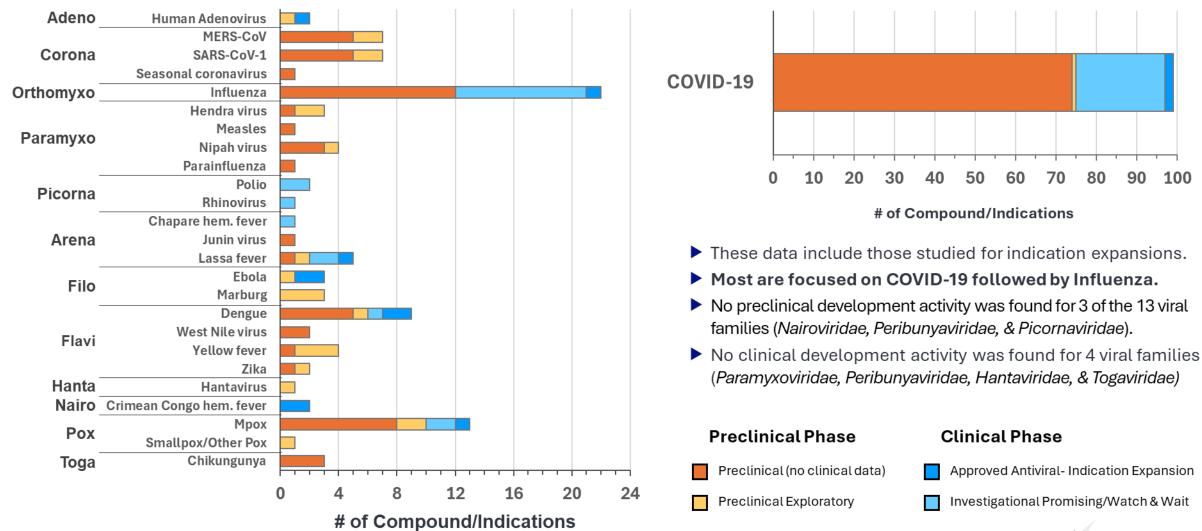




<sup>\*</sup>December 18, 2024 data with "Promising" Analysis defined in March 2024.

# INTREPID Alliance Antiviral Landscape: Overview of 13 Priority Viral Families\*

As of Dec 18, 2024, for the 13 viral families with greatest risk of pandemic potential, clinical phase & approved antiviral compounds fall into 9 of 13 and preclinical into 10 of 13.



<sup>\*</sup>As of December 18, 2024:

\*\*Number of compounds in ongoing development.

Indication

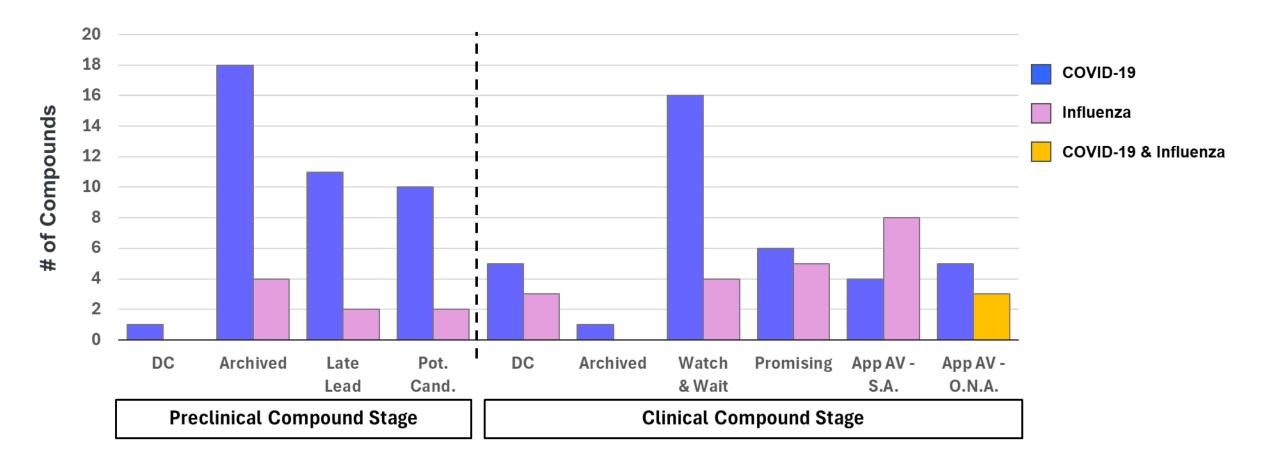
Viral Disease

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## Antiviral Compounds for COVID-19 and Influenza Span the Stages of Preclinical & Clinical Development\*

COVID-19 has more compounds in later stages of preclinical development than Influenza or any other virus indication. Three compounds are approved for both COVID-19 and Influenza.

The number of COVID-19 compounds categorized as Archived or Discontinued increased since previous reports.



<sup>\*</sup>As of December 18, 2024; DC: discontinued, Pot. Cand.:Potential Candidate, App AV: approved antiviral, S.A.: stringent authority, O.N.A.: other national authority; 3 compounds are approved for both COVID-19 and Influenza



# Preclinical Compounds by Stage of Preclinical Development: COVID-19 Indications

The majority of preclinical compounds are under evaluation for SARS-CoV-2/COVID-19 (74/125, 59.2%).

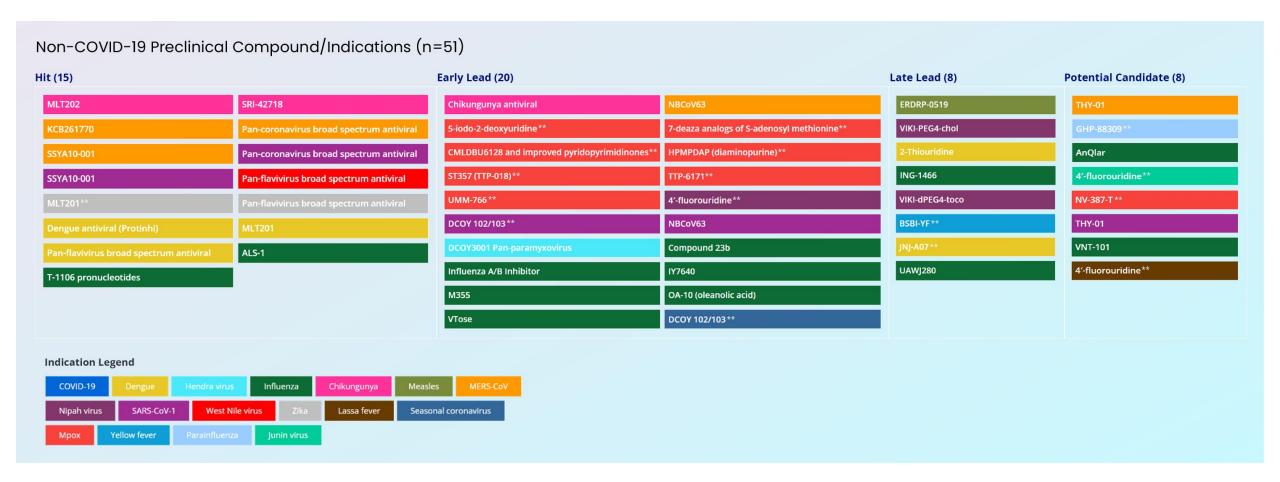
| t (36)                         |  | Early Lead (17)  |   | Late Lead (11) | Potential Candidate (10) |
|--------------------------------|--|------------------|---|----------------|--------------------------|
| i-72-2a                        | Anisodamine                              | 21i              | C6G25S                                    | 2-Thiouridine  | CDI-45205                |
| AVI-8053                       | Borneol Ester, PROTACs                   | D6               | EDDC-2214                                 | Beta-521       | COR803                   |
| CD04872SC                      | Epigallocatechin-3-gallate               | EK1C4            | FBP (frog-defensin-derived basic peptide) | HT-002         | GC376**                  |
| H84T-BanLec                    | IPB02                                    | GRL0617**        | NBCoV63                                   | LNA ASOs       | P315V3                   |
| IPB19                          | Lycium barbarum glycopeptide             | PLpro Inhibitors | RCYM002                                   | Mpro inhibitor | SY110                    |
| MCULE-5948770040               | MPI5                                     | SBCoV202         | Small molecule inhibitor                  | PF-07957472    | CDI-873                  |
| MPI8                           | MRX-18                                   | STI 4398         | SWC423                                    | 3N39v4-Fc      | COV-X                    |
| MXB-4                          | MXB-9                                    | TDI-015051**     | Therapeutic interfering particles         | DCOY 102/103   | NV-387-R                 |
| Napthoquinones                 | Pan-coronavirus broad spectrum antiviral | TNX-3500         |   | Jun12682       | RCYM003                  |
| Penciclovir                    | Pentosan Polysulfate                     |                  |   | ML2006a4       | THY-01                   |
| Protegrin-2                    | RECCE 529                                |                  |   | MVR-V001       |                          |
| RU-0415529**                   | SACT-Covid19                             |                  |   |                |                          |
| Sangivamycin                   | Saquinavir                               |                  |   |                |                          |
| SARS-CoV-2 PLpro Inhibitor     | SBFM-PL4                                 |                  |   |                |                          |
| SPIKENET                       | Spirooxindole                            |                  |   |                |                          |
| SSYA10-001                     | TEAR-CoV                                 |                  |   |                |                          |
| Urtica dioica agglutinin (UDA) | ViruSAL                                  |                  |   |                |                          |
| YH-6                           | ZINC000000639429                         |                  |   |                |                          |

<sup>\*</sup>As of December 18, 2024. Archived and Discontinued compound/indications are not included in this summary; \*\*New.



## Preclinical Compounds by Stage of Preclinical Development: Non-COVID-19 Indications

For Non-COVID-19 preclinical compounds, Influenza has the highest number under evaluation (12/51, 23.5%).





<sup>\*</sup>As of December 18, 2024. Archived and Discontinued compound/indications are not included in this summary; \*\*New.

# COVID-19 & Influenza Compounds Approved by a Stringent Regulatory Authority (S.A.)\*

COVID-19 (n=4), Influenza (n=8)

| Compound               | Developer/Sponsor  | Mechanism/Target           |
|------------------------|--|----------------------------|
| COVID-19               |  |                            |
| Ensitrelvir            | Shionogi, Ildong   | Protease - 3CL pro         |
| Molnupiravir           | Merck & Co./Merck Sharp & Dohme (MSD), Ridgeback Biotherapeutics | Replication - RdRp         |
| Nirmatrelvir/ritonavir | Pfizer   | Protease - 3CL pro         |
| Remdesivir             | Gilead Sciences  | Replication - RdRp         |
| INFLUENZA              |  |                            |
| Amantadine             | Novartis   | Entry - Proton Channel M2  |
| Baloxavir Marboxil     | Shionogi, Roche  | Replication - Endonuclease |
| Favipiravir**          | FUJIFILM Toyama Chemical   | Replication - RdRp         |
| Laninamivir            | Daiichi Sankyo   | Assembly/Release - NA      |
| Oseltamivir            | Roche  | Assembly/Release - NA      |
| Peramivir              | BioCryst Pharmaceuticals   | Assembly/Release - NA      |
| Rimantadine            | Allergan   | Entry - Proton Channel M2  |
| Zanamivir              | GlaxoSmithKline (GSK)  | Assembly/Release - NA      |



<sup>\*</sup>As of December 18, 2024; \*\*Favipiravir also has an O.N.A. approval.

# COVID-19 & Influenza Compounds Approved by Other National Authority (O.N.A.)\*

COVID-19 (n=5), Influenza (n=0), COVID-19 & Influenza (n=3)

| Compound               | Developer/Sponsor  | Mechanism/Target   |
|------------------------|--|--------------------|
| COVID-19               |  |                    |
| Azvudine               | HeNan Sincere Biotech, Zhengzhou Granlen PharmaTech, Genuine<br>Biotech, Fosun Pharma                  | Replication - RdRp |
| Favipiravir **         | Promomed,R-Pharm   | Replication - RdRp |
| Leritrelvir (RAY1216)  | Guangdong Zhongsheng Pharmaceutical  | Protease - 3CL pro |
| Mindeudesivir (VV116)  | Shanghai Junshi Biosciences  | Replication - RdRp |
| Simnotrelvir/ritonavir | Simcere Pharmaceutical, Shanghai Institute of Materia Medica (SIMM),<br>Jiangsu Simcere Pharmaceutical | Protease - 3CL pro |
| INFLUENZA              |  |                    |
| -                      | -  | -                  |
| COVID-19 & INFLUENZA   |  |                    |
| Enisamium (VR17-04)    | Farmak   | Replication - RdRp |
| Triazavirin            | Medsintez Pharmaceutical   | Replication - RdRp |
| Umifenovir             | Pharmstandard  | Entry - Fusion     |

<sup>\*</sup>As of December 18, 2024; \*\*Favipiravir also has an S.A. approval.



# 11 "Promising" Novel Clinical Antiviral Compounds for COVID-19 or Influenza\*

COVID-19 (n=6), Influenza (n=5)

| Viral Disease | Compound            | Developer/Sponsor   | Country       | Mechanism/Target           | Phase of<br>Development |
|---------------|---------------------|---|---------------|----------------------------|-------------------------|
|               | EDP-235             | Enanta Pharmaceuticals  | U.S.          | Protease - 3CL pro         | 2                       |
|               | GST-HG171/ritonavir | Fujian Cosunter Pharmaceutical                                    | China         | Protease - 3CL pro         | 3                       |
| COV/ID 10     | lbuzatrelvir        | Pfizer  | U.S.          | Protease - 3CL pro         | 2                       |
| COVID-19      | QLS1128             | Qilu Pharmaceutical   | China         | Protease - 3CL pro         | 3                       |
| SH            | SHEN26              | Kexing Biopharm   | China         | Replication - RdRp         | 2                       |
|               | STI-1558            | Sorrento Therapeutics   | U.S.          | Protease - 3CL pro         | 3                       |
|               | CD388               | Cidara Therapeutics, Johnson & Johnson Innovative Medicine (JJIM) | U.S., Belgium | Entry - Fc Drug Conjugate  | 2                       |
|               | GP681               | Jiangxi Qingfeng Pharmaceutical                                   | China         | Replication - Endonuclease | 3                       |
| Influenza     | Onradivir           | Raynovent   | China         | Replication - DdRp         | 3                       |
|               | TG-1000             | TaiGen Biotechnology  | Taiwan        | Replication - DdRp         | 3                       |
|               | ZX-7101A            | Nanjing Zenshine Pharmaceuticals                                  | China         | Replication - Endonuclease | 3                       |



<sup>\*</sup>As of December 18, 2024.

# 20 "Watch & Wait" Novel Clinical Antiviral Compounds for COVID-19 or Influenza\*

COVID-19 (n=16) of 20

| Viral<br>Disease | Compound                | Developer/Sponsor   | Country              | Mechanism/Target   | Phase of<br>Development |
|------------------|-------------------------|---|----------------------|--------------------|-------------------------|
|                  | ALG-097558              | Aligos Therapeutics   | U.S.                 | Protease - 3CL pro | 1                       |
|                  | ASC11/Ritonavir         | Ascletis Pharma   | China                | Protease - 3CL pro | 1                       |
|                  | CDI-988                 | CoCrystal Pharma  | U.S.                 | Protease - 3CL pro | 1                       |
|                  | Delcetravir             | Esfam Biotech   | Australia            | Entry - Attachment | 1                       |
|                  | FB2001                  | Frontier Biotechnologies  | China                | Protease - 3CL pro | 3                       |
|                  | GS-00202                | Gusen Pharma  | China                | Protease - 3CL pro | 1                       |
|                  | HS 10517/Ritonavir      | Abbott Laboratories, AbbVie,<br>Gilead Sciences, Jiangsu Hansoh<br>Pharmaceutical | U.S., U.S.,<br>China | Protease - 3CL pro | 2                       |
| COVID-19         | HY3000                  | Hybio Pharmaceutical (formerly<br>Hanyu Pharmaceutical)                           | China                | Entry - Fusion     | 1                       |
|                  | IPD-52520               | IAVI  | U.S.                 | Entry              | 1                       |
|                  | ISM3312                 | Insilico Medicine   | Hong Kong            | Protease - 3CL pro | 1                       |
|                  | Limnetrelvir (ABBV 903) | AbbVie  | U.S.                 | Protease - 3CL pro | 1                       |
|                  | NV-387                  | NanoViricides   | U.S.                 | Entry - Attachment | 1                       |
|                  | RQ-01                   | Red Queen Therapeutics  | U.S.                 | Entry              | 1                       |
|                  | S-892216                | Shionogi  | Japan                | Protease - 3CL pro | 1                       |
|                  | WPV01                   | Westlake University   | China                | Protease - 3CL pro | 3                       |
|                  | YKYY017                 | Yuekang Pharmaceutical  | China                | Entry - Fusion     | 3                       |

<sup>\*</sup>As of December 18, 2024.



## 20 "Watch & Wait" Novel Clinical Antiviral Compounds for COVID-19 or Influenza\*

Influenza (n=4) of 20

| Viral Disease | Compound        | Developer/Sponsor                         | Country | Mechanism/Target           | Phase of<br>Development |
|---------------|-----------------|---|---------|----------------------------|-------------------------|
| Influenza     | AV5080          | Viriom                                    | Russia  | Assembly/Release - NA      | 2                       |
| Influenza     | CC-42344        | CoCrystal Pharma                          | U.S.    | Replication - Flu A Pol    | 2                       |
| Influenza     | HNC042          | Guangzhou Henovcom<br>Bioscience Co. Ltd. | China   | Assembly/Release - NA      | 2                       |
| Influenza     | TRX100 (AV5124) | Traws Pharma                              | U.S.    | Replication - Endonuclease | 1                       |



# **Preclinical Compounds for COVID-19 (n=21)\***

Potential Candidates (n=10), Late Leads (n=11)

| Phase of<br>Development | Viral<br>Disease | Compound       | Developer/Sponsor  | Country     | Mechanism/Target   |
|-------------------------|------------------|----------------|--|-------------|--------------------|
|                         |                  | CDI-45205      | CoCrystal Pharma   | U.S.        | Protease - 3CL pro |
|                         |                  | CDI-873        | CoCrystal Pharma   | U.S.        | Protease - 3CL pro |
|                         |                  | COR803         | Quince Therapeutics (formerly Cortexyme)                     | U.S.        | Protease - 3CL pro |
|                         |                  | COV-X          | Infex Therapeutics   | U.K.        | Protease - PL pro  |
| <b>.</b>                |                  | GC376          | Anivive Lifesciences   | U.S.        | Protease - 3CL pro |
| Potential candidate     | COVID-19         | NV-387-R       | NanoViricides  | U.S.        | Entry              |
|                         |                  | P315V3         | Institute of Microbiology of the Chinese Academy of Sciences | China       | Entry - Fusion     |
|                         |                  | RCYM003        | Raynovent  | China       | Protease - 3CL pro |
|                         |                  | SY110          | Sichuan University   | China       | Protease - 3CL pro |
|                         |                  | THY-01         | Thylacine Biotherapeutics Inc.                               | U.S.        | Entry - Fusion     |
|                         |                  | 2-Thiouridine  | Hokkaido University  | Japan       | Replication - RdRp |
|                         |                  | 3N39v4-Fc      | Juntendo University  | Japan       | Entry - Spike      |
|                         |                  | Beta-521       | Benevira   | U.S.        | Entry              |
|                         |                  | DCOY 102/103   | Decoy Therapeutics   | U.S.        | Entry - Decoy      |
|                         |                  | HT-002         | Hoth Therapeutics  | U.S.        | Entry              |
| Late lead               | COVID-19         | Jun12682       | Rutgers University   | U.S.        | Protease - PL pro  |
|                         |                  | LNA ASOs       | University of California Berkeley                            | U.S.        | Replication -RNA   |
|                         |                  | ML2006a4       | Stanford University  | U.S.        | Protease - 3CL pro |
|                         |                  | Mpro inhibitor | Exscientia   | U.K.        | Protease - 3CL pro |
|                         |                  | MVR-V001       | MVRIX  | South Korea | Entry - Decoy      |
|                         |                  | PF-07957472    | Pfizer   | U.S.        | Protease - PL pro  |

# **Preclinical Compounds for Influenza (n=4)\***

Potential Candidates (n=2), Late Leads (n=2)

| Phase of<br>Development | Viral<br>Disease | Compound | Developer/Sponsor  | Country    | Mechanism/Target |
|-------------------------|------------------|----------|--|------------|------------------|
| Potential Candidate     | Influenza        | AnQlar   | Virpax Pharmaceuticals                                     | U.S.       | Entry            |
|                         | Influenza        | VNT-101  | Via Nova Therapeutics                                      | U.S.       | Replication      |
| Late Lead               | Influenza        | ING-1466 | University of Illinois at Chicago,<br>Chicago BioSolutions | U.S.       | Entry - Flu HA   |
|                         |                  | UAWJ280  | University of Georgia,<br>University of Arizona            | U.S., U.S. | Entry - Flu M2   |



# **Archived Compounds for COVID-19\***

Clinical (n=1), Preclinical (n=18)

| Phase of<br>Development      | Viral<br>Disease | Compound                             | Developer/Sponsor   | Country          | Mechanism/Target                     |
|------------------------------|------------------|--------------------------------------|---|------------------|--------------------------------------|
| Clinical                     | COVID-19         | WPV01/ritonavir                      | Westlake University   | China            | Protease - 3CL pro                   |
| Preclinical                  |                  | 4'-Fluorouridine                     | Georgia State Univ., Emory Univ., Texas Biomed.<br>Res. Inst.             | U.S., U.S., U.S. | Replication - RdRp                   |
|                              |                  | AB-343                               | Arbutus Biopharma   | U.S.             | Protease - 3CL pro                   |
|                              |                  | Antisense Oligonucleotides           | Sarepta Therapeutics  | U.S.             | Viral RNA                            |
|                              |                  | ATV006                               | Guangdong Provincial Center for Disease Control and Prevention            | China            | Replication - RdRp                   |
|                              |                  | GDI-4405                             | Jiangsu Hansoh Pharmaceutical   | China            | Protease - 3CL pro                   |
|                              | COVID-19         | GS-621763                            | Gilead Sciences   | U.S.             | Replication - RdRp                   |
|                              |                  | GS-6620                              | Gilead Sciences   | U.S.             | Protease - 3CL pro                   |
|                              |                  | Oral nsp12 inhibitor                 | Arbutus Biopharma   | U.S.             | Replication - RdRp                   |
|                              |                  | PF-00835231                          | Pfizer  | U.S.             | Protease - 3CL pro                   |
|                              |                  | 1KJ0-7                               | Shahid Chamran University   | Iran             | Protease - 3CL pro                   |
|                              |                  | 2ERW-9                               | Shahid Chamran University   | Iran             | Protease - 3CL pro                   |
|                              |                  | Ab001                                | Agastiya Biotech  | U.S.             | Entry - ACE2;<br>Replication - NSP15 |
|                              |                  | Bananin                              | Medsintez Pharmaceutical  | Russia           | NSP13 helicase                       |
|                              |                  | chromone-4c                          | Pritzker School of Molecular Engineering                                  | U.S.             | NSP13 helicase                       |
|                              |                  | Coumarin-EM04                        | Sambalpur University  | India            | Protease - 3CL pro                   |
|                              |                  | LMed-052                             | State University of Londrina, Federal University of Rio de Janeiro (UFRJ) | Brazil           | Replication - RdRp                   |
|                              |                  | LMed-087                             | State University of Londrina, Federal University of Rio de Janeiro (UFRJ) | Brazil           | Replication - RdRp                   |
|                              |                  | Monomethylated<br>Triazolopyrimidine | University of Hyderabad, National Institute of Anima<br>Biotechnology     | l<br>India       | Replication - RdRp                   |
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# **Archived Compounds for Influenza\***

Clinical (n=0), Preclinical (n=4)

| Phase of<br>Development | Viral<br>Disease | Compound           | Developer/Sponsor    | Country     | Mechanism/Target       |
|-------------------------|------------------|--------------------|----------------------|-------------|------------------------|
|                         | Influenza        | CD-SA cyclodextrin | University of Geneva | Switzerland | Entry - Viral Envelope |
| Deceliais al            |                  | Oral FluCide       | NanoViricides        | U.S.        | Not yet confirmed      |
| Preclinical             |                  | STP-702            | SirnaOmics           | U.S.        | Replication - siRNA    |
|                         |                  | Tamiphosphor       | TaiMed Biologics     | Taiwan      | Assembly/Release - NA  |



# **Discontinued Clinical Compounds for COVID-19 or Influenza\***

COVID-19 (n=5), Influenza (n=3)

| Phase of Development | Viral<br>Disease | Compound       | Developer/Sponsor                 | Country     | Mechanism/Target           |
|----------------------|------------------|----------------|-----------------------------------|-------------|----------------------------|
| Clinical             |                  | Bemnifosbuvir  | Atea Pharmaceuticals              | U.S.        | Replication - RdRp         |
|                      | COVID-19         | BIT-225        | Biotron                           | Australia   | Assembly/Release           |
|                      |                  | Galidesivir    | BioCryst Pharmaceuticals, NIAID   | U.S., U.S.  | Replication - RdRp         |
|                      |                  | Obeldesivir    | Gilead Sciences                   | U.S.        | Replication - RdRp         |
|                      |                  | Valganciclovir | Roche                             | Switzerland | Replication - DNA pol      |
|                      | Influenza        | AL-794         | Johnson & Johnson Innovative Med. | Belgium     | Replication - Endonuclease |
|                      |                  | Flufirvitide-3 | Autoimmune Technologies           | U.S.        | Entry - Flu HA             |
|                      |                  | Radavirsen     | Sarepta Therapeutics              | U.S.        | Replication - Translation  |



# **Discontinued Preclinical Compounds for COVID-19 or Influenza\***

COVID-19 (n=1), Influenza (n=0)

| Phase of Development | Viral<br>Disease | Compound       | Developer/Sponsor | Country   | Mechanism/Target   |
|----------------------|------------------|----------------|-------------------|-----------|--------------------|
| Preclinical          | COVID-19         | ISM036-076 PCC | Insilico Medicine | Hong Kong | Protease - 3CL pro |

