INTREPID ALLIANCE

INTERNATIONAL READINESS FOR PREVENTING INFECTIOUS VIRAL DISEASE

APRIL 30, 2025

Antiviral Clinical and Preclinical Development Landscape – 4th Edition

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INTREPID Alliance. Antiviral Clinical and Preclinical Development Landscape – 4th Edition. 30 APRIL 2025. Available at intrepidalliance.org.

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.

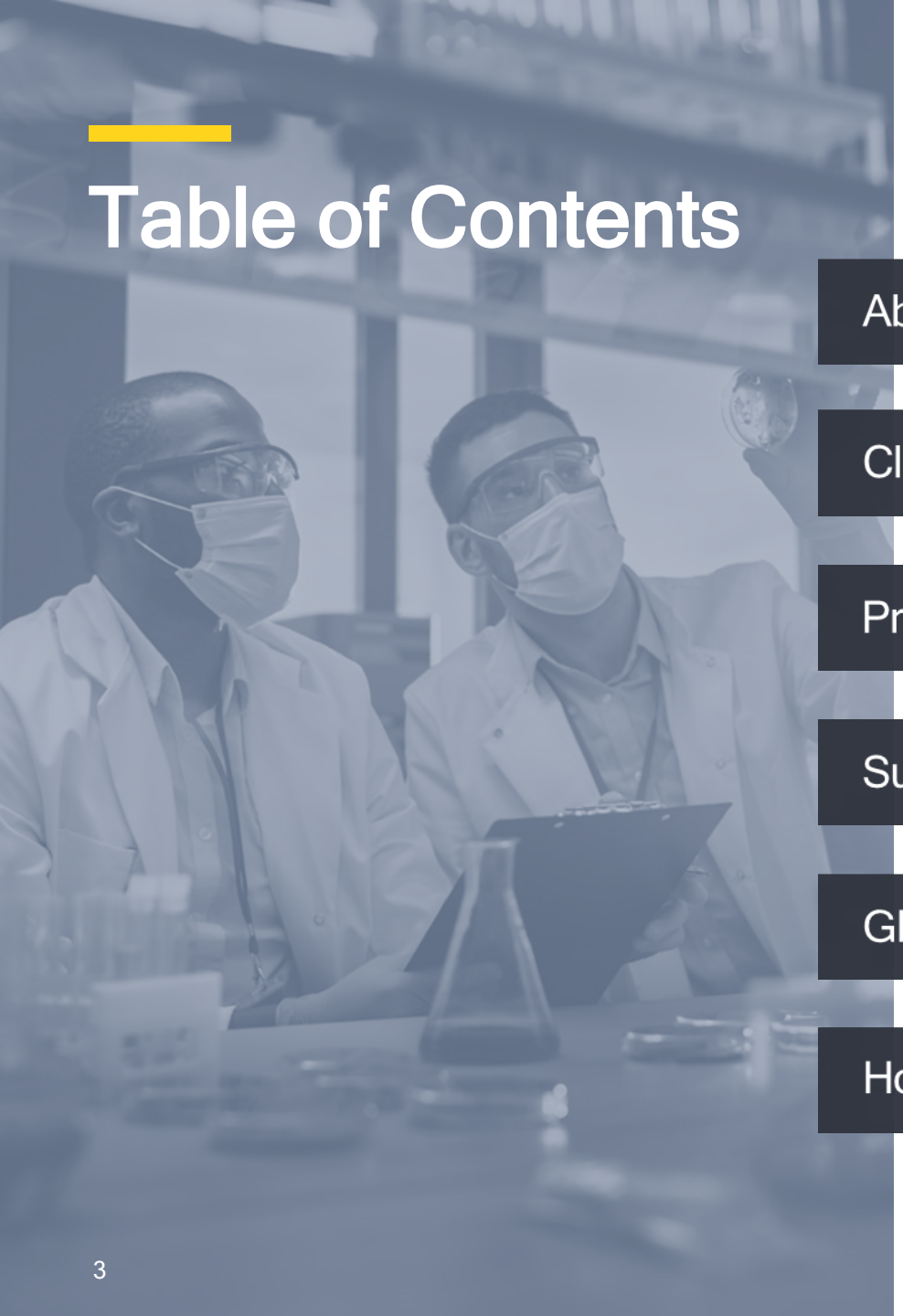

Table of Contents

INTREPID ALLIANCE

About the INTREPID Alliance Antiviral Development Landscape

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
  - **3rd 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.

*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.

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 Viral Families

Primarily Respiratory Transmission

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

X = absence of preclinical or clinical phase antivirals

Primarily Contact/Vector-Mediated Transmission

	Disease Indication (n)**	
Pillar	Preclinical (22)	Clinical (13)
Arenaviridae	• Junin virus (1) • Lassa fever (1)	• Lassa fever (3) • Chapare hem. fever (1)
Filoviridae	X	• Ebola (2)
Flaviviridae	• Dengue (5) • West Nile (1) • Yellow fever (1) • Zika (2)	• Dengue (3)
Hantaviridae	X	X
Nairoviridae	X	• Crimean Congo hem. fever (2)
Peribunyaviridae	X	X
Poxviridae	• Mpox (8)	• Mpox (2)
Togaviridae	• Chikungunya (3)	X

*As of December 18, 2024; **Number of compounds in ongoing development.

Clinical Antiviral Development Landscape as of December 2024

INTREPID Alliance Clinical Antiviral Landscape: Clinical Antiviral Compounds Analysis Update (4th Edition)*

- Clinical Landscape Analyses previously reported on the INTREPID Alliance website:
  - 1st edition (January 2024) with data through November 2023. Available here.
  - 2nd edition (April 2024) with data through March 2024. Available here.
  - 3rd edition (October 2024) with data through July 2024. Available here.
- This 4th Edition analysis of the data through December 2024 shows that there are **67** distinct antiviral compounds in the antiviral clinical development landscape.
  - **25** have prior regulatory approval and **42** are novel unapproved
- Data were organized based on stage of clinical development and regulatory approval:
  - Novel Unapproved Clinical Phase Antiviral Compounds (e.g., not yet approved for a virus disease indication)
  - Approved-Indication Expansion Antiviral Compounds (e.g., initial approval for one viral indication and under evaluation for other viral indication(s))
- Additional scientific analysis** of only the novel compounds categorized them as follows:
  - **Promising**
  - **Watch & Wait**
  - **Archived**
  - **Discontinued**

*As of December 18, 2024; **See criteria and references on slides 10-11.

Criteria* for Promising Clinical Antiviral Compounds Analysis**

- FIH trial completed and data at adequate doses and dosing duration available.
- POC study ongoing *or* completed and data available.
  - POC demonstration via viral endpoint, symptom alleviation, etc.
  - POC in animal model may be applicable for certain viral diseases where clinical POC is not feasible.
- Adequate PK/PD to support Phase 2/3 dose selection and route of administration.
- Safety and tolerability consistent with the target dose/exposure and no difficult-to-manage clinical safety signals.
- Other criteria such as chemical structure, synthesis, scalability, etc., are taken into account where data are available.

*In addition to the collective antiviral drug development experience of INTREPID Alliance member companies, guidance documents from Regulatory Authorities such as the U.S. FDA routinely used by drug developers, and publicly available Target Product Profiles such as the NIH/NIAID Target Product Profiles for Antivirals, were used to inform the clinical phase triage.

**As defined in 2nd and 3rd Editions of the Clinical Antiviral Landscape (available here); see disclaimer information on slide 2. FIH: first-in-human; POC: proof-of-concept; PK/PD: pharmacokinetic/pharmacodynamic.

Categories for Clinical Antiviral Compound Analysis*

- **Promising** (e.g., meets “Promising Criteria”)
  - 100 Days Mission Ready
  - Registration & Approval for established viral diseases
- **Watch & Wait**
  - FIH or POC Study just starting/ongoing or data are unavailable for a completed study
  - Unable to make a data-driven evaluation
- **Archived**
  - Development paused, no recent information >5 years
  - May be useful to inform new screening or medicinal chemistry efforts
- **Discontinued**
  - Development stopped for known reasons; e.g., change in business strategy, lack of efficacy or funding, low enrollment, PK variability preventing effective dosing, other
  - May be useful to inform new screening or medicinal chemistry efforts

*As also defined in 2nd and 3rd Editions of the Clinical Antiviral Landscape (available here), with addition of “Discontinued” in the 4th Edition.
FIH: first-in-human; POC: proof-of-concept; PK: pharmacokinetic.

Changes in Clinical Antiviral Pipeline (4th Edition)*

New Additions and Changes in Status from 3rd to 4th Edition

Virus Family	Indication	Compound	Discontinued	Archived	Preclinical Exploratory	Phase 1	Phase 2	Phase 3	Approved
Adenoviridae	Human Adeno	Brincidofovir (IV)					NEW AppAV-IE Prom		
		Cidofovir		←	←				
		Valganciclovir	←	←	←				
		Brincidofovir (Oral)	←	←					
Coronaviridae	COVID-19	Obeldesivir	←	←	←	←	←	Prom	
		Bemnifosbuvir	←	←	←	←	←	W&W	
		BIT225	←	←	←	←	W&W		
		WPV01/Ritonavir		←	←	W&W			
		Valganciclovir	←	←	←				
	MERS-CoV	Remdesivir			NEW AppAV-IE				
	SARS-CoV-1	Remdesivir			NEW AppAV-IE				
		Galidesivir		←	←				
Orthomyxoviridae	Influenza	CD388					W&W to Prom		
		TG-1000						W&W to Prom	
		ZX7101A						W&W to Prom	
		AL794	←	←					
		Flufirvitide-3	←	←					
Flaviviridae	Dengue	Zanamivir				→	→		
		Molnupiravir					NEW AppAV-IE W&W		
		Remdesivir			NEW AppAV-IE				
		Mosnodenvir	←	←	←	←	Prom		
Poxviridae	Mpox	Adefovir			NEW AppAV-IE				

*As of December 18, 2024.

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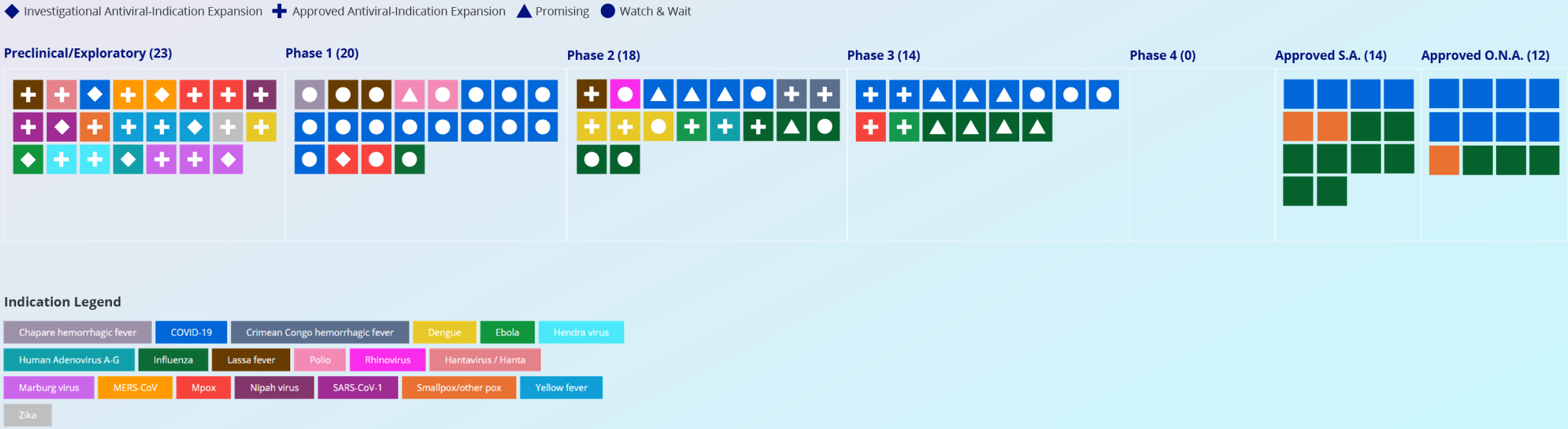
Summary of Updated Antiviral Clinical Development Landscape with Promising Clinical Compounds (4th Edition)*

- Identified 67 distinct antiviral compounds with ongoing clinical phase activity
  - 22 Approved Compounds: 19 Approved for COVID-19 and/or Influenza; 3 for Smallpox/Other Poxviruses
    - 13 by Stringent Authority (S.A.)
    - 8 by Other National Authority (O.N.A.)
    - 1 by S.A. and O.N.A.
  - 3 Compounds approved for viral indications outside the 13 viral families
    - These are under evaluation as potential indication expansions within the 13 viral families
  - 42 Unapproved Compounds
- There are 103 indications associated with the 67 distinct antiviral compounds**
  - 23 Approved indications for COVID-19 (n=8), Influenza (n=7), or both (n= 4 x 2)
  - 5 Approved indications for Smallpox (n=3), Cowpox (n=1), Mpox (n=1)
  - 28 other viral indications under evaluation for 10 of the distinct Approved antiviral compounds
  - 47 indications for Unapproved compounds; 2 compounds being evaluated for two indications and 1 for four indications
- Unapproved Promising and Watch & Wait clinical compounds target entry (n=11), protease (n=16), replication (n=9), and assembly-release (n=2).

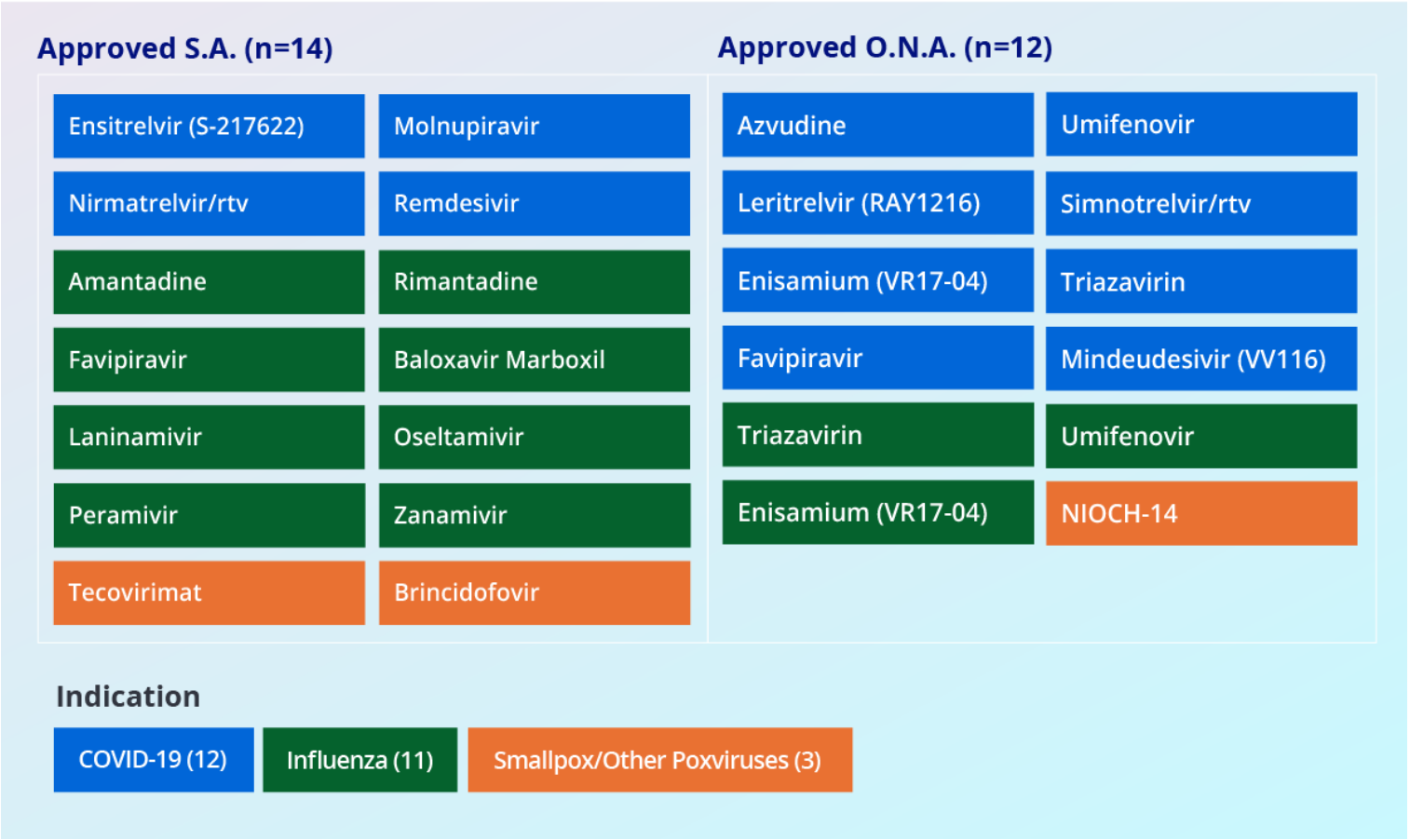
*As of December 18, 2024; **Some compounds are being evaluated for more than one viral indication.

Static View of Interactive Antiviral Clinical Development Pipeline: INTREPID Alliance Analysis (4th Edition)*



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

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

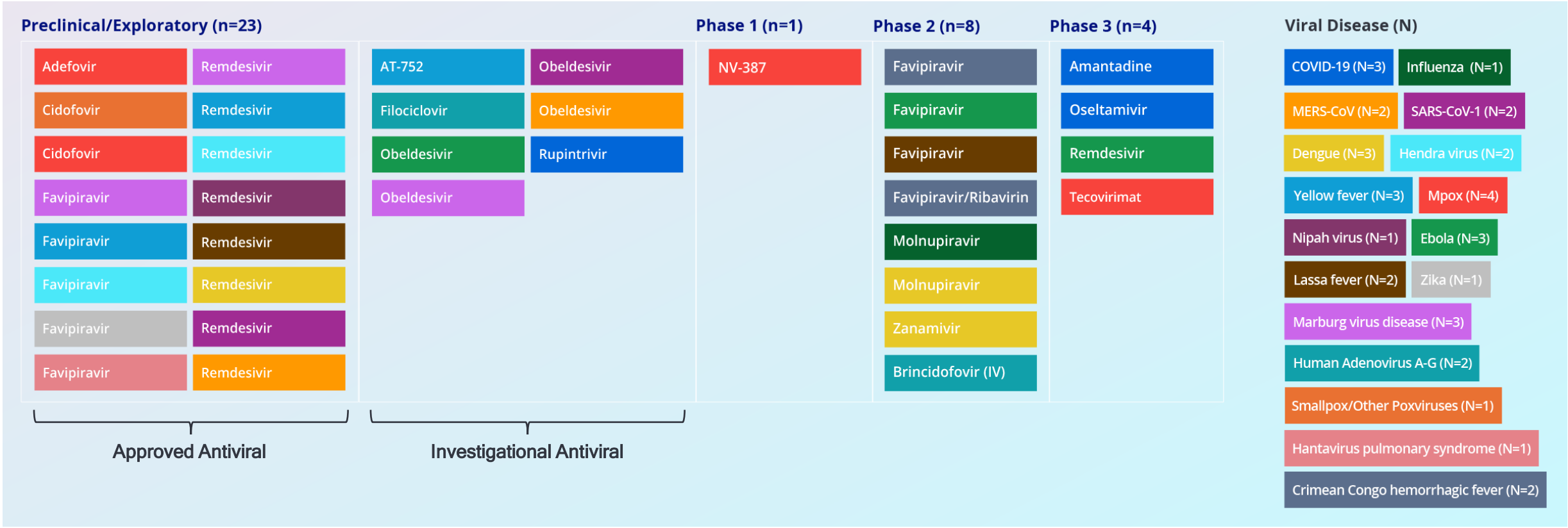


- 22 distinct antiviral compounds have received regulatory approval for COVID-19, Influenza, or Smallpox/Other Poxviruses
- 4 compounds are approved for COVID-19 and Influenza (favipiravir, triazavirin, umifenovir, and enisamium)
- 3 compounds have regulatory authorization by Animal Rule Development 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

*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).

*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)*

*December 18, 2024 data with “Promising” Analysis defined in March 2024.

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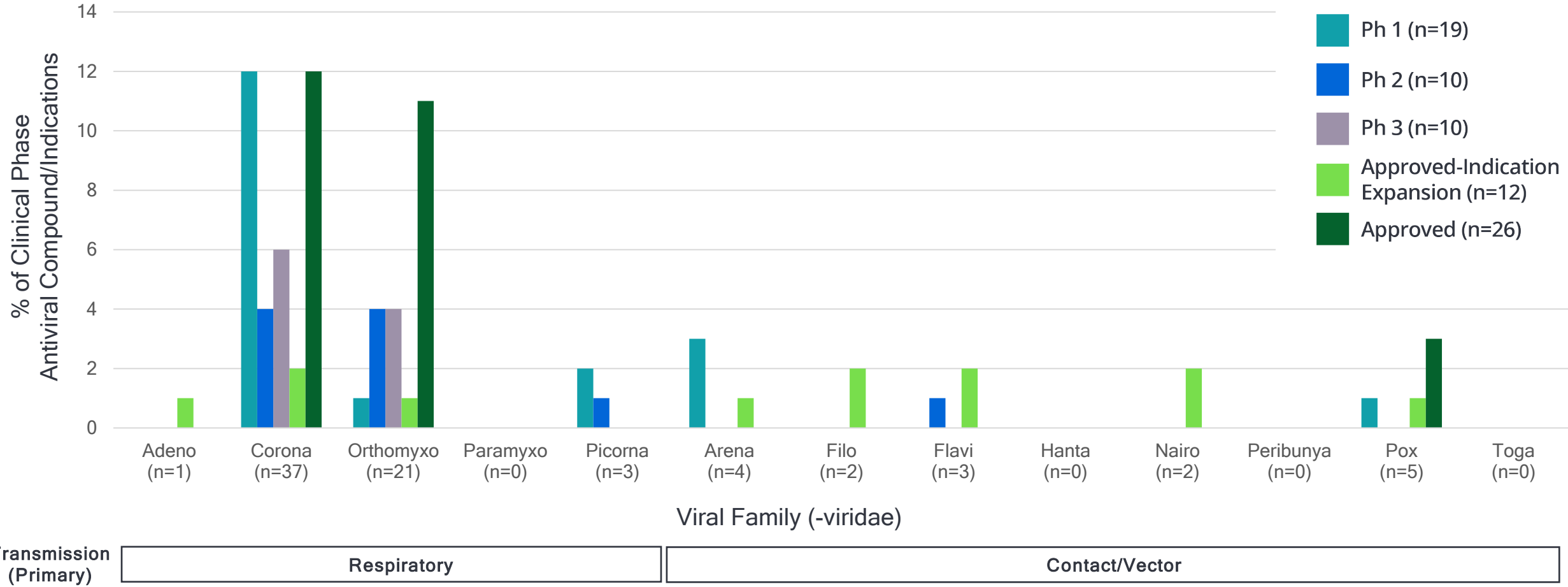
The Majority of Clinical Phase Antiviral Compound/Indications Are Targeting Coronaviruses and Orthomyxoviruses*

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



*As of December 18, 2024. Adenoviridae has 1 clinical phase program listed in Archived.

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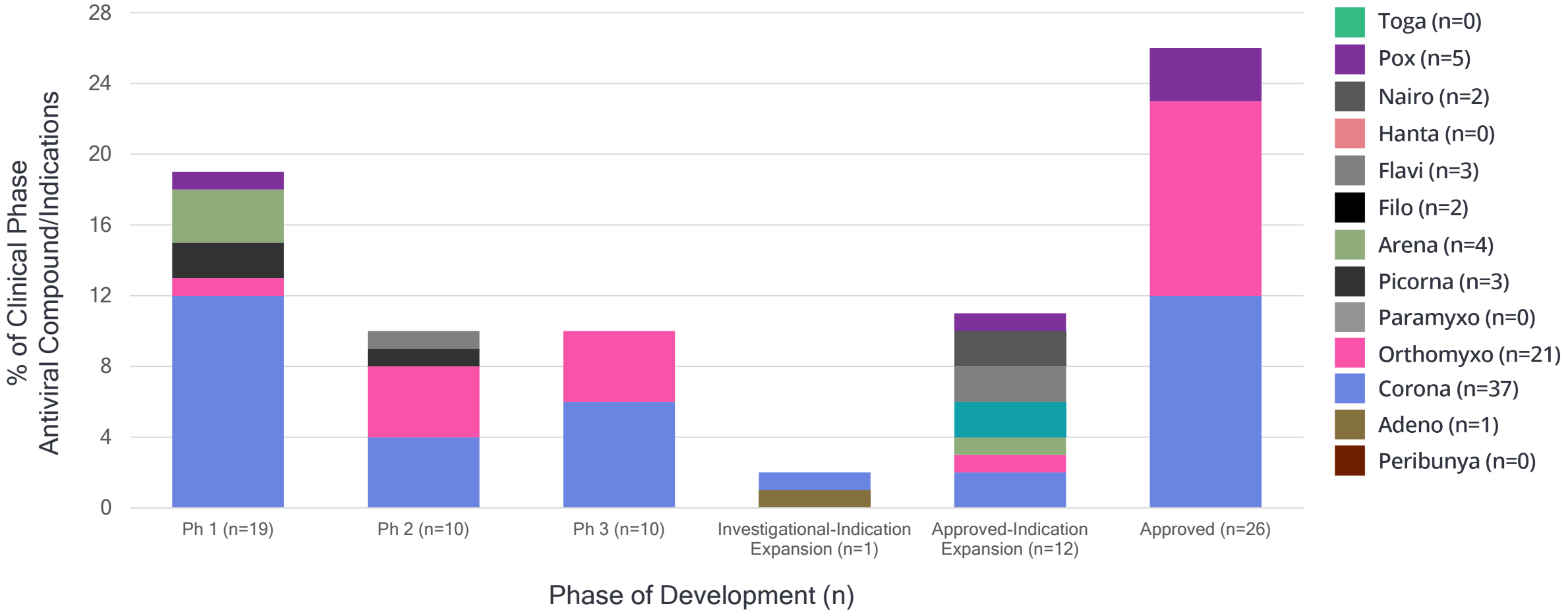
The Majority of Clinical Phase Antiviral Compound/Indications Are Targeting Coronaviruses and Orthomyxoviruses*

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



*As of December 18, 2024.

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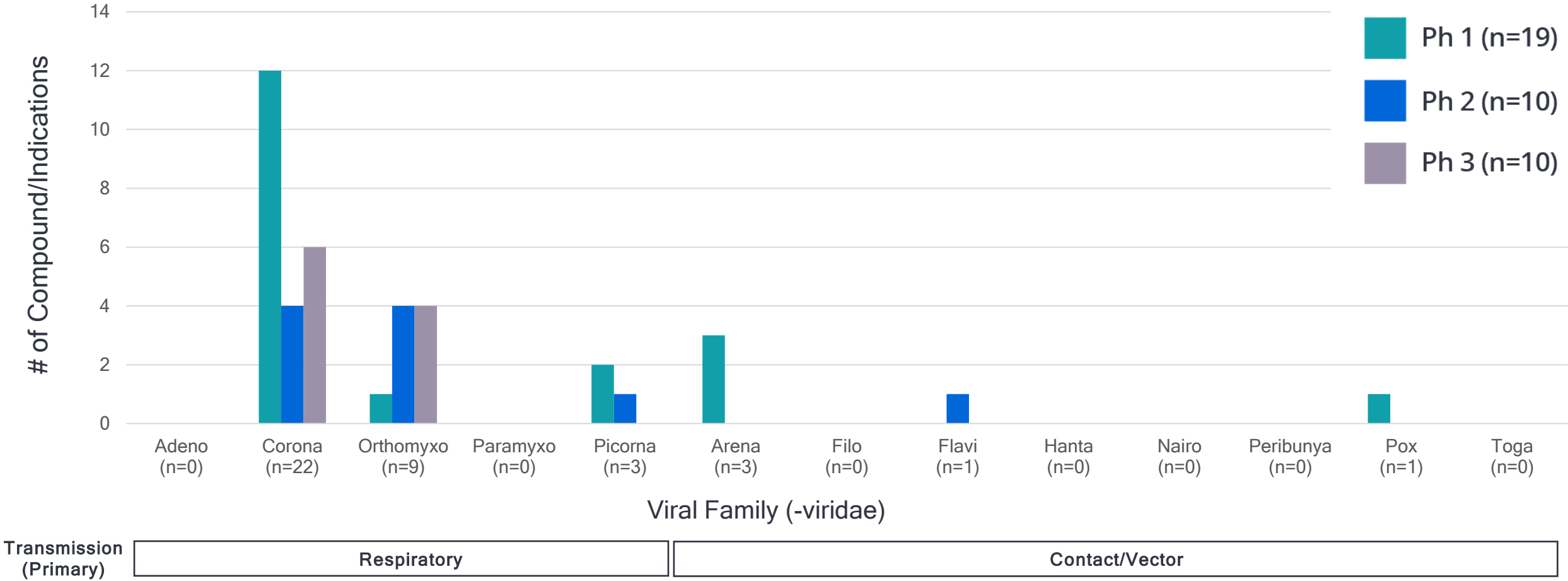
“Promising” Clinical Compounds Analysis (4th Edition)*

Unapproved Compounds (Promising and Watch & Wait) by Virus Family (N=39)



*As of December 18, 2024.

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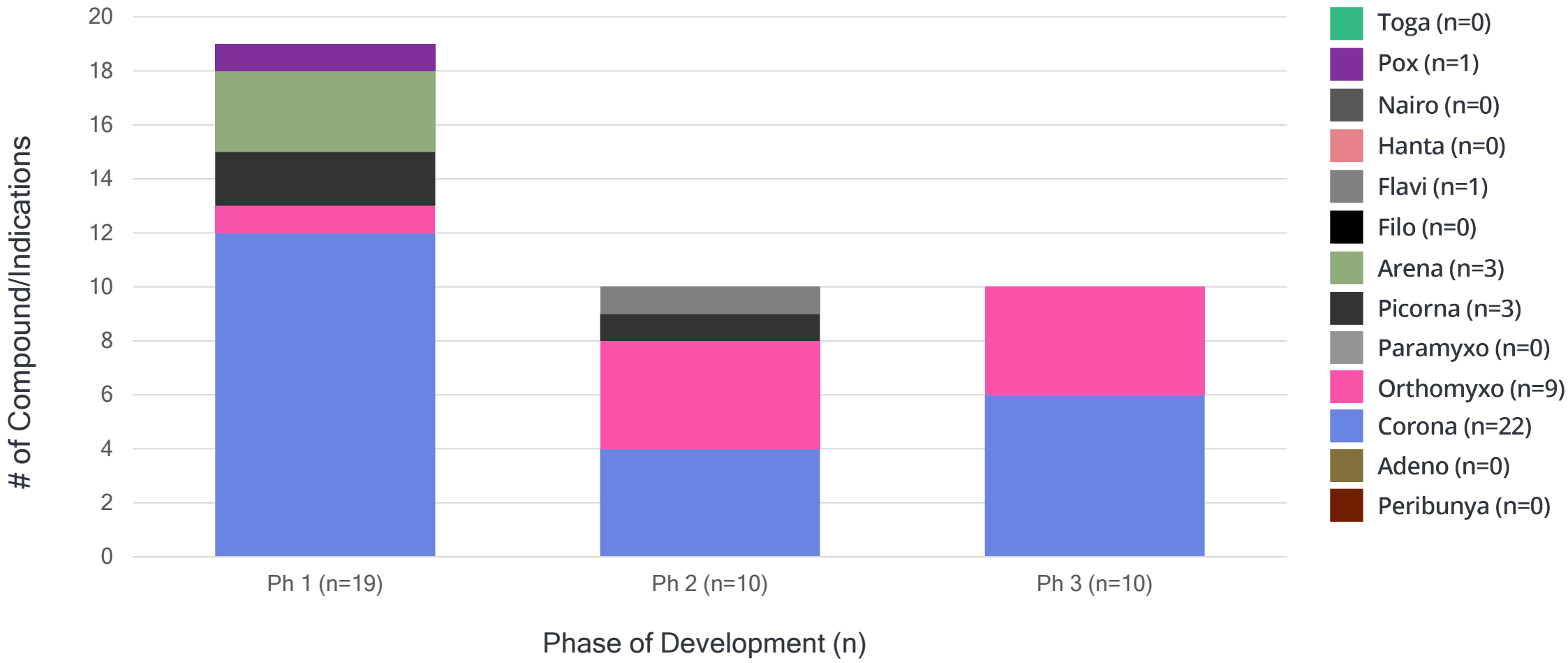
“Promising” Compounds Analysis (4th Edition)*

Novel Compound/Indications (Promising and Watch & Wait) by Phase of Development (N=39)



*As of December 18, 2024.

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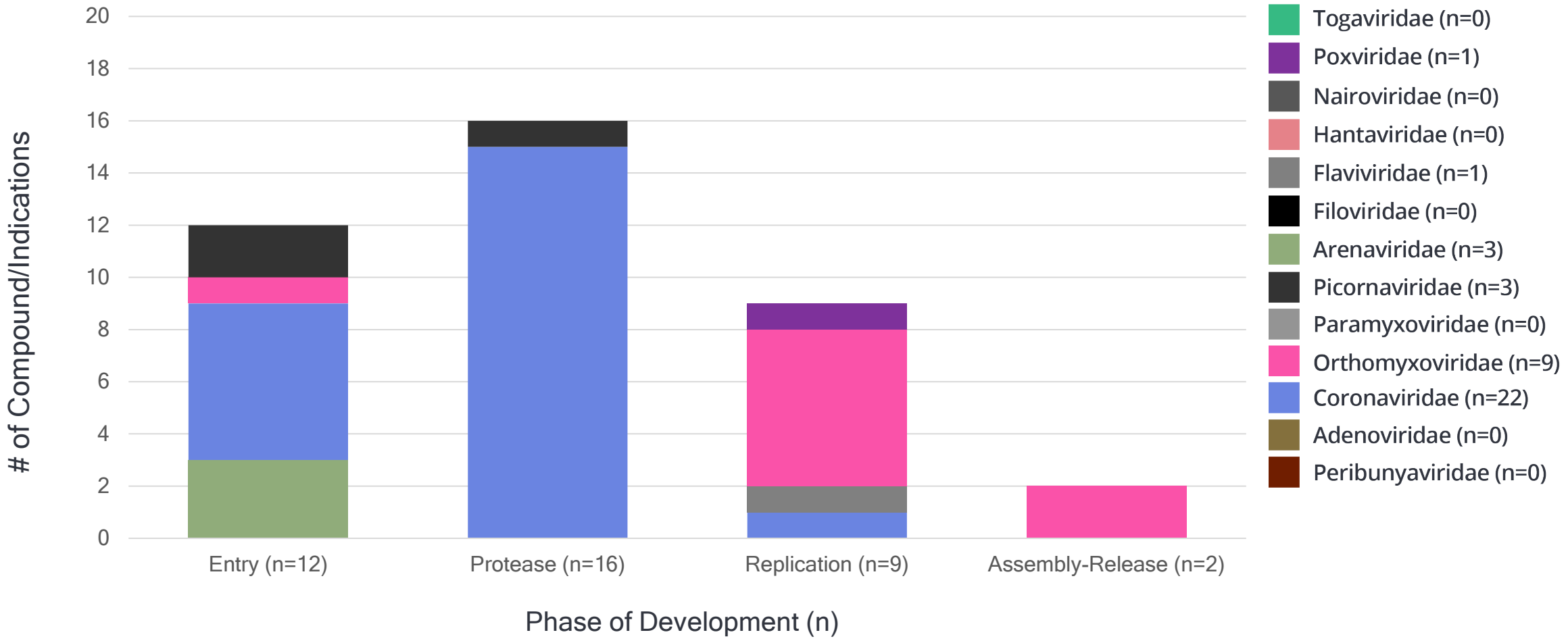
“Promising” Compounds Analysis (4th Edition)*

Novel Compound/Indications (Promising and Watch & Wait) by MOA and Viral Family (N=39)



*As of December 18, 2024.

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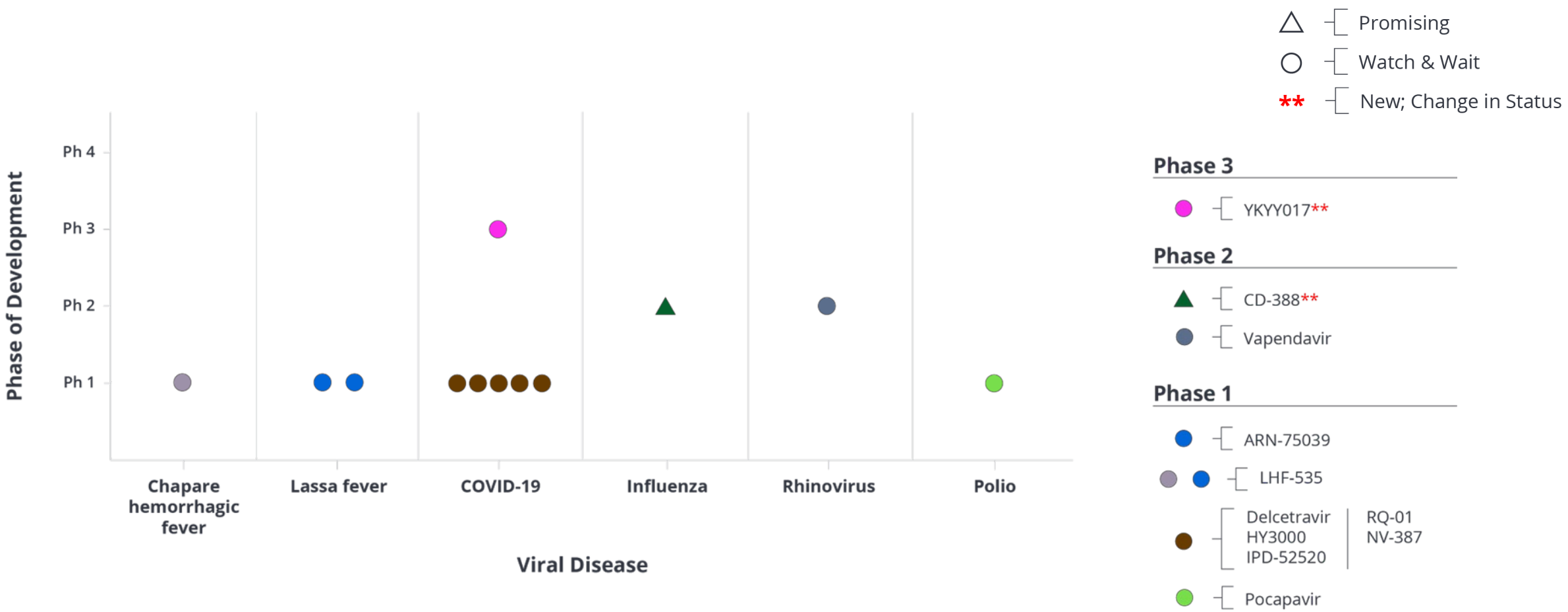
Novel Clinical Antiviral Entry Inhibitors*

Novel Compound/Indications (Promising, Watch & Wait (N=12))



*As of December 18, 2024; Attachment, Capsid (Rhinovirus), Fusion.

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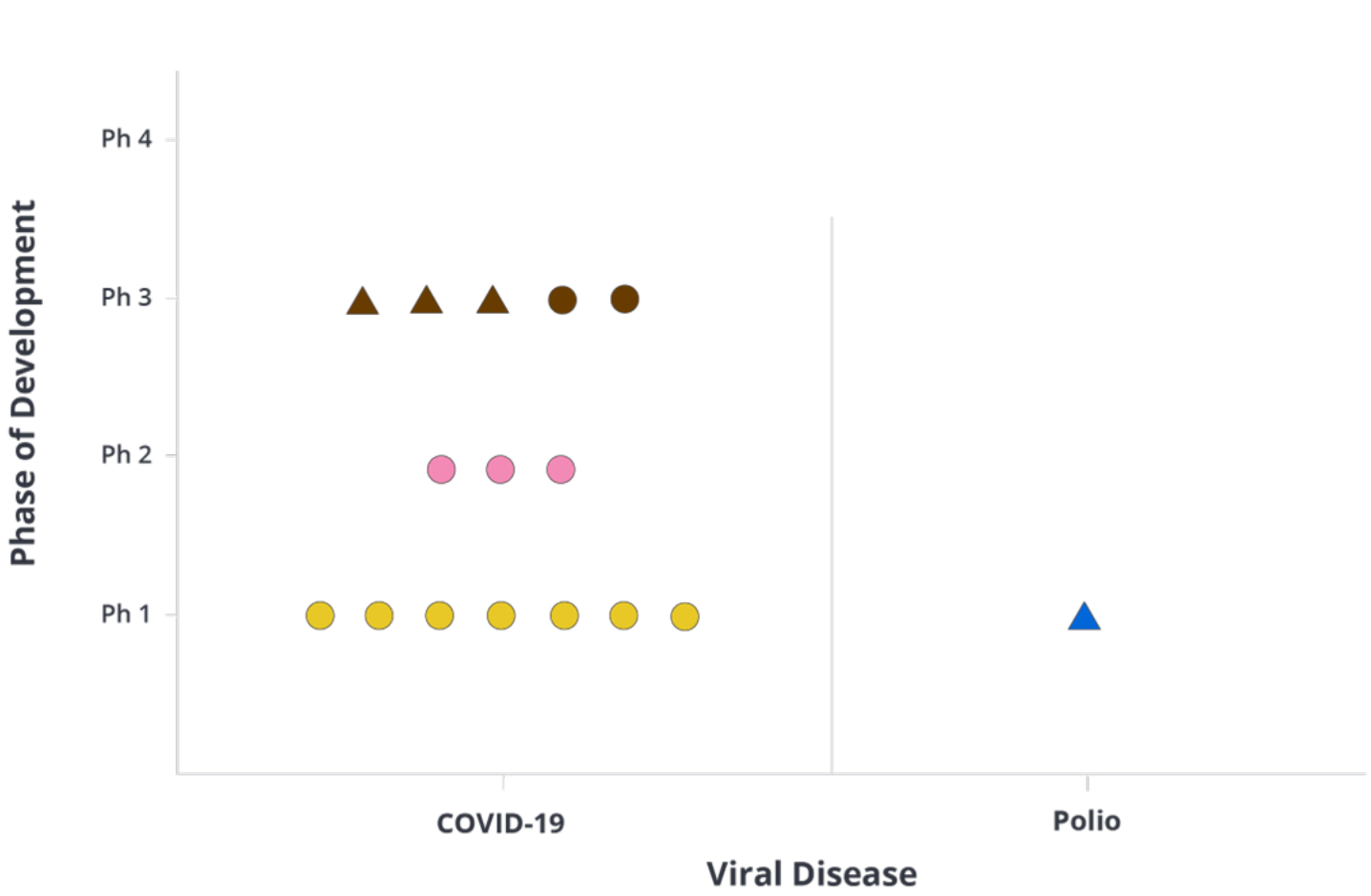
Novel Clinical Antiviral Protease Inhibitors*

Novel Compound/Indications (Promising, Watch & Wait, Archived (N=16))



△ Promising
○ Watch & Wait

Phase 3

△ GST-HG171, QLS1128, STI-1558

● FB2001, WPV01

Phase 2

● EDP-235, Ibuzatrelvir, HS 10517/Ritonavir

Phase 1

▲ V-7404

● ALG-097558, ASC11/rtv, CDI-988, GS-00202, ISM3312, S-892216, Limnetrelvir (ABBV 903)

*As of December 18, 2024; Mpro (Coronavirus and Enterovirus).

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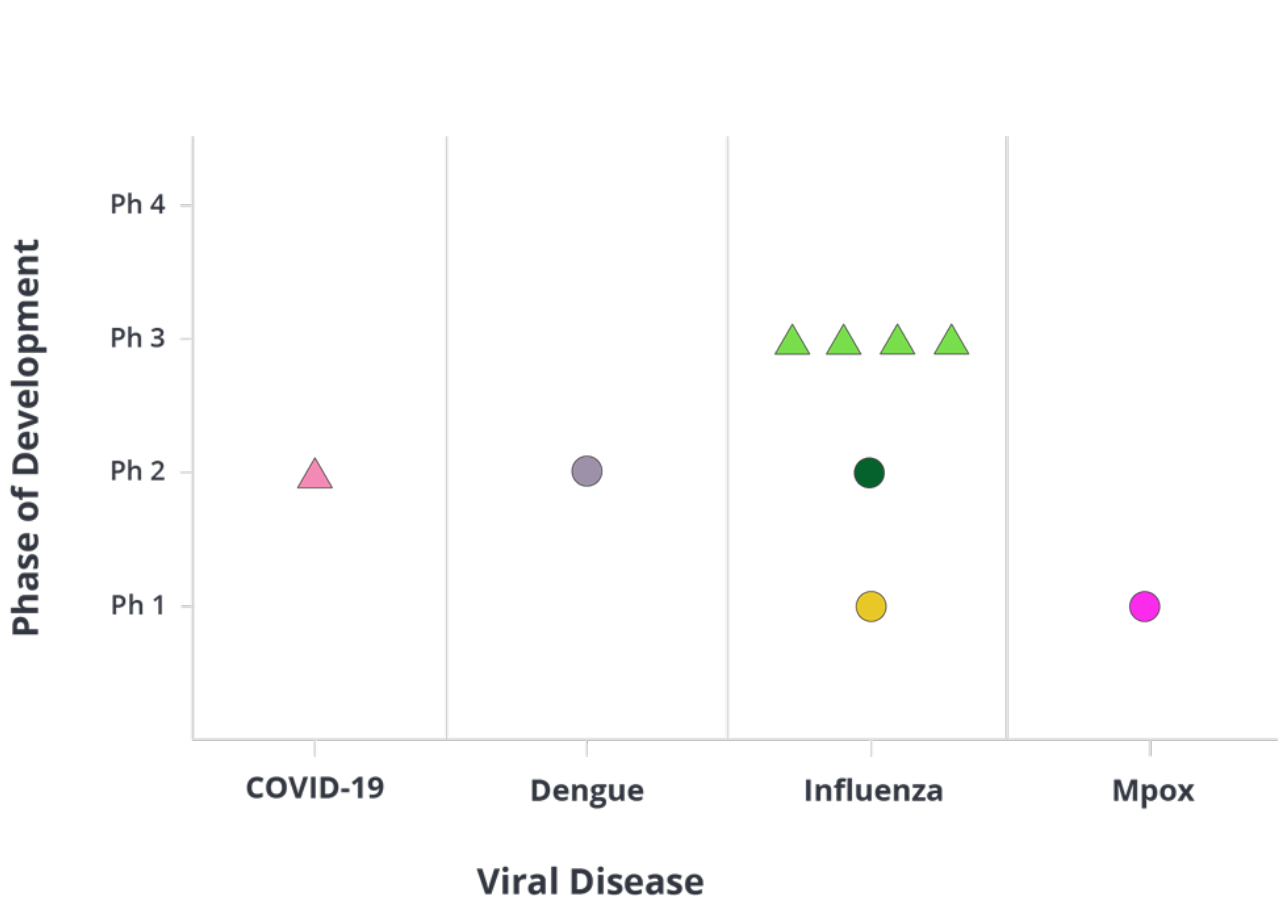
Novel Clinical Antiviral Replication Inhibitors*

Novel Compound/Indications (Promising, Watch & Wait (N=9))



△ Promising

○ Watch & Wait

** New; Change in Status

Phase 3

△ Onradivir
GP681
ZX-7101A
TG-1000

Phase 2

△ SHEN26

○ EYU688

● CC-42344**

Phase 1

● TRX100 (AV5124)

● ASC10

*As of December 18, 2024; Polymerase, Endonuclease, Replicase, DENV NS4B.

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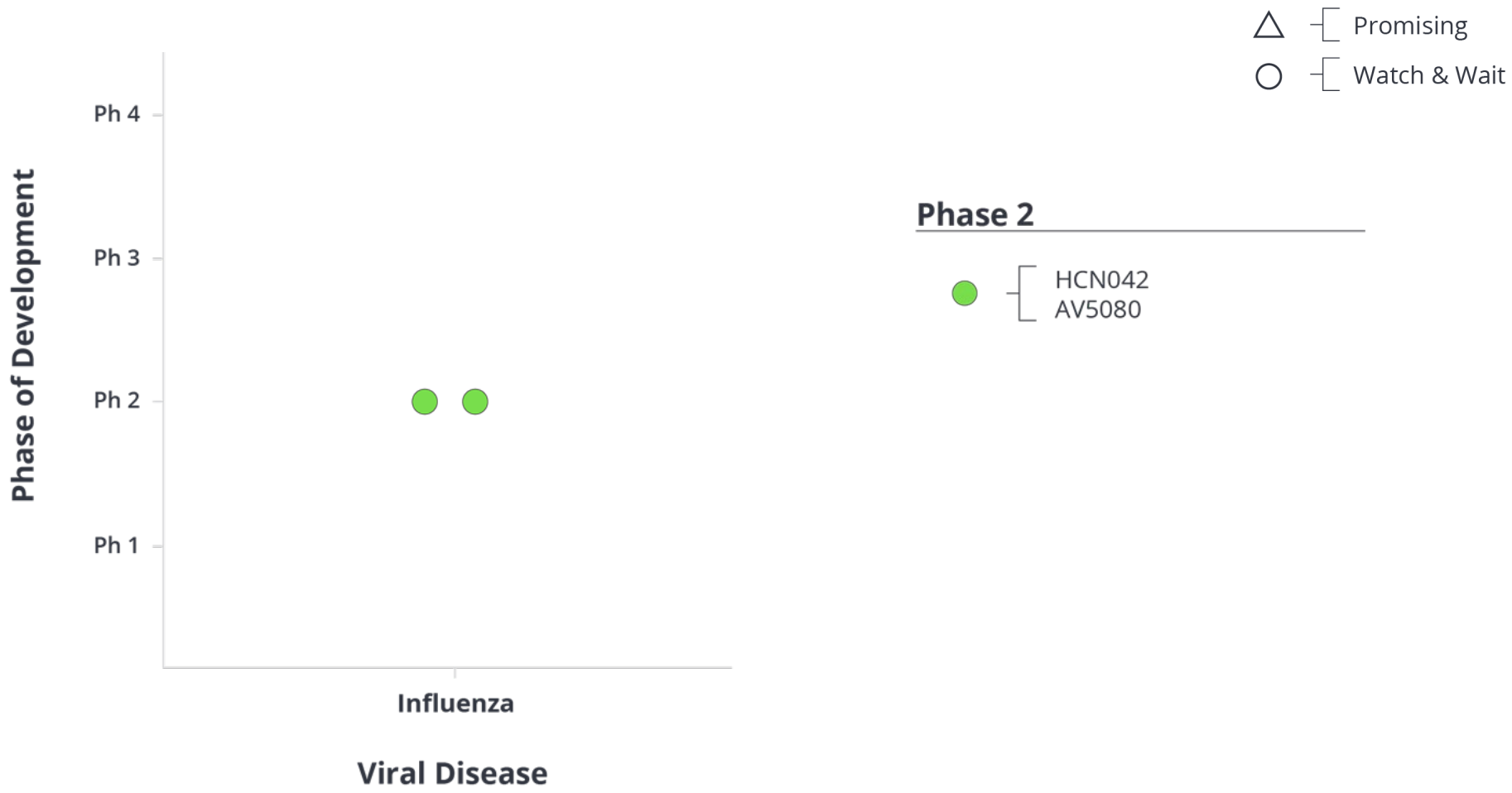
Novel Clinical Antiviral Assembly-Release Inhibitors*

Novel Compound/Indications (Promising, Watch & Wait, Archived (N=2))



*As of December 18, 2024; Neuraminidase.

Summary of Updated Antiviral Clinical Development Landscape with Promising Clinical Compounds (4th Edition)*

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*As of December 18, 2024; **Some compounds are being evaluated for more than one viral indication.

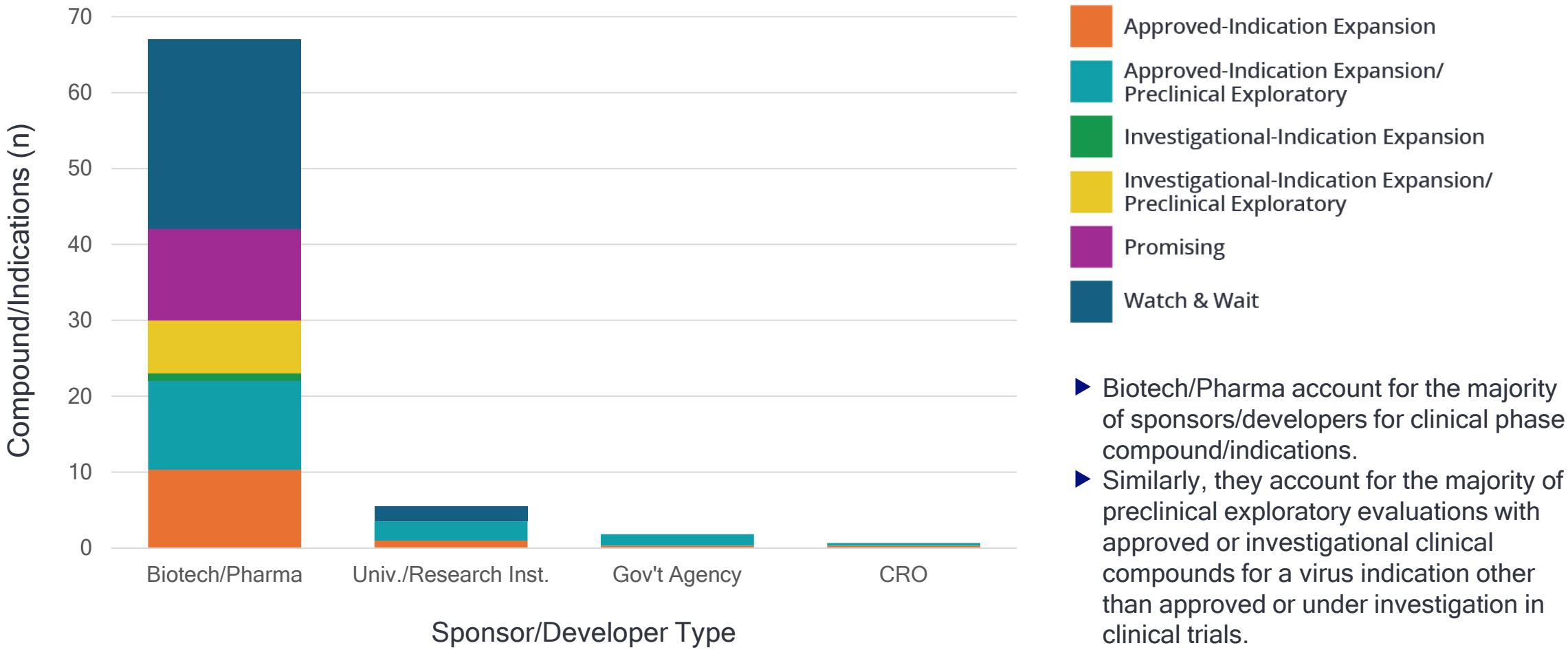
Clinical Antiviral Sponsors and Developers

Clinical Antiviral Landscape: Sponsors & Developers*

- The biopharmaceutical industry (both large and small companies) represents **67 (89.3%)** of the global antiviral clinical developers (**75**).
  - Academia **7.3%**
  - Government groups **2.4%**
  - Contract Research Organizations (CRO) **<1%**
- For the **39** Promising and Watch & Wait clinical compound/indications:
  - The countries most represented by developers/sponsors are the United States (**46.6%**) and China (**36.8%**). Others include:
    - Australia, Hong Kong, Japan, Russia, Switzerland, Taiwan, each at **2.6%**
    - Belgium at **1.3%**
  - The majority (**63.2%**) of developers/sponsors are located in countries with high-income economies.
    - The remainder are located in China which has an upper-middle income economy class.

*As of December 18, 2024; Includes clinical compounds categorized as Approved/Investigational Antivirals-Indication Expansions, Promising, and Watch & Wait.

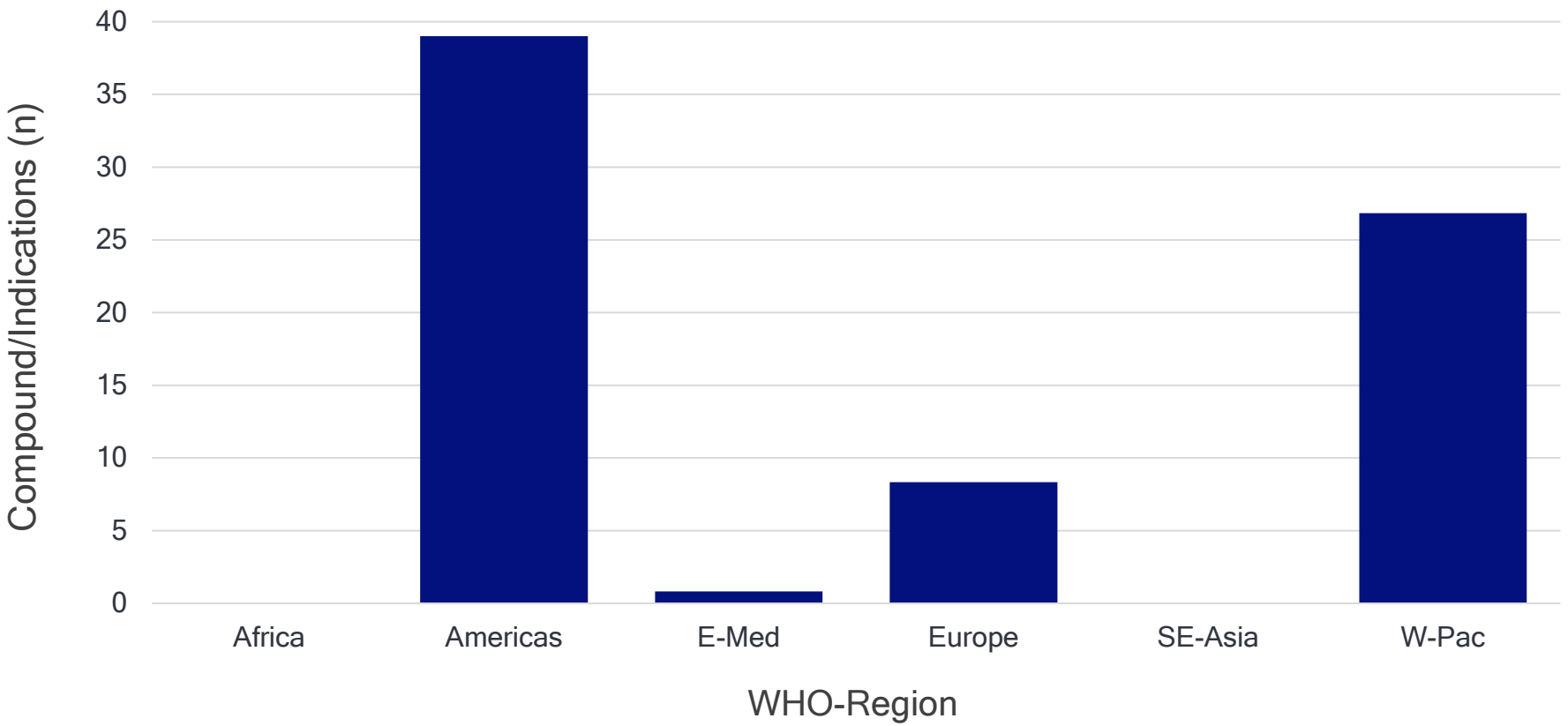
Clinical Antiviral Compound/Indications by Sponsor/Developer Type*



- Biotech/Pharma account for the majority of sponsors/developers for clinical phase compound/indications.
- Similarly, they account for the majority of preclinical exploratory evaluations with approved or investigational clinical compounds for a virus indication other than approved or under investigation in clinical trials.

*As of December 18, 2024; Includes clinical compounds categorized as Approved/Investigational Antivirals-Indication Expansions, Promising, and Watch & Wait.
CRO: contract research organization.

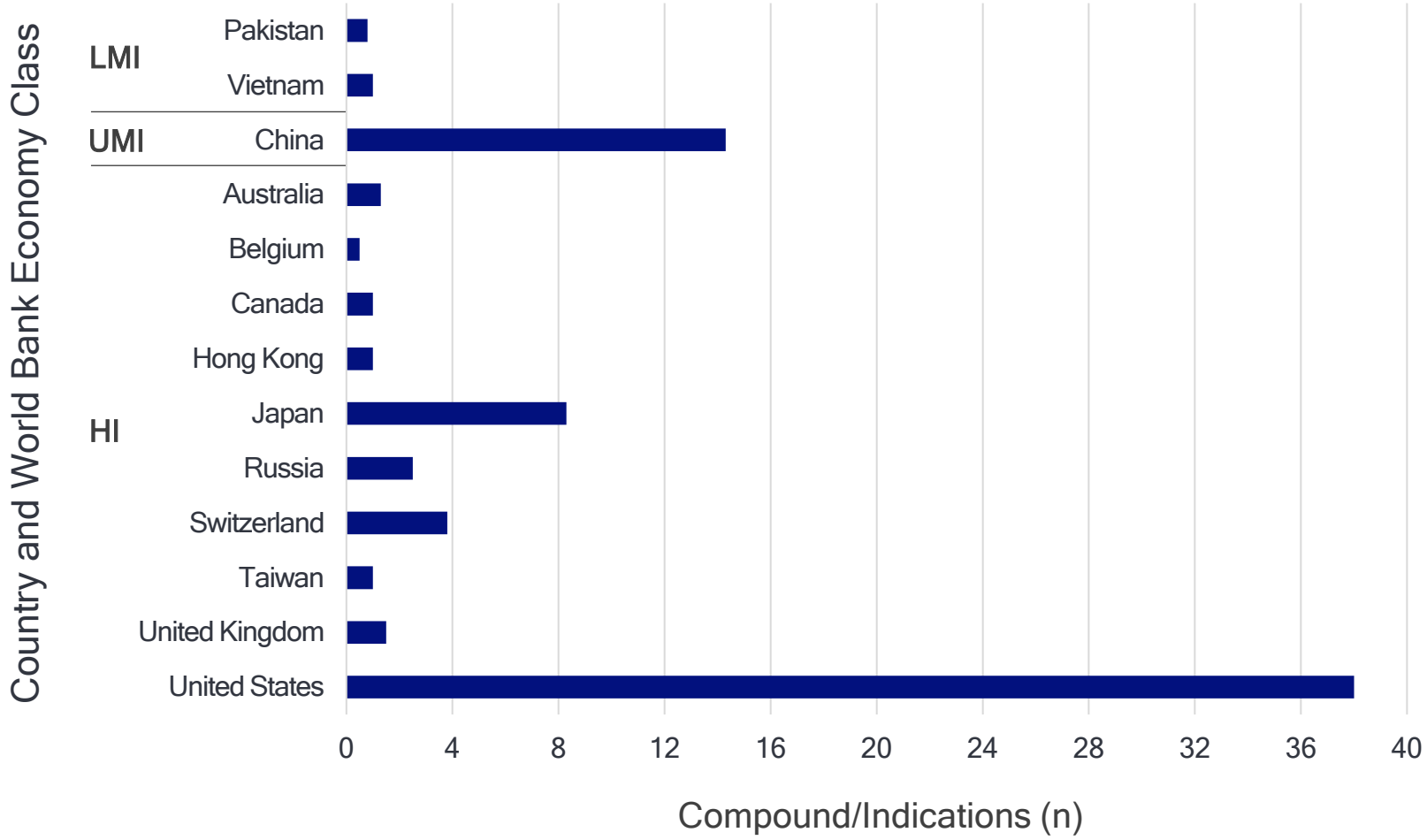
Clinical Antiviral Compound/Indications by Sponsor/Developer WHO-Region* (N=75)



- The Americas and Western Pacific regions are primarily driven by the United States and China.

*As of December 18, 2024; Includes clinical compounds categorized as Approved/Investigational Antivirals-Indication Expansions, Promising, and Watch & Wait.

Clinical Antiviral Compound/Indications* by Country and World Bank Economy Class** (N=75)



- The majority (**78.5%**) of sponsors/developers of Indication Expansion, Promising and Watch & Wait clinical antiviral compound/indications are located in countries with high-income economies.
  - The remainder are those with upper-middle (**19.1%**) and lower-middle (**2.4%**) income economies.
- The United States (HI) and China (UMI) have the most representation.

*As of December 18, 2024; Includes clinical compounds categorized as Approved/Investigational Antivirals-Indication Expansions, Promising, and Watch & Wait.
**World Bank country classifications by income level for 2024-2025; LMI: lower-middle income; UMI: upper-middle income; HI: high-income.

Preclinical Antiviral Development Landscape as of December 2024

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.

INTREPID Alliance Preclinical Triage and Classification

- Preclinical compounds in Airfinity database:
  - Triage based on publicly available data into general therapeutic categories/mechanism
  - Airfinity provided the key references/citations associated with the preclinical compounds
- Challenges in classifying preclinical compounds:
  - Amount/Type of data available varies substantially
  - Not every "published" preclinical compound is or will be a clinical candidate
    - Tool compound, lead series, etc. in publications
- Proposed classification on type of data available consistent with industry stages of discovery R&D:
  - Preclinical compounds designated as "Hit", "Early Lead", "Late Lead", "Potential Candidate"
  - Archived preclinical compounds lack of published data suggesting no further development; only computational-based antiviral data reported.
  - Compounds with prior clinical data designated as Approved Antiviral-Indication Expansion, Investigational Antiviral-Indication Expansion, or Repurposed (non-antiviral)

Examples of publicly available data for INTREPID Alliance review of preclinical compound/indications:

in vitro	Structure/Sequence	*in vivo* Exposure (animal)	*in vivo* Efficacy (animal)	Prior Clinical Data Available
Biochemical Cell-based (e.g., replicon, pseudovirus) Cell-based antiviral (wild-type, variants) ADME Resistance profile	Chemical structure Amino acid sequence RNA sequence	PK Safety/Toxicology	Treatment Prevention	Yes No

ADME: absorption, distribution, metabolism, and excretion; PK: pharmacokinetic.

INTREPID Alliance Preclinical Antiviral Landscape: Preclinical Antiviral Compounds Analysis Update (4th Edition)*

- Preclinical Landscape Analyses previously reported on the INTREPID Alliance website:
  - Initial post within 3rd Edition with data through July 2024 was reported in October 2024. Available here.
- This 4th edition analysis of the data through December 2024 shows:
  - **168** distinct antiviral compounds in the antiviral preclinical development landscape associated with **189** indications; **93** for COVID-19 and **96** for Non-COVID.
- Data were organized based on stage of development:
  - **Preclinical** are novel unapproved antiviral compounds with only preclinical data and no clinical data.
  - **Preclinical Exploratory** are unapproved clinical phase or approved antivirals exploring activity against a different virus from the primary antiviral indication, including:
    - **Approved Antiviral-Indication Expansion** – antiviral approved for one or more viral disease indications.
    - **Investigational Antiviral-Indication Expansion** – antiviral in clinical development, not yet approved.
- Additional scientific analysis** of only the novel preclinical compounds categorized them based on the relative stage of preclinical development from “Hit” to “Potential Candidate”.

*As of December 18, 2024; **See criteria on slide 37.

INTREPID Alliance Preclinical Triage: Stages of Preclinical Development

Categories generally align with movement of a compound across the stages of drug discovery.

- Preclinical Compounds with only preclinical data and no clinical data designated as:
  - **Hit** – high-throughput or compound library screening hit, initial antiviral activity requiring significant optimization. Limited or no *in vitro* data available supporting antiviral mechanism of action (MOA).
  - **Early Lead** – limited Structure-Activity Relationship (SAR), antiviral activity associated with MOA, may have limited *in vitro/in vivo* pharmacokinetic data reported.
  - **Late Lead** – potency consistent with candidate quality for the specific MOA, more extensive *in vitro* characterization (e.g., ADME profile, activity against clinically relevant virus strains/isolates), *in vivo* PK and/or animal efficacy model data reported.
  - **Potential Candidate** – *in vivo* efficacy and safety dataset consistent with preparation for FDA IND (or similar) submission; compound has been reported by developer as a pipeline clinical candidate and/or in IND (or similar) enabling studies.
  - **Archived** – progress on the compound has been stopped (timeframe stopped, >5 years); antiviral evidence is only computational; previously optimized drug from another antiviral/other indication that only has weak activity. May be useful to inform new screening or medicinal chemistry efforts.
  - **Discontinued** – compound progression has been stopped for known reasons; for example, compound failed preclinical "IND" toxicology, change in business strategy, etc. May be useful to inform new screening or medicinal chemistry efforts.
- Preclinical Exploratory are Investigational ("unapproved") and Approved antivirals exploring antiviral activity against a different virus from the Investigational/Approved antiviral indication, including:
  - **Approved Antiviral-Indication Expansion** – antiviral approved for one or more viral disease indications.
  - **Investigational Antiviral-Indication Expansion** – antiviral in clinical development, not yet approved.

ADME: absorption, distribution, metabolism, and excretion; PK: pharmacokinetic; IND: Investigational New Drug.

Triage of Preclinical Data (3rd Edition Landscape)*

- Initial triage of preclinical antiviral landscape data as of July 12, 2024, show 362 preclinical compound/indications.
- Preclinical antiviral compounds of interest are those that are directed at specific viral targets.

General Category	N	%
Antiviral	157	43
Ribavirin	10	3
Other/Excluded	195	54
TOTAL	362	100

Initial Triage

Airfinity Data by Compound/Indications

106 with confirmed antiviral mechanism of action

- 72 (68%) for COVID-19
- 34 (32%) for Non-COVID-19

2nd Triage

INTREPID Alliance Triage by Antiviral Mechanism

Preclinical Compound/Indication Category:

- Hit
- Early Lead
- Late Lead
- Approved Antiviral-Indication Expansion
- Investigational Antiviral-Indication Expansion
- Ribavirin-Indication Expansion
- Archived

Exclusion Criteria:

- Antibodies
- Antibiotics & Anti-infectives
- HIV or HCV-specific
- Host Targets (incl. Imm. Mod.)
- Natural Products/Nutraceuticals/Herbals
- Vaccines

Inclusion Criteria:

- Known Antiviral MOA
- *In Vitro/In Vivo* Activity
- Small Molecules
- Peptides
- RNA-based
- Preclinical Exposure & Efficacy
- Prior Clinical Data Available

*As previously shown in the 3rd Edition of the Preclinical Antiviral Landscape based on data up through July 12, 2024.

Summary of Preclinical Antiviral Compounds & Stage of Development (4th Edition)*

Stage of Preclinical Development	Distinct Compounds	# Compound/Indications**		
		All	COVID-19	Non-COVID
Preclinical* **	**168**	**189**	**93**	**96**
On-going Activity	108	125	74	51
Potential Candidate	15	18	10	8
Late Lead	17	19	11	8
Early Lead	33	37	17	20
Archived & Discontinued	60	64	19	45
Archived	55	57	18	39
Discontinued	5	7	1	6
Preclinical Exploratory	**8**	**23**	**1**	**22**
App. AV-Ind. Exp.	4	16	0	16
Inv. AV-Ind. Exp.	4	7	1	6
Overall Total	**176**	**212**	**94**	**118**

- **108** distinct **Preclinical** compounds have on-going activity
- These are associated with **125** viral disease indications
  - **74** (59.2%) target COVID-19

- **8** distinct **Preclinical Exploratory** investigational or approved antivirals have on-going activity
- These are associated with **23** viral disease indications
  - **22** (95.7%) target Non-COVID

*As of December 18, 2024; **Some compounds are being evaluated for more than 1 viral indication;
***App. AV-Ind. Exp.: Approved Antiviral-Indication Expansion; Inv. AV-Ind. Exp.: Investigational Antiviral-Indication Expansion.

Summary of Preclinical Antiviral Compounds & Mechanism of Action (4th Edition)*

Mechanism of Action	# Distinct Compounds**		
	All	COVID-19	Non-COVID
Preclinical	**108**	**73**	**35**
Entry	34	24	10
Protease	40	35	5
Replication	31	13	18
Assembly/Release	2	0	2
Unspecified	1	1	0
Preclinical Exploratory* **	**8**	**1**	**7**
App. AV-Ind. Exp. Replication	4	0	4
Inv. AV-Ind. Exp. Protease	1	1	0
Inv. AV-Ind. Exp. Replication	3	0	3
Overall Total	**116**	**74**	**42**

- **108** distinct **Preclinical** compounds have on-going activity
- Primary target **MOA**:
  - **Overall: 40** protease (37%)
  - **COVID-19: 35** protease (47.9%)
  - **Non-COVID: 18** replication (51.4%)

- **8** distinct **Preclinical Exploratory** investigational or approved antivirals have on-going activity
- Primary target **MOA**:
  - **Overall: 7** replication (87.5%)
  - **COVID-19: 1** protease (100%)
  - **Non-COVID: 7** replication (100%)

*As of December 18, 2024; **Some compounds are being evaluated for more than 1 viral indication;
***App. AV-Ind. Exp.: Approved Antiviral-Indication Expansion; Inv. AV-Ind. Exp.: Investigational Antiviral-Indication Expansion.

Changes in Preclinical Antiviral Pipeline (4th Edition)*

New Additions and Changes in Status from 3rd to 4th Edition

Virus Family	Indication	Compound	Hit (2)	Early Lead (12)	Late Lead (2)	Potential Candidate (5)
Coronaviridae	COVID-19	GC-376				NEW
		GRL-0617		NEW		
		TDI-015051		NEW		
		RU-0415529	NEW			
	SARS-CoV-1	DCOY 102/103		NEW		
	Seasonal Coronavirus	DCOY 102/103		NEW		
Paramyxoviridae	Nipah virus	4′-fluorouridine		NEW		
	Parainfluenza	GHP-88309				NEW
Arenaviridae	Junin virus	4′-fluorouridine				NEW
	Lassa fever	4′-fluorouridine				NEW
Flaviviridae	Dengue	JNJ-A07			NEW	
	Yellow fever	BSBI-YF			NEW	
	Zika virus	MLT201	NEW			
Poxviridae	Mpox	NV-387-T				NEW
		5-iodo-2-deoxyuridine		NEW		
		7-deaza analogs of S-adenosyl methionine		NEW		
		CMLDBU6128 and improved pyridopyrimidinones		NEW		
		HPMPDAP (diaminopurine)		NEW		
		ST357 (TTP-018)		NEW		
		TTP-6171		NEW		
		UMM-766		NEW		

*As of December 18, 2024.

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%).

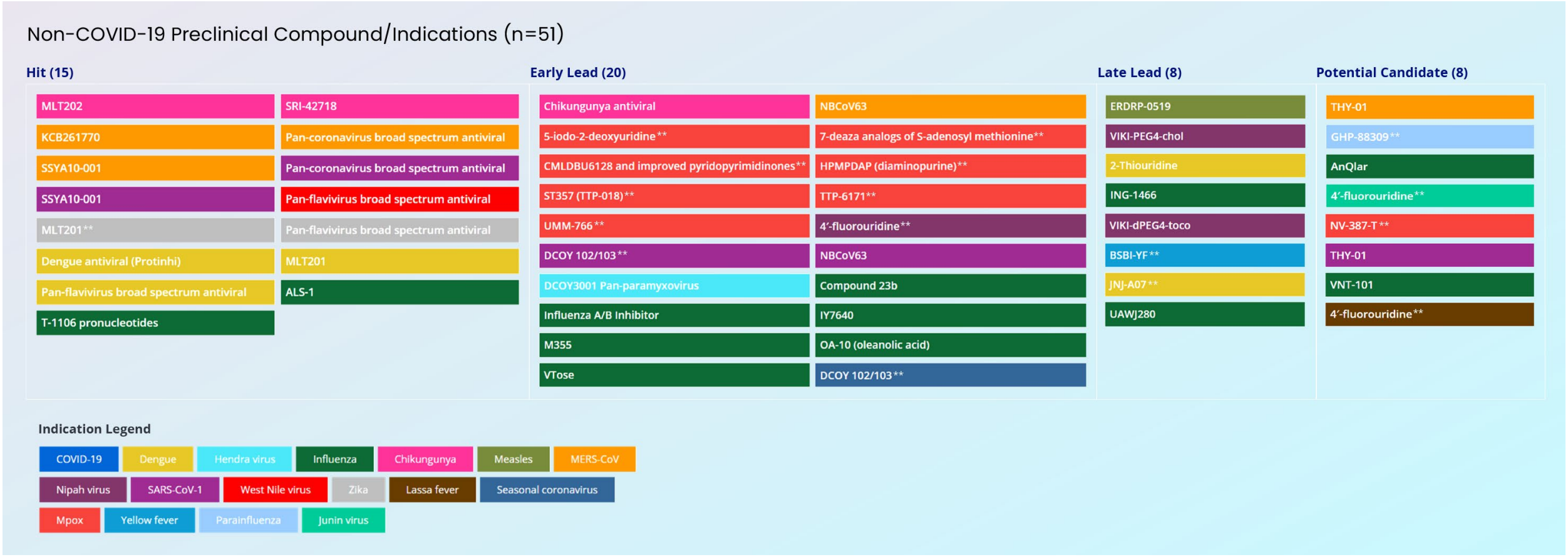
COVID-19 Preclinical Compound/Indications (n=74)

Hit (36)		Early Lead (17)		Late Lead (11)	Potential Candidate (10)
6-72-2a	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				

*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%).



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

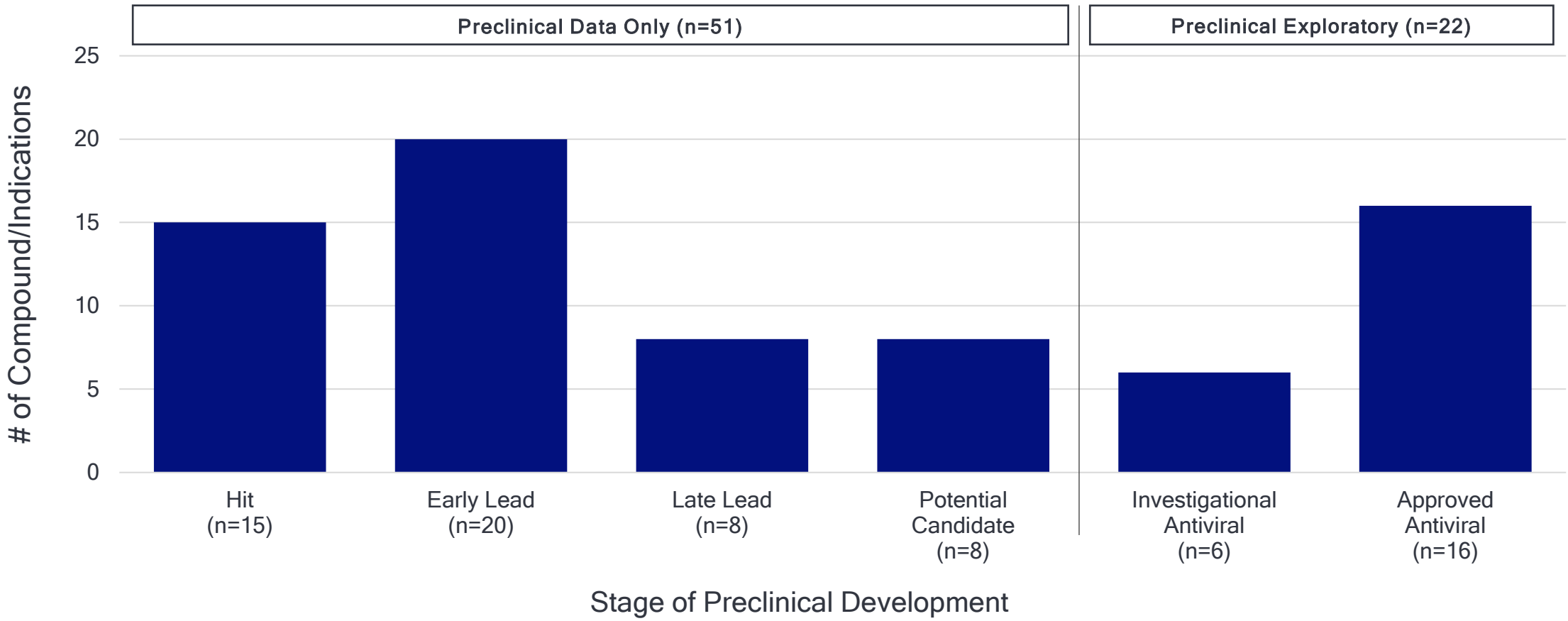
INTREPID Alliance Preclinical Antiviral Landscape (4th Edition): Key Takeaways

- A total of **168 preclinical antiviral compounds** under evaluation for the **13 viral families** of pandemic potential; the majority of preclinical compounds are targeting COVID-19.
  - Non-COVID-19 preclinical compounds are targeting primarily Influenza (9.6%), mpox (6.4%), MERS-CoV and SARS-CoV-1 and Dengue (each at 4%); the remaining 17 indications are each below 3%.
  - Ribavirin is being evaluated for 10 potential expanded virus indications.
- No preclinical development activity was found for **6** of the **13** viral families (*Adenoviridae, Picornaviridae, Filoviridae, Hantaviridae, Nairoviridae, & Peribunyaviridae*).
- In view of the 100 Days Mission for Non-COVID-19 indications, there are **16** compounds (preclinical data only) at the Late Lead or Potential Candidate stage of preclinical development.
  - Influenza (n=2 potential candidates, n=2 late leads)
  - Junin virus, Lassa fever, Mpox, Parainfluenza, SARS-CoV-1, and MERS-CoV (each with n=1 potential candidate)
  - Nipah & Dengue (each with n=2 late leads)
  - Measles & Yellow fever (each with 1 late lead)

*As of December 18, 2024.

Preclinical Non-COVID-19 Indications

Preclinical Compound/Indications by Stage of Preclinical Development (Non-COVID-19; N=73)*

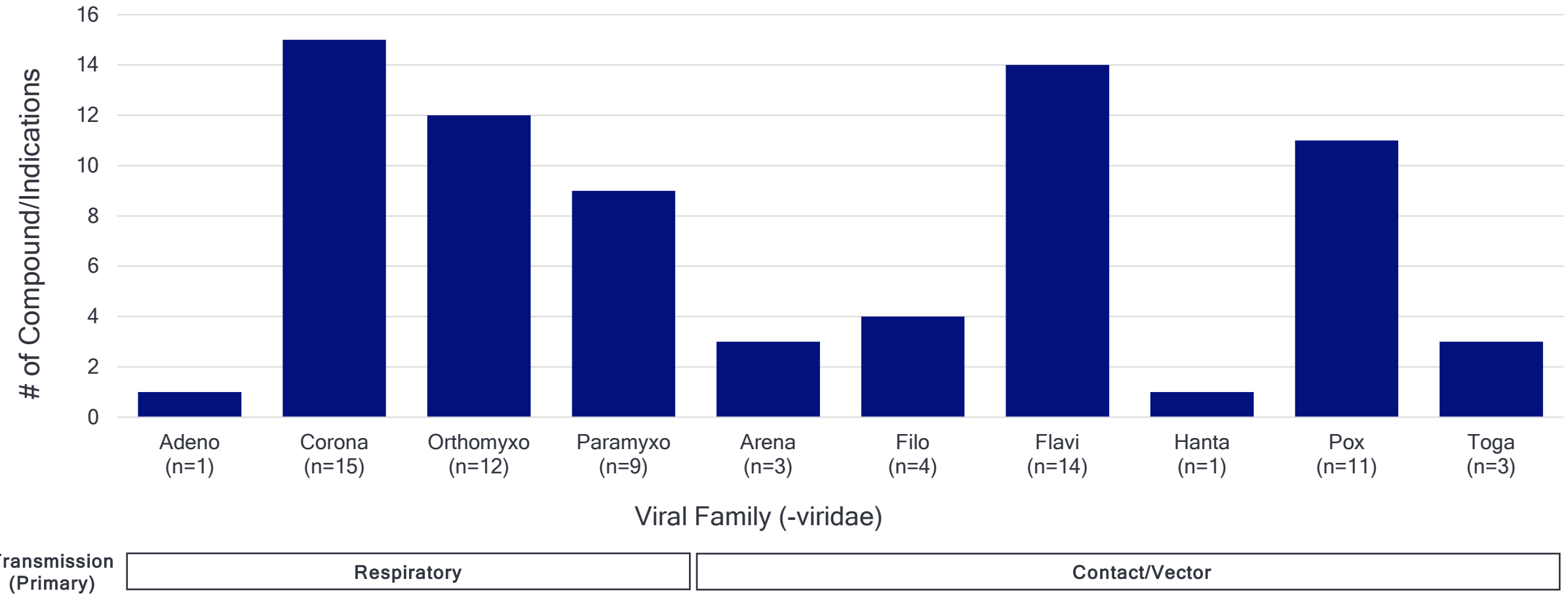


- Compound/Indications span the various stages of preclinical development.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indications by Viral Family (Non-COVID-19; N=73)*

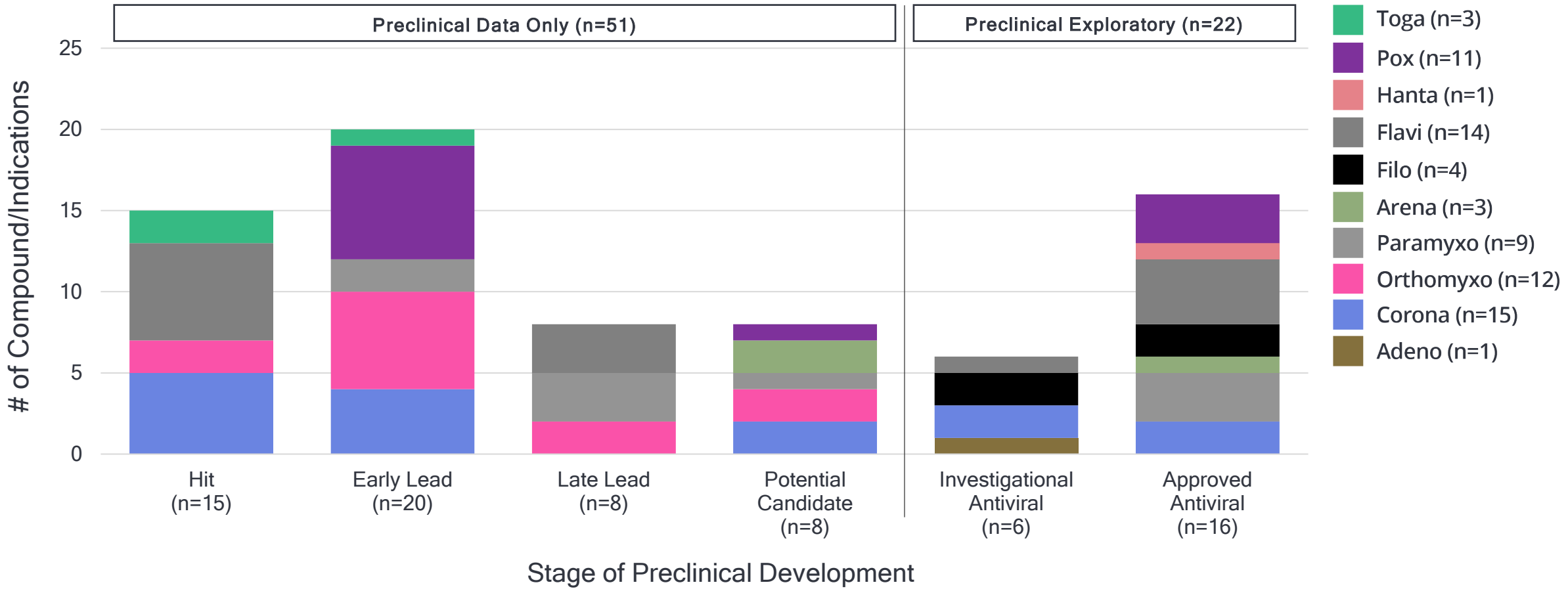


- Ten of the 13 viral families with pandemic potential have preclinical compound/indications.
  - *Orthomyxoviridae* has the most compounds and is focused on Influenza.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indications by Stage of Preclinical Development and Viral Family (Non-COVID-19; N=73)*

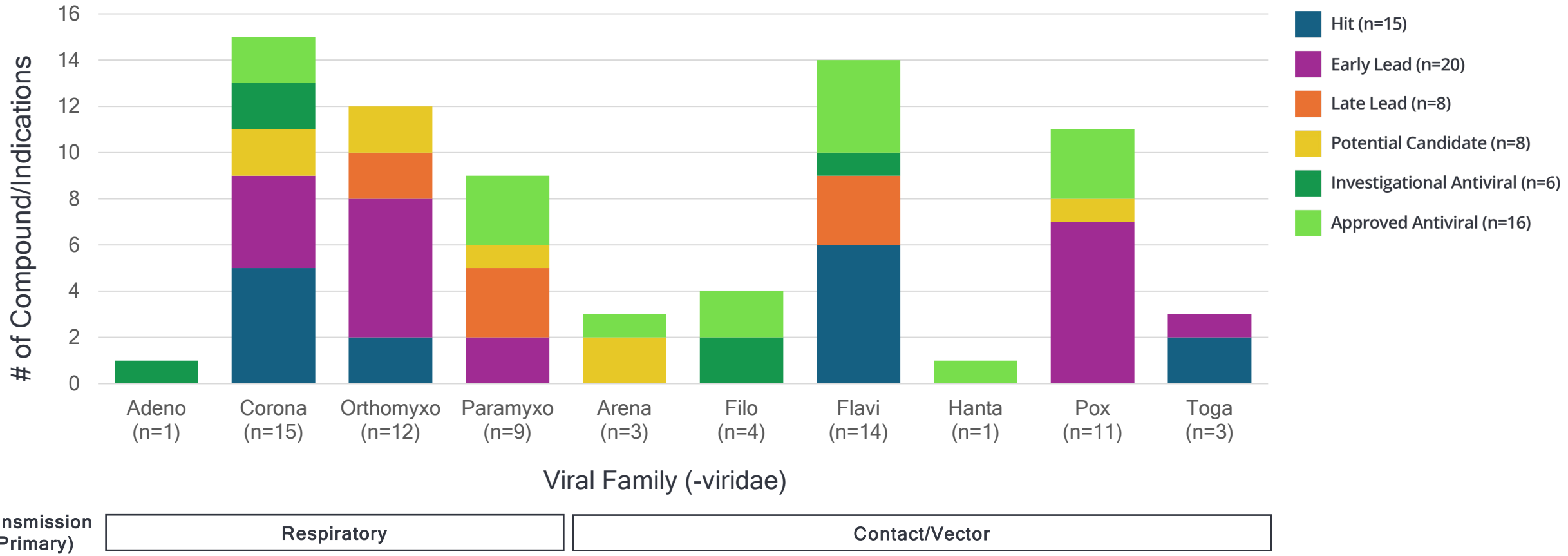


- Compound/Indications span the various stages of preclinical development.
  - *Orthomyxoviridae* (Influenza) has the most compound/indications.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indications by Viral Family and Stage of Preclinical Development (Non-COVID-19; N=73)*

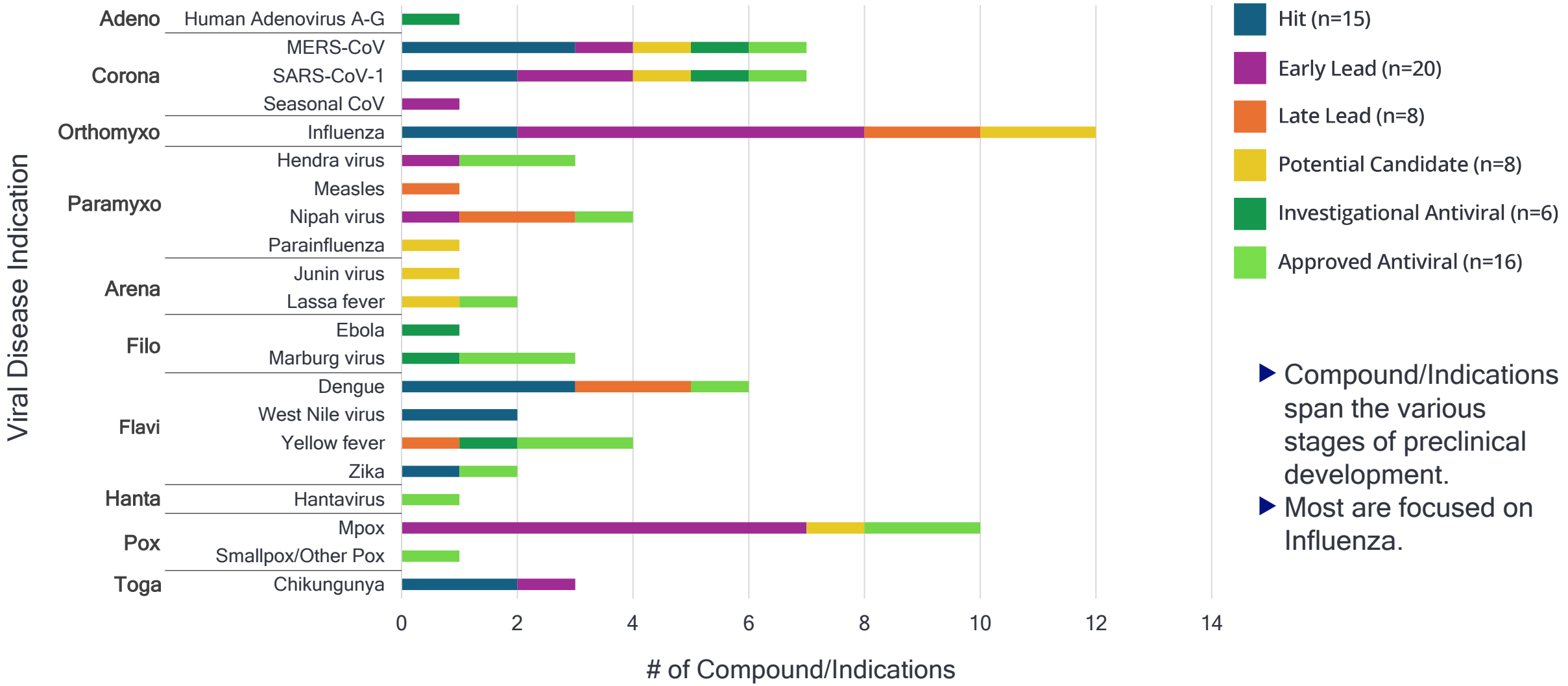


- Compound/Indications span the various stages of preclinical development.
- The highest activity (12/51, 23.5%) is focused on *Orthomyxoviridae* (Influenza).

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indications by Viral Disease and Stage of Preclinical Development (Non-COVID-19; N=73)*

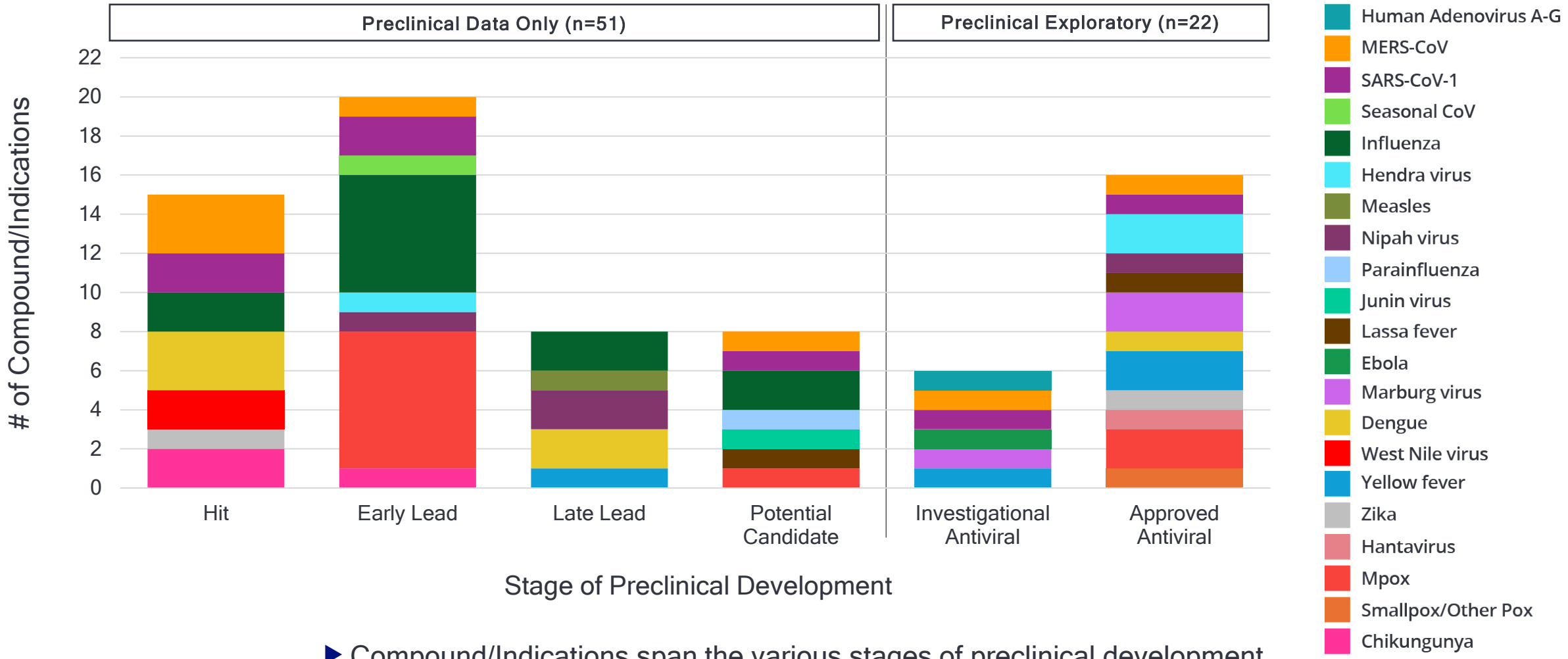


- Compound/Indications span the various stages of preclinical development.
- Most are focused on Influenza.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indications by Stage of Preclinical Development and Viral Disease (Non-COVID-19; N=73)*

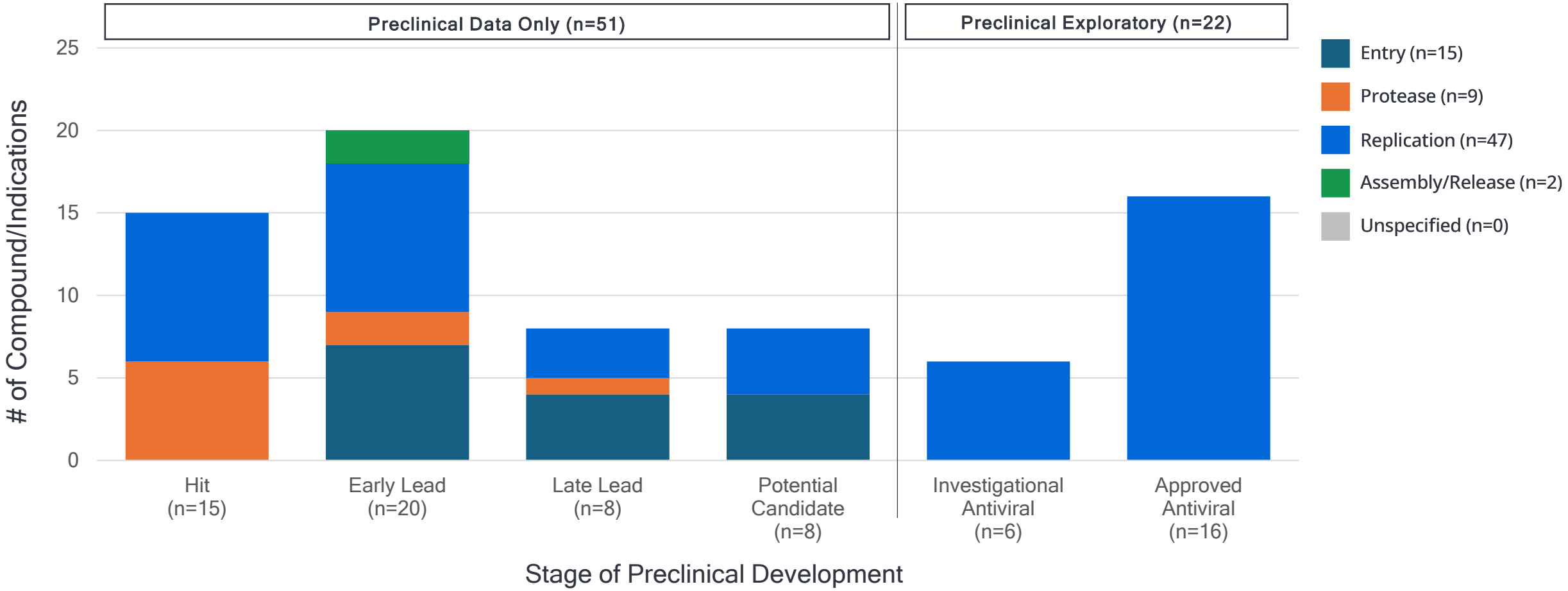


- Compound/Indications span the various stages of preclinical development.
- Most are focused on Influenza.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indication Category by Stage of Preclinical Development and Mechanism of Action (Non-COVID-19; N=73)*

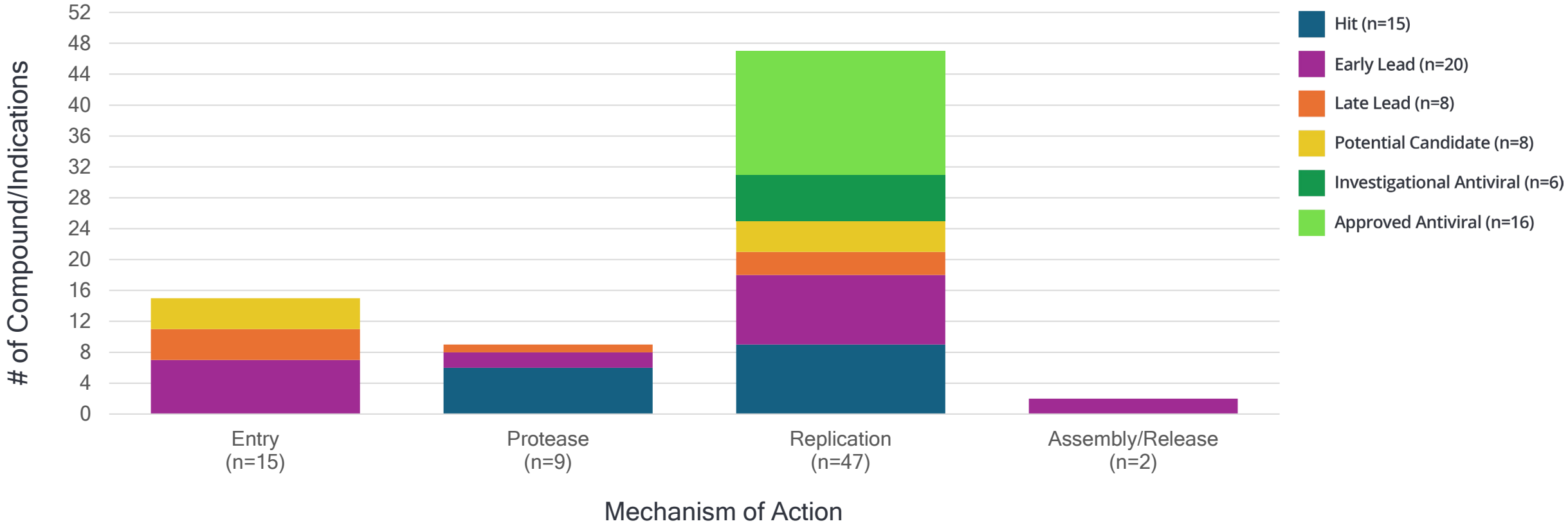


- MOAs for Compound/Indications span the various stages of preclinical development.
- All of the Approved or Investigational Antivirals for indication expansion are replication inhibitors.

*As of December 18, 2024.

INTREPID ALLIANCE

Preclinical Compound/Indication Category by Mechanism of Action and Stage of Preclinical Development (Non-COVID-19; N=73)*

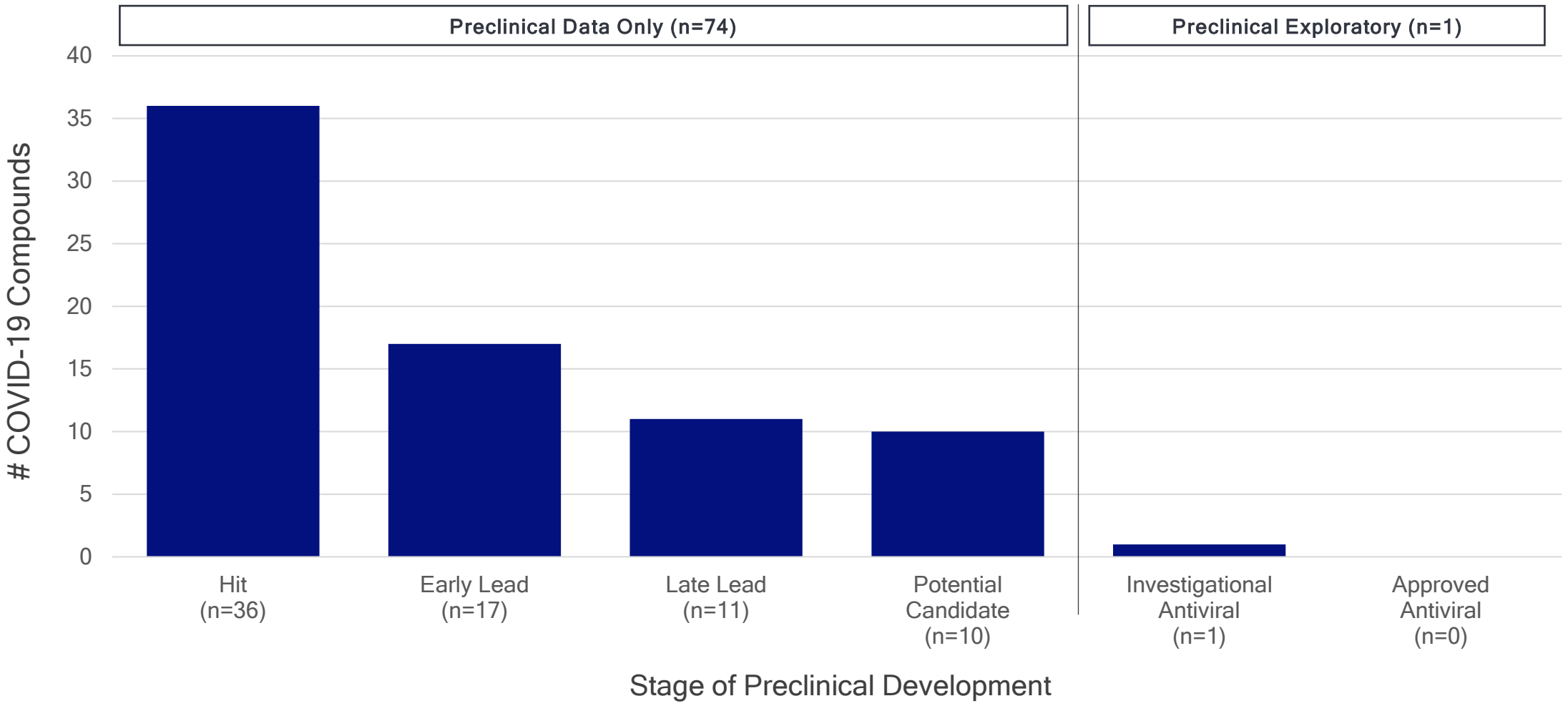


- Compound/Indications span the various stages of preclinical development and MOAs.
- The MOA rank order is Replication, Entry, Protease, Assembly/Release.

*As of December 18, 2024.

Preclinical COVID-19 Indications

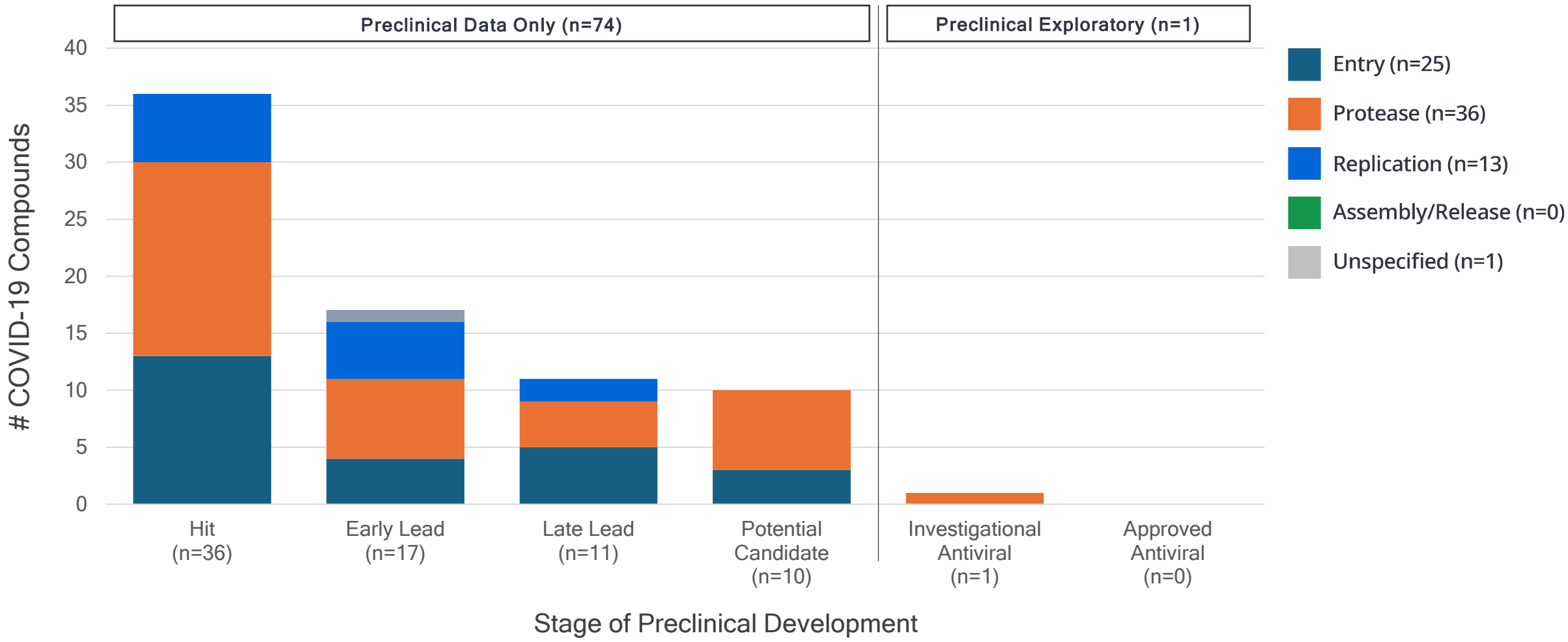
COVID-19 Compounds by Stage of Preclinical Development (N=75)*



*As of December 18, 2024.

INTREPID ALLIANCE

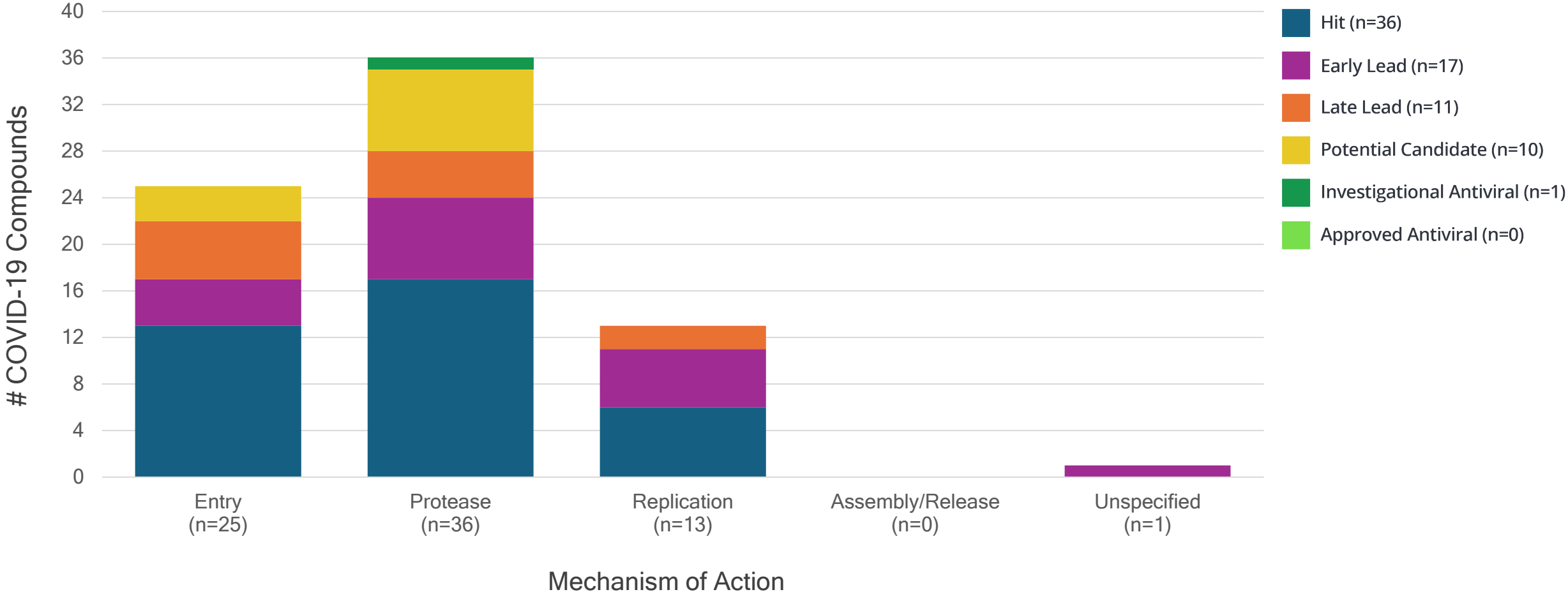
COVID-19 Compounds by Stage of Preclinical Development and Mechanism of Action (N=75)*



*As of December 18, 2024.

INTREPID ALLIANCE

COVID-19 Compounds by Mechanism of Action and Stage of Preclinical Development (N=75)*



*As of December 18, 2024.

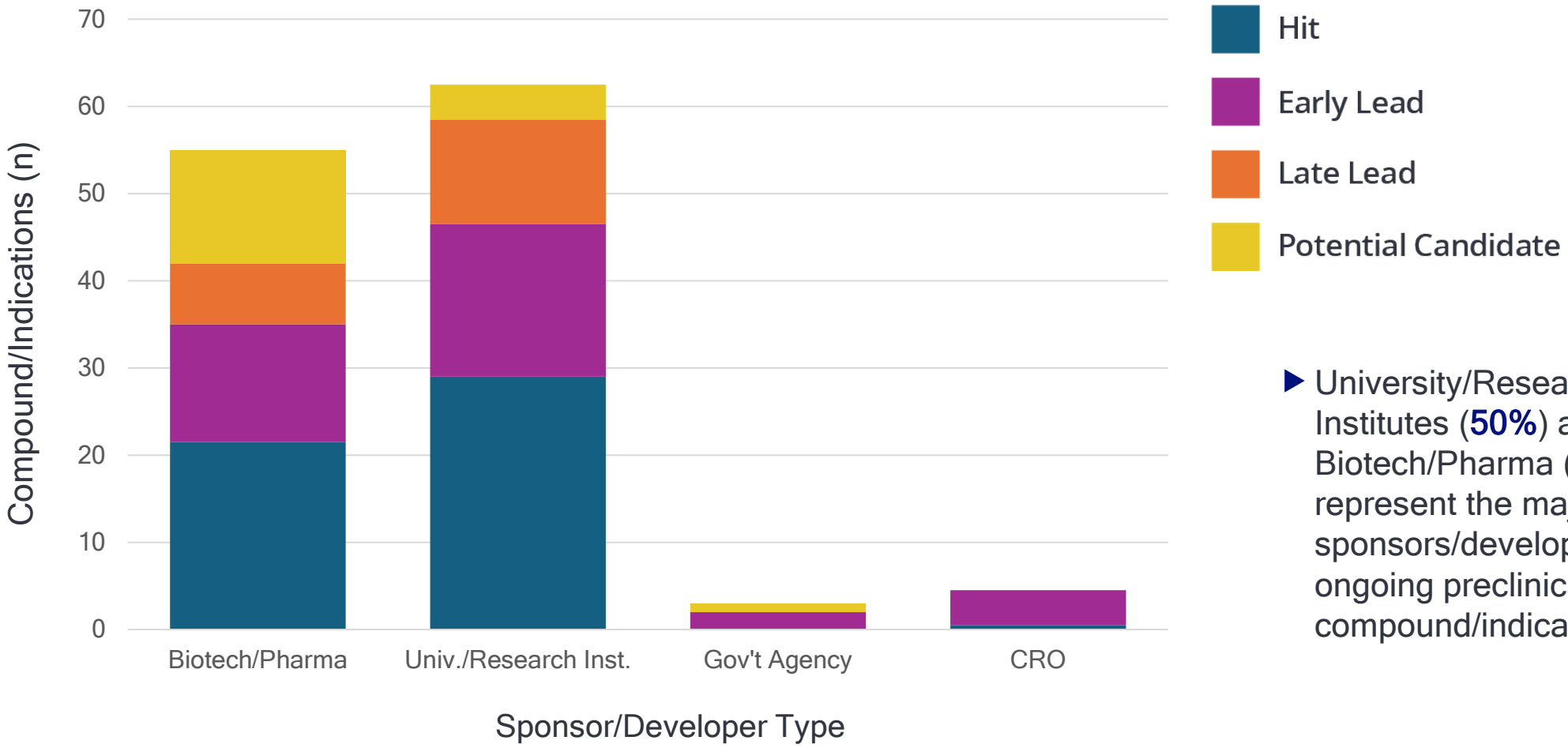
Preclinical Antiviral Sponsors and Developers

Preclinical Antiviral Landscape: Sponsors & Developers*

- Biotech/Pharma (44%) and University/Research Institutes (50%) represent **94%** of **125** sponsors/developers for preclinical compound/indications.
  - As programs move towards Potential Candidate, the relative contribution of sponsors/developers shifts more towards Biotech/Pharma. This is consistent with the increased resources needed to prepare for regulatory submissions and entry into clinical development.
- Sponsors/Developers of preclinical antiviral compound/indications are located in **24** countries across **5** of the **6** WHO-Regions.
  - The majority (**87.5%**) are located in countries with high-income economies.
  - The remainder have upper-middle income (**8.3%**) or lower-middle income (**4.2%**) economies.
- The United States (WHO Americas; High income) and China (WHO Western Pacific; Upper-middle income) have the most representation at **48.8%** and **12.8%**, respectively.

*As of December 18, 2024; Includes preclinical compounds categorized as Hit, Early Lead, Late Lead, or Potential Candidate.

Preclinical Antiviral Compound/Indications by Sponsor/Developer Type (N=125)*

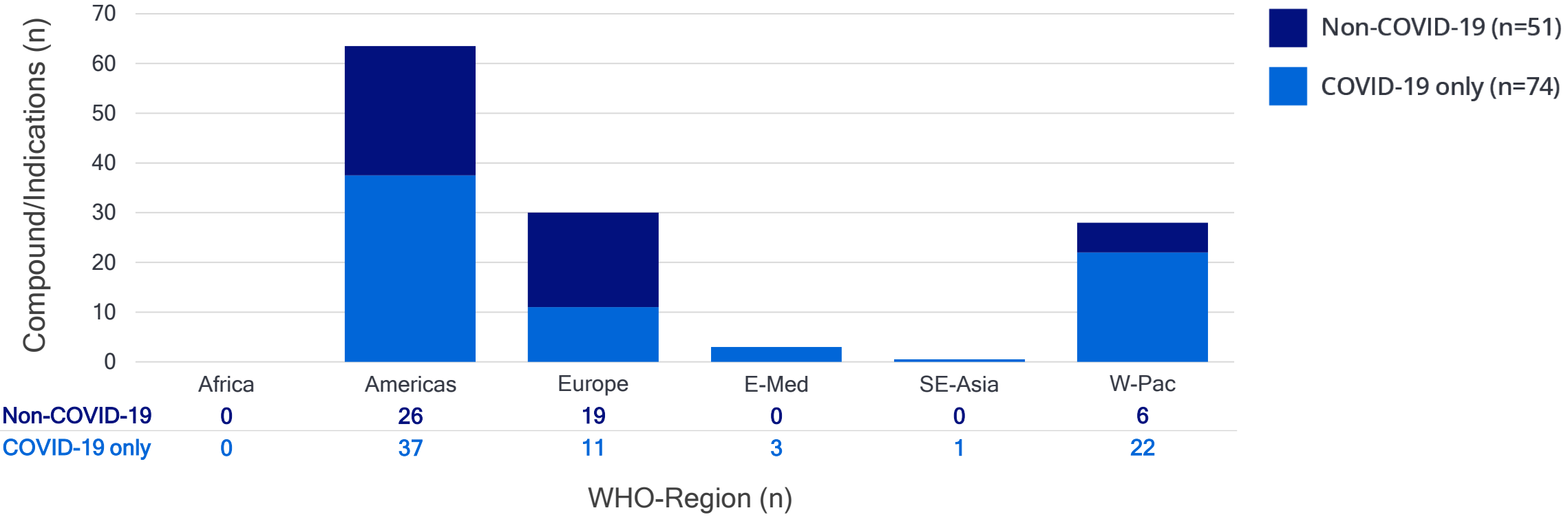


- University/Research Institutes (**50%**) and Biotech/Pharma (**44%**) and represent the majority of sponsors/developers for ongoing preclinical compound/indications.

*As of December 18, 2024; Includes preclinical compounds categorized as Hit, Early Lead, Late Lead, or Potential Candidate.
CRO: contract research organization.

Preclinical Antiviral Compound/Indications by Sponsor/Developer WHO-Region*

(COVID-19 only and Non-COVID-19; N=125)

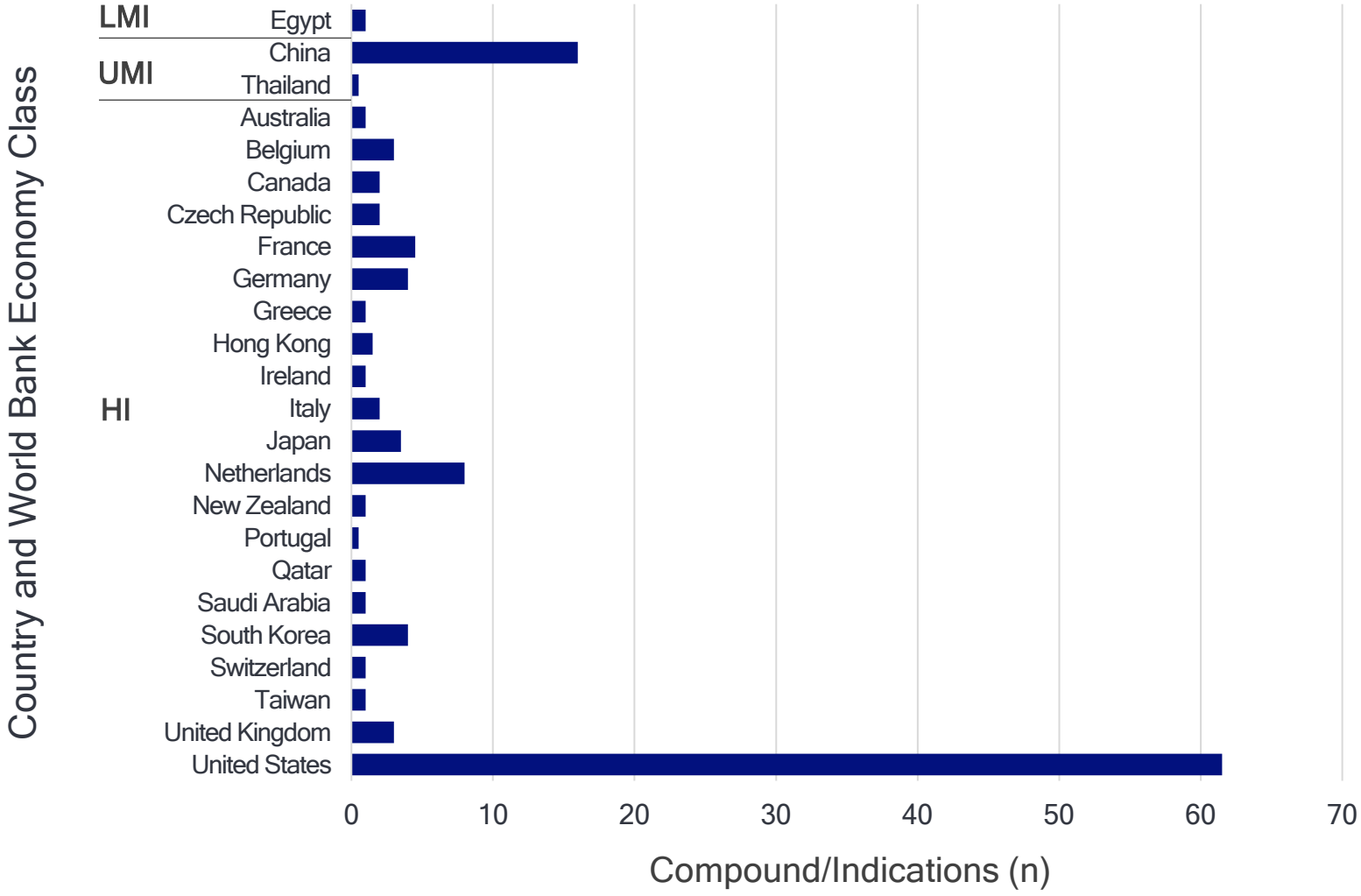


	Africa	Americas	Europe	E-Med	SE-Asia	W-Pac
Non-COVID-19	0	26	19	0	0	6
COVID-19 only	0	37	11	3	1	22

- There are twice as many COVID-19-specific versus Non-COVID-19 preclinical compound/indications.
  - COVID-19-specific: 74 are located in 5 of the 6 WHO-Regions.
  - Non-COVID-19-specific: 51 are located in 3 of 6 WHO-Regions.
- The Americas and Western Pacific regions are primarily driven by the United States and China.

*As of December 18, 2024; Includes preclinical compounds categorized as Hit, Early Lead, Late Lead, or Potential Candidate.

Promising and Watch & Wait Clinical Antiviral Compound/Indications* by Country and World Bank Economy Class**



- The majority (**86%**) of sponsors/developers of are located in countries with high-income economies.
  - The remainder are those with upper-middle income (**13.2%**) or lower-middle income (**0.8%**) economies.
- The United States (HI) and China (UMI) have the most representation across the **24** countries.

*As of December 18, 2024; Includes preclinical compounds categorized as Hit, Early Lead, Late Lead, or Potential Candidate;
**World Bank country classifications by income level for 2024-2025; LMI: lower-middle income; UMI: upper-middle income; HI: high-income.

Supplemental Information

INTREPID Alliance Clinical Antiviral Landscape: Clinical Antiviral Compounds Analysis Update (4th Edition)*

New Additions and Changes in Status from 3rd to 4th Edition

Compound	Indication	3rd Edition Category	4th Edition Category
Brincidofovir (IV)**	Human Adenovirus	–	Approved Antiviral – Indication Expansion Phase 2
Molnupiravir**	Dengue	–	Approved Antiviral – Indication Expansion Phase 2
Adefovir**	Mpox	–	Approved Antiviral – Indication Expansion Preclinical Exploratory
Remdesivir**	Dengue, MERS-CoV, SARS-CoV-1	–	Approved Antiviral – Indication Expansion Preclinical Exploratory
Zanamavir	Dengue	Approved – Indication Expansion Phase 1	Approved – Indication Expansion Phase 2
CD388	Influenza	Watch & Wait	Promising
TG-1000	Influenza	Watch & Wait	Promising
ZX-7101A	Influenza	Watch & Wait	Promising
WPV01/Ritonavir	COVID-19	Watch & Wait – Phase 1	COVID-19 Archive
Cidofovir	Human Adenovirus	Approved Antiviral – Indication Expansion Preclinical Exploratory	Non-COVID Archive
Galidesivir	SARS-CoV-1	Investigational Antiviral – Indication Expansion Preclinical Exploratory	Non-COVID Archive
Valganciclovir	COVID-19; Human Adenovirus	Approved Antiviral – Indication Expansion Preclinical Exploratory	Discontinued – Lack of Activity
Mosnodenvir	Dengue	Promising – Phase 2	Discontinued – Business Strategy
Obeldesivir	COVID-19	Promising – Phase 3	Discontinued – Lack of Efficacy
Bemnifosbuvir	COVID-19	Watch & Wait – Phase 3	Discontinued – Lack of Efficacy
BIT-225	COVID-19	Watch & Wait – Phase 2	Discontinued – Lack of Efficacy
AL-794	Influenza	Archived	Discontinued – PK Variability
Radavirsen	Influenza	Archived	Discontinued – Lack of Funding
Brincidofovir (Oral)	Human Adenovirus	Archived	Discontinued – Low Enrollment
Flufirvitide-3	Influenza	Archived	Discontinued – Lack of Efficacy

*As of December 18, 2024; See criteria and references on slides 10-11; **New additions.

14 Compounds Approved by a Stringent Regulatory Authority (S.A.)*

COVID-19 (n=4), Influenza (n=8), Smallpox/Other Poxviruses (n=2)

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
SMALLPOX/OTHER POXVIRUSES		
Brincidofovir	Emergent BioSolutions	Replication – DNA Polymerase
Tecovirimat	Siga Technologies	Assembly/Release – VP37

*As of December 18, 2024; WHO defined Stringent Authority (https://www.who.int/publications/m/item/list-of-transitional-wlas);
**Favipiravir also has O.N.A. approval; ***Zanamivir also has Dengue study via Investigator Sponsored Study.

9 Compounds Approved by Other National Authority (O.N.A.)*

COVID-19 (n=5), Influenza (n=0), COVID-19 & Influenza (n=3), Smallpox/Other Poxviruses (n=1)

Compound	Developer/Sponsor	Mechanism/Target
COVID-19		
Azvudine	HeNan Sincere Biotech, Zhengzhou Granlen PharmaTech, Genuine 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), 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
SMALLPOX/OTHER POXVIRUSES		
NIOCH-14	Vector Center	Assembly/Release

*As of December 18, 2024; WHO defined Other National Authority (https://www.who.int/publications/m/item/list-of-transitional-wlas);
**Favipiravir also has S.A. approval.

12 “Promising” Novel Clinical Antiviral Compounds*

COVID-19 (n=6), Influenza (n=5), Polio (n=1)

Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target	Phase of Development
COVID-19	EDP-235	Enanta Pharmaceuticals	U.S.	Protease – 3CL pro	2
	GST-HG171/Ritonavir	Fujian Cosunter Pharmaceutical	China	Protease – 3CL pro	3
	Ibuzatrelvir	Pfizer	U.S.	Protease – 3CL pro	2
	QLS1128	Qilu Pharmaceutical	China	Protease – 3CL pro	3
	SHEN26	Kexing Biopharm	China	Replication – RdRp	2
	STI-1558	Sorrento Therapeutics	U.S.	Protease – 3CL pro	3
Influenza	CD388**	Cidara Therapeutics, Janssen Pharmaceuticals	U.S., Belgium	Entry – Fc Drug Conjugate	2
	GP681	Jiangxi Qingfeng Pharmaceutical	China	Replication – Endonuclease	3
	Onradivir	Raynovent	China	Replication – DdRp	3
	TG-1000**	TaiGen Biotechnology	Taiwan	Replication – DdRp	3
	ZX-7101A**	Nanjing Zenshine Pharmaceuticals	China	Replication – Endonuclease	3
Polio	V-7404	ViroDefense, Pfizer	U.S.	Protease – EV 3C pro	1

*As of December 18, 2024; **CD388 new addition, TG-1000 and ZX-7101A moved forward from Watch & Wait.

“Watch & Wait” Novel Clinical Antiviral Compounds (N=16 of 27)*

COVID-19 (n=16)

Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target	Phase of Development
COVID-19	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, Gilead Sciences, Jiangsu Hansoh Pharmaceutical	U.S., U.S., China	Protease – 3CL pro	2
	HY3000	Hybio Pharmaceutical (formerly 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

*As of December 18, 2024; **YKYY017 moved forward from Phase 2 to Phase 3.

“Watch & Wait” Novel Clinical Antiviral Compounds (N=11 of 27)*

Influenza (n=4), Lassa fever (n=2), and Chapare hemorrhagic fever, Dengue, Mpox, Polio, and Rhinovirus (each with n=1)

Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target	Phase of Development
Influenza	AV5080	Viriom	Russia	Assembly/Release – NA	2
	CC-42344	CoCrystal Pharma	U.S.	Replication – Flu A Pol	2
	HNC042	Guangzhou Henovcom Bioscience Co. Ltd.	China	Assembly/Release – NA	2
	TRX100 (AV5124)	Traws Pharma	U.S.	Replication – Endonuclease	1
Lassa fever	ARN-75039	Arisan Therapeutics	U.S.	Entry – Fusion	1
	LHF 535**	Kineta	U.S.	Entry – Fusion	1
Chapare hemorrhagic fever	LHF 535**	Kineta	U.S.	Entry – Fusion	1
Dengue	EYU688	Novartis	Switzerland	Replication – NS4B	2
Mpox	ASC10	Ascletis Pharma	China	Replication	1
Polio	Pocapavir	ViroDefense	U.S.	Entry	1
Rhinovirus	Vapendavir	Vaxart, Altesa Biosciences	U.S., U.S.	Entry – Capsid	2

*As of December 18, 2024; **LHF535 under evaluation for two viral diseases.

Preclinical Compounds for COVID-19 (N=21)*

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

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Potential Candidate	COVID-19	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
		GC376**	Anivive Lifesciences	U.S.	Protease – 3CL pro
		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
Late Lead	COVID-19	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
		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

*As of December 18, 2024; **GC376 is a new addition.

Preclinical Compounds for Non-COVID-19 (N=16)*

Potential Candidates (n=8), Late Leads (n=8)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Potential Candidate	Junin virus	4'-fluorouridine**	U.S. CDC and Utah State University	U.S., U.S.	Replication – RdRp
	Lassa fever	4'-fluorouridine**	U.S. CDC and Utah State University	U.S., U.S.	Replication – RdRp
	MERS-CoV	THY-01	Thylacine Biotherapeutics Inc.	U.S.	Entry – Fusion
	SARS-CoV-1	THY-01	Thylacine Biotherapeutics Inc.	U.S.	Entry – Fusion
	Influenza	AnQlar	Virpax Pharmaceuticals	U.S.	Entry
		VNT-101	Via Nova Therapeutics	U.S.	Replication
	Parainfluenza	GHP-88309**	Georgia State Univ., Icahn School of Medicine at Mount Sinai, Emory Univ., Univ. of Washington	U.S., U.S., U.S.	Replication – RdRp
	Mpox	NV-387-T	NanoViricides	U.S.	Entry
Late Lead	Dengue	2-Thiouridine	University of Porto, Institute for Antiviral Research	Portugal, U.S.	Replication – RdRp
		JNJ-A07**	Johnson & Johnson Innovative Medicine	Belgium	Protease
	Yellow fever	BSBI-YF**	Blumberg Institute	U.S.	Replication – NS4B
	Influenza	ING-1466	University of Illinois at Chicago, Chicago BioSolutions	U.S.	Entry – Flu HA
		UAWJ280	University of Georgia, University of Arizona	U.S., U.S.	Entry – Flu M2
	Measles	ERDRP-0519	Paul Ehrlich Institute	Germany	Replication – RdRp
	Nipah virus	VIKI-dPEG4-toco	Columbia University, Claude Bernard University	U.S., France	Entry – Fusion
		VIKI-PEG4-chol	Columbia University, Claude Bernard University	U.S., France	Entry – Fusion

*As of December 18, 2024; **4'-fluorouridine, GHP-88309, JNJ-A07, and BSBI-YF are new additions.

Ribavirin has several ongoing activities in both the Clinical and Preclinical space*

Clinical Studies (n=5); Preclinical Exploratory (n=10)

Phase of Development	Viral Disease	Developer/Sponsor	Country	Mechanism/ Target
Phase 3	COVID-19	Bausch Health	Canada	IMPDH1**
Phase 2	Crimean Congo hemorrhagic fever***	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Influenza	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Japanese encephalitis	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Lassa fever	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
Preclinical Exploratory	Argentine hemorrhagic fever	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Dengue	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Hendra virus	Bausch Health	Canada	IMPDH1
	Human Adenovirus A-G	Bausch Health	Canada	IMPDH1
	Lujo hemorrhagic fever	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Measles	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Mpox	Bausch Health, Roche	Canada, Switzerland	IMPDH1
	Nipah virus	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Parainfluenza	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1
	Zika	Bausch Health, Roche, Chugai Pharmaceutical	Canada, Switzerland, Japan	IMPDH1

*As of December 18, 2024; **IMPDH1: Inosine-5'-Monophosphate Dehydrogenase 1;
***A second Phase 2 study is also ongoing for ribavirin in combination with favipiravir.

Archived Antiviral Compounds for COVID-19* (N=19)

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

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Clinical	COVID-19	WPV01/Ritonavir**	Westlake University	China	Protease – 3CL pro
Preclinical	COVID-19	4′-Fluorouridine	Georgia State Univ., Emory Univ., Texas Biomedical Research Institute	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
		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; 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 Triazolopyrimidine***	University of Hyderabad, National Institute of Animal Biotechnology	India	Replication – RdRp

*As of December 18, 2024; **WPV01/ritonavir does not require ritonavir and is progressing as WPV01; ***These compounds only have *in silico* modeling data.

Archived Antiviral Compounds for Non-COVID-19* (N=14 of 46)

Clinical (n=7), Preclinical (n=7)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Clinical	Human Adenovirus A-G	Cidofovir	Investigator Initiated - compassionate use	U.S.	Replication DNA pol
	MERS-CoV	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	SARS-CoV-1	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	Ebola	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	Marburg	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	Dengue	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	Zika	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
Preclinical	Influenza	CD-SA cyclodextrin	University of Geneva	Switzerland	Entry – Viral Envelope
		Oral FluCide	NanoViricides	U.S.	Not yet confirmed
		STP-702	SirnaOmics	U.S.	Replication – siRNA
		Tamiphosphor	TaiMed Biologics	Taiwan	Assembly/Release – NA
	Parainfluenza	GS-441524	Gilead Sciences	U.S.	Replication – RdRp
	SARS-CoV-1	Bananin	Medsintez Pharmaceutical	Russia	NSP13 helicase
	Mpox	Simeprevir	Johnson & Johnson Innovative Medicine	U.S.	Assembly/Release – Capsid

*As of December 18, 2024.

Archived Antiviral Compounds for Non-COVID-19* (N=20 of 46)

Clinical (n=0), Preclinical (n=20)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Preclinical	Dengue	166347	PanThera Biopharma, LLC, Aiea, HI, USA	U.S.	Protease – NS2/3
		2'-C-Methylcytidine (NM107)	University of Porto, Utah State University Institute for Antiviral Research	Portugal, U.S.	Replication – RdRp
		6A49	Univ. Texas Medical Branch	U.S.	Protease – NS2/3
		7-Fluoro MK608	Emory University	U.S.	Replication – RdRp
		Allosteric NS5 inhibitor	Novartis	Switzerland	Replication – RdRp
		ARDP0006	Univ. Texas Medical Branch	U.S.	Protease – NS2/3
		ARDP0009	Univ. Texas Medical Branch	U.S.	Protease – NS2/3
		Carnosine	Georgia State University, USA	U.S.	Protease – NS2/3
		Compound 14a in NITD manuscript	Novartis	Switzerland	Replication – NS4b
		Compound 6 Entry inhibitor - NITD	Novartis	Switzerland	Entry - not yet confirmed
		Compound 104	Heidelberg University	Germany	Protease – NS2/3
		Compound 14	Nankai University	China	Protease – NS2/3
		Compound 32	Heidelberg University	Germany	Protease – NS2/3
		Compound 45a	Heidelberg University	Germany	Protease – NS2/3
		Compound 7n	Georgetown University	U.S.	Protease – NS2/3
		Compound C/D/F	Georgetown University	U.S.	Protease – NS2/3
		Compound 1	Novartis Institute for Tropical Diseases (NITD), Singapore	Singapore	Protease – NS2/3
		Compound 1/6/8 - diarylthioethers	Marburg/Heidelberg University	Germany	Protease – NS2/3
		Ltc1	University of Malaysia	Malaysia	Protease – NS2/3
		MB21	Birla Institute of Technology and Science	India	Protease – NS2/3

*As of December 18, 2024.

Archived Antiviral Compounds for Non-COVID-19* (N=12 of 46)

Clinical (n=0), Preclinical (n=12)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Preclinical	Dengue	Methyl transferase inhibitor	Novartis	Switzerland	Replication – RNA Methyl transferase
		MK608	Merck	U.S.	Replication – RdRp
		Nelfinavir	Lund University, Sweden	Sweden	Protease – NS2/3
		NITD-618	Novartis	Switzerland	Replication – NS4b
		Policresulin	Zheijiang University	China	Protease – NS2/3
		Potegrin 1	University of Malaysia	Malaysia	Protease – NS2/3
		Protease inhibitor	Heidelberg University	Germany	Protease – NS2/3
		Retrocyclin 1	University of Malaysia	Malaysia	Protease – NS2/3
		RK-0404678	RIKEN, Japan	Japan	Replication – NS5
		ST-148	SIGA	U.S.	Assembly/Release – Capsid
		ST-610	SIGA	U.S.	Replication – Helicase
		Thiazolidinone-peptide	Heidelberg University	Germany	Protease – NS2/3

*As of December 18, 2024.

Discontinued Clinical Antiviral Compounds* (N=16)

COVID-19 (n=5), Non-COVID-19 (n=11)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Clinical	COVID-19	Bemnifosbuvir**	Atea Pharmaceuticals	U.S.	Replication – RdRp
		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
	Human Adenovirus A-G	Brincidofovir (Oral)**	Chimerix	U.S.	Replication – DdDp
		Valganciclovir**	Roche	Switzerland	Replication – DNA pol
	Dengue	AT-752**	Atea Pharmaceuticals	U.S.	Replication – DdRp
		Balapiravir**	Roche	Switzerland	Replication – RdRp
		Mosnodenvir**	Johnson & Johnson Innovative Medicine	Belgium	Replication DENV NS3 (Helicase) /NS4B (immune evasion)
	Yellow fever	Galidesivir	BioCryst Pharmaceuticals, NIAID	U.S., U.S.	Replication – RdRp
	Influenza	AL-794**	Johnson & Johnson Innovative Medicine	Belgium	Replication – Endonuclease
		Flufirvitide-3**	Autoimmune Technologies	U.S.	Entry – Flu HA
		Radavirsen**	Sarepta Therapeutics	U.S.	Replication – Translation
	Hendra virus	Balapiravir**	Roche	Switzerland	Replication – RdRp
	Nipah virus	Balapiravir**	Roche	Switzerland	Replication – RdRp

*As of December 18, 2024; **New additions.

Discontinued Preclinical Antiviral Compounds* (N=7)

COVID-19 (n=1), Non-COVID-19 (n=6)

Phase of Development	Viral Disease	Compound	Developer/Sponsor	Country	Mechanism/Target
Preclinical	COVID-19	ISM036-076 PCC	Insilico Medicine	Hong Kong	Protease – 3CL pro
	Dengue	NITD - cyclic phosphoramidate compound 17	Novartis	Switzerland	Replication – NS5 polymerase
		NITD008	NITD, Singapore	Singapore	Replication – RdRp
	Yellow fever	NITD008	NITD, Singapore	Singapore	Replication – RdRp
	Zika	NITD008	NITD, Singapore	Singapore	Replication – RdRp
	Dengue	NITD203	Novartis	Switzerland	Replication – NS5 polymerase
	Parainfluenza	BCX 2798	BioCryst Pharmaceuticals	U.S.	Entry – parainfluenza HN

*As of December 18, 2024.

Select References for "Promising" Novel Clinical Antiviral Compounds*

These were cited in addition to information provided by Airfinity.

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*As of December 18, 2024.

Select References for "Promising" Novel Clinical Antiviral Compounds* (cont'd)

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*As of December 18, 2024.

Glossary of Terms

Glossary of Terms

- **ADME:** absorption, distribution, metabolism, and excretion
- **Approved Antiviral-Indication Expansion:** antiviral approved for one or more viral disease indications (e.g., cidofovir, favipiravir, molnupiravir, remdesivir, valganciclovir)
- **'Archived' Compound:** clinical compound where development has paused or no recent information available from the past 5 years
- **CRO:** contract research organization
- **'Discontinued' Compound:** clinical compound where development has stopped for known reasons (e.g., change in business strategy, lack of efficacy or funding, low enrollment, PK variability preventing effective dosing, other)
- **'Exclude' Compound:** clinical compound with known disqualifying data related to safety and tolerability, efficacy, developability, chemical structure, etc.
- **FIH:** first-in-human
- **HI:** high-income
- **IND:** Investigational New Drug
- **Investigational Antiviral-Indication Expansion:** antiviral in clinical development, not yet approved (e.g., AT-752, filociclovir, galidesivir, GC736, GRL0167, NV-387-T, obeldesivir, rupintrivir)
- **LMI:** lower-middle income
- **MOA:** mechanism of action
- **O.N.A.:** other national authority
- **PD:** pharmacodynamic
- **PK:** pharmacokinetic
- **POC:** proof-of-concept

Glossary of Terms (cont'd)

- **Preclinical Compounds with only preclinical data and no clinical data:**
  - **Hit** – high-throughput or compound library screening hit, initial antiviral activity requiring significant optimization. Limited or no *in vitro* data available supporting antiviral mechanism of action (MOA).
  - **Early Lead** – limited Structure-Activity Relationship (SAR), antiviral activity associated with MOA, may have limited *in vitro/in vivo* pharmacokinetic data reported.
  - **Late Lead** – potency consistent with candidate quality for the specific MOA, more extensive *in vitro* characterization (e.g. ADME profile, activity against clinically relevant virus strains/isolates), *in vivo* PK and/or animal efficacy model data reported.
  - **Potential Candidate** – *in vivo* efficacy and safety dataset consistent with preparation for FDA IND (or similar) submission. Compound has been reported by developer as a pipeline clinical candidate and/or in IND (or similar) enabling studies.
  - **Archived** – progress on the compound has been stopped (timeframe stopped, 5 years); antiviral evidence is only computational; previously optimized drug from another antiviral/other indication that only has weak activity.
  - **Discontinued** – compound progression has been stopped for known reasons; for example, compound failed preclinical "IND" toxicology, change in business strategy, etc. May be useful to inform new screening or medicinal chemistry efforts.
- **Preclinical Exploratory:** Investigational ("unapproved") and Approved antivirals exploring antiviral activity against a different virus from the Investigational/Approved antiviral indication
- **'Promising' Compound:** clinical compound that aligns with 100 Days Mission goals and/or has been registered and approved for established viral diseases
- **S.A.:** stringent authority
- **SAD/MAD:** Single Ascending Dose/Multiple Ascending Dose
- **UMI:** upper-middle income
- **'Watch & Wait' Compound:** clinical compound that has FIH or POC studies just starting/ongoing or data are available for a completed study or unable to make a data-driven evaluation at the time of the analysis

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