Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Clinical and Molecular Medicine

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Discovery of Broad-Spectrum Antiviral Agents by Drug Repurposing for Rapid Response to Emergent Viral Pandemics

Building Digital Tools to Advance Translational Research

Master's thesis in Molecular Medicine
Supervisor: Denis Kainov
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Acknowledgements

Like all human works of science, art, and innovation, the work for this master's thesis was not created in a vacuum; rather, it was only reachable by standing on the shoulders of giants. Therefore, I would like to take this opportunity to indulge in some words of appreciation for all who have helped me complete this work.

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Thank you All,

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Publications

Some of the work undertaken in this master's thesis have been previously presented and published elsewhere in two scientific articles. They are as follows:

1. Ianevski, A., et al., *Potential Antiviral Options against SARS-CoV-2 Infection.* Viruses, 2020. **12**(6): p. 642.

2. Ianevski, A., et al., *Identification and Tracking of Antiviral Drug Combinations.* Viruses, 2020. **12**(10).

Additional academic contributions outside of the scope of this thesis that have been written and published in the course of this master's project are listed below:

1. Castañeda-Zegarra, S., et al., *Leaky severe combined immunodeficiency in mice lacking non-homologous end joining factors XLF and MRI.* Aging (Albany NY), 2020. **12**(23): p. 23578-23597.

2. Castañeda-Zegarra, S., et al., *Genetic interaction between the non-homologous end-joining factors during B and T lymphocyte development: In vivo mouse models.* Scand J Immunol, 2020. **92**(4): p. e12936.

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Abstract

The ongoing COVID-19 pandemic caused by the emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in 2019 has highlighted urgency for a more efficient and comprehensive paradigm for antiviral development. The majority of antiviral development in the past has relied on the 'one drug, one virus' model, which focuses on a method of drug discovery wherein one drug exploits the biological mechanisms of one specific species of virus. However, this is an inefficient method for drug development which often dissuades many pharmaceutical companies from investing resources towards antiviral discovery. Broad spectrum antivirals agents (BSAAs) are compounds that have antiviral activity against a broad range of viruses. They have become the subject of increasing attention in antiviral development because of the advantages they confer in potentially treating multiple viral infections with one drug. Drug repurposing is also an increasingly utilized technique in antiviral development that relies on the discovery of new indications for previously developed drugs, and offers the advantage of saving time and money in the drug development process. These two approaches to antiviral drug discovery can be combined to drastically cut down on time, money, and other resource requirements of traditional drug development. If these techniques are successful, they could yield a broad arsenal of antiviral drugs that will not only help combat current viral epidemics, but also increase global preparedness for emerging viruses in the future. In this master's thesis, I intend to describe my efforts that contributed to the building of a web-based database, DrugVirus.info, that aggregates information to promote discovery and development of novel BSAA candidates. Additionally, I will present SARS-Coronavirus-2.info, a highly accessible, multilingual website which served as a method for rapid dissemination of information in the early days of the COVID-19 pandemic. Finally, using information gathered from work on both resources, I will discuss the impact of each in the context of the emergence of SARS-CoV-2, as well as how the pharmaceutical response to COVID-19 will impact the future of BSAA development.

Abbreviations

ADME	Absorption, distribution, metabolism, and excretion
ANZCTR	Australian New Zealand Clinical Trials Registry
BSAA	Broad-spectrum antiviral agent
CC50	Half-maximal cytotoxic concentration
ChiCTR	Chinese Clinical Trials Register
COVID-19	Coronavirus Disease 2019
CRiS	Clinical Research Information Services Korea
CTRI	Clinical Trials Registry India
DMPK	Drug metabolism and pharmacokinetics
DNA	Deoxyribonucleic acid
DRKS	German Clinical Trials Register
EBOV	Ebolavirus
EC50	Half-maximal effective concentration
EU-CTR	EU Clinical Trials Register
FDA	United States Food and Drug Administration
HIV	Human immunodeficiency virus
ICTRP	International Clinical Trials Registry Platform
iPSC	Induced pluripotent stem cell
IRCT	Iranian Registry of Clinical Trials
JPRN	Japan Primary Registries Network
LBCTR	Lebanese Clinical Trials Registry
MERS	Middle East respiratory syndrome
mRNA	Messenger ribonucleic acid
NTR	The Netherlands National Clinical Trials Register
PACTR	Pan-African Clinical Trials Register
PD	Pharmacodynamics
PK	Pharmacokinetics
ReBec	Brazilian Clinical Trials Registry
REPEC	Peruvian Clinical Trials Registry
RPCEC	Cuban Public Registry of Clinical Trials
RT-PCR	Reverse transcriptase polymerase chain reaction
SARS	Severe acute respiratory syndrome
SARS-CoV-2	SARS coronavirus 2
SI	Selectivity index
SLCTR	Sri Lanka Clinical Trials Registry
TCTR	Thai Clinical Trials Registry

1 Introduction

1.1 Drug repurposing and broad-spectrum antivirals

Viruses are a populous and diverse group of non-living, infectious particles that rely on living organisms to reproduce. Despite their small size and relative lack of complexity, they are a mainstay of human infectious disease and give rise to epidemics around the world each year, accounting for 75% of all emerging infectious diseases in current times [1]. Emerging viruses that arise from natural reservoirs such as wild animals are particularly dangerous to human health due to lack of established virus-host equilibrium. This can be plainly seen in emergent viral epidemics of the past and is especially well illustrated by the ongoing COVID-19 global pandemic, which has already killed over 2 million people within only one year of widespread circulation.

Traditionally, antiviral viral drug development has followed a 'one drug, one virus' schema, wherein each antiviral drug targets a unique viral infection (Figure 1a). However, this approach is neither efficient nor profitable, and has led antiviral development being largely ignored by the pharmaceutical industry. Indeed, currently there are only a handful of approved drugs used to treat viral infections, leaving the majority of the 259 known pathogenic human viruses without a readily available antiviral treatment [2, 3]. Such untreatable viruses include those that have caused deadly outbreaks in the past, such as SARS coronavirus, MERS coronavirus, and ebolavirus [4-6]. While this deficit in our antiviral repertoire is largely ignored in times of human-virus equilibrium, it poses a serious public health threat in the face of emerging virus outbreaks such as the one we are currently experiencing.

To reduce the costs and increase financial incentives of developing an antiviral drug, researchers may take existing drugs that have already been fully or partially developed for one indication and conduct smaller, supplementary studies that allow them to be used for another indication (Figure 1b). This process can be referred to by a wide variety of names, including drug repurposing, repositioning, reprofiling, redirecting, or re-tasking. Compared to traditional drug development methods, drug repurposing requires both drastically shortened development time and resources while providing similar therapeutic benefits [7].

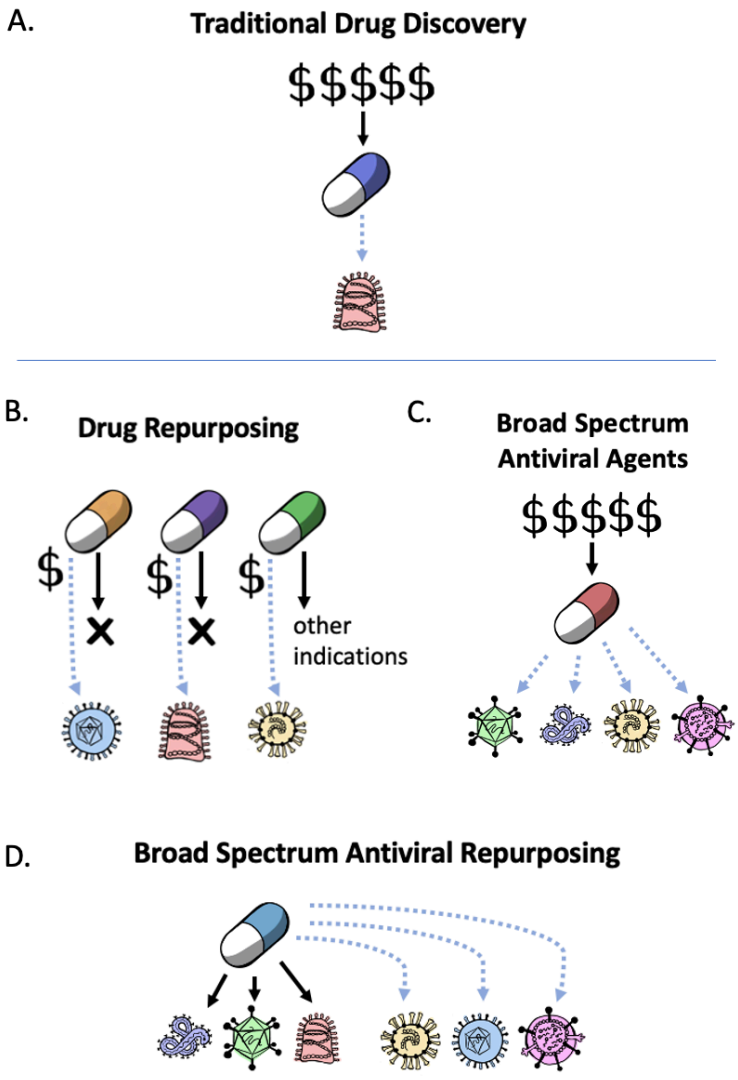

Figure 1. Broad spectrum antiviral agent discovery and drug repurposing compared to traditional drug discovery methods. (A) Traditional antiviral drug discovery follows the 'one drug, one virus' paradigm, which focuses on the development of antivirals that work against a specific virus. (B) Broad spectrum antiviral agents focus the same resources on developing treatments that target common pathways in viral infections, thereby allowing one agent to potentially treat multiple viruses. (C) Drug repurposing probes for antiviral activity among failed drugs or drugs initially developed for other indications, thereby reducing the cost to bring an antiviral to market. (D) By focusing on safe-in-man BSAAs, one can expedite the development of new antiviral treatments with minimal time and resources.

Another method that can boost our antiviral repertoire is focusing research on antiviral compounds that can target more than one virus, shifting away from the existing 'one drug, one virus' paradigm to a new 'one drug, many viruses' paradigm. Such drugs that target two or more families of viruses are termed broad spectrum antiviral agents (BSAAs) [8]. These drugs target

common infection pathways shared by multiple viruses, such as nucleic acid synthesis, viral proteases, or host factors associated with viral infection. Similar to antibiotics which are able to stop a wide range of bacterial infections, the ideal BSAA would have the ability to treat a broad range of viral diseases within a range of viral families, regardless of the specific type of virus (Figure 1c).

To further increase the efficiency of antiviral research, BSAAs can also be repurposed from existing drugs, compounding the benefits of each method (Figure 1d) [9]. BSAAs that have been repurposed from fully- or partially developed drugs and have at least passed Phase I clinical trials are termed safe-in-man BSAAs [8]. These agents can be brought to market with particular speed and affordability, as they have been previously characterized and their safety profile in humans have already been established.

1.2 Advantages of BSAA discovery through repurposing

Drug repurposing and BSAA discovery have gained popularity in recent years, likely due to the several advantages that these methods have when compared to traditional *de novo* drug discovery. These range from financial incentives for pharmaceutical companies to environmental and societal benefits that have global impact.

One principal hinderance to pharmaceutical innovation is characterized by the high attrition rates that occur between basic scientific research and a drug's clinical approval process, often referred to as the pharmaceutical 'Valley of Death'. To illustrate this point, over 900,000 new biomedical and life science articles were registered in the MEDLINE database and over 600,000 new biomedical and life science articles were added on PubMed Central in the year 2019 alone [10, 11]. However, in spite of the staggering amount of information and data generated over the course of that year, only 48 new drugs were approved by the FDA [10, 12]. This lack of translatability between research and industry ultimately means that many lead compounds and drug candidates will fail to demonstrate the appropriate safety or efficacy, often during preclinical or clinical development [13]. Drug repurposing takes advantage of this high failure rate by drawing from the pool of partially characterized compounds and finding new indications for them. This is beneficial for pharmaceutical companies by allowing them to fully utilize their

intellectual property while also improving the overall efficiency of drug discovery by increasing the success rate of each lead compound.

Another advantage that is conferred by both drug repurposing and BSAA development is the ability to save both time and money. On average, drug development is incredibly time- and resource draining, with the whole development process taking a minimum of 10 years and having an average cost of $1.5 billion [14]. However, repurposed drugs could potentially bypass toxicology, DMPK (drug metabolism and pharmacokinetics), and ADME (adsorption, distribution, metabolism, and excretion) studies, as well as the first phases of clinical trials, depending on the extent of prior testing. The ability to skip some of these difficult hurdles offers a sizeable advantage, decreasing the development time to as low as 5 years while decreasing the cost of drug development to as low as $8.4 million per drug [14, 15]. Similarly, BSAA development saves time and resources by allowing pre-clinical and early clinical studies for multiple indications to be consolidated for each distinct drug. Although steps cannot be skipped during BSAA development if the compound has not been previously characterized, an approved BSAA makes up for this by having a wider range of activity that could treat more conditions. Thus, even *de novo* BSAA development can allow for more efficient use of resources compared to traditional drug development approaches.

Because steps can be eliminated or consolidated during drug repurposing and BSAA development, the two processes are also beneficial from an environmental point of view. The global pharmaceutical industry is a global leader in energy use, waste production, and pollution, releasing 48.55 metric tons of CO_2 equivalents per million dollars earned [16]. The ability to bypass pre-clinical and early clinical studies would reduce environmental costs associated with burdensome processes such as single-use plastic production, chemical waste disposal, and overnight and cold-chain transportation. In this way, the environmental footprint of drug development could also be lessened through the implementation of these techniques.

Finally, and perhaps most saliently in light of the ongoing pandemic, an important function of both drug repurposing and BSAA development is providing an increased ability to prevent deaths during emergent viral outbreaks. Due to their high propensity for mutation, the emergence of new, pandemic-causing viruses among the human population should be expected.

Currently, our most common method of combating viral infections is vaccination. However, although vaccines are often effective at stopping outbreaks once a virus has been discovered and characterized, they cannot be developed in preparation of an emerging disease. Moreover, vaccines are a public health-oriented measure and do not protect each individual with the same efficacy, meaning that antivirals would still be necessary for the treatment of individual infections that may still occur [17-19].

Because of their broad mechanisms of action, BSAAs are the only potentially effective treatment that could be developed and manufactured before a virus even emerges. The more diverse the arsenal of pre-developed BSAAs, the higher the probability of being effective against new viruses. However, if no existing BSAA is effective against an emerging virus, the process of finding an effective antiviral treatment could still be drastically shortened through drug repurposing. Finding potent antivirals among the pool of existing drugs and drug candidates is not impossible; in fact, promising antiviral activity has already been discovered in many existing non-antiviral drugs *in vitro* and *in vivo* [20-26]. Notably, already-approved drugs that have been repurposed as antivirals could be prescribed for off-label use immediately after establishing efficacy, potentially parrying years of delay that could otherwise be attributed the drug approval process [27].

1.3 Current strategies for BSAA discovery through drug repurposing

The initial stages of drug repurposing can be done using a variety of methods, including *in silico* and experimental methods. *In silico* screening methods are often utilized to begin exploratory studies, due to their low cost and potential for high throughput. These studies often return a list of drugs or drug candidates that are more likely to have antiviral activity against a selected virus, or vice-versa. Following this, experimental screening methods can be carried out to confirm the nature of these drug-virus interactions and identify the extent of antiviral activity.

In silico drug discovery can be categorized into two main methods: manual literature review and algorithm-based screening. Both methods rely on existing data from journal articles and databases to direct further experimental research (Figure 2). Manual literature review involves synthesizing information from published scientific articles to form hypotheses about

potential drug candidates. While this can be very low-throughput and time-consuming work, it is also the most thorough method to find potential drug candidates or targets. Thus, manual literature reviews are preferable for targeted research where there is little information on a subject matter, such as in the beginning stages of an emerging viral outbreak. On the other hand, algorithm-based screening is preferable where there is already a wealth of data available and during untargeted drug discovery. These methods are higher throughput but can return a higher rate of false positives while missing false negatives, depending on the algorithm and parameters used. The most common algorithm-based discovery tools are molecular docking studies, network modeling, and text mining.

Molecular docking is the process of using an algorithm to simulate drug-target interactions with existing 3D structural data [28]. Databases which contain detailed structural data from viral proteins such as the RCSB Protein Data Bank [29] or from small bioactive compounds such as PubChem [30, 31] and DrugBank [32, 33] are particularly important resources for molecular docking studies. Common software used for molecular docking studies are the Amber [34] and AutoDOCK [35] suites, as well as publicly accessible online tools such as ParDOCK [36] and Sanjeevini [37]. These algorithms return an affinity score based on the physical attributes of each interaction, and the highest scoring interactions can then be selected for experimental investigation.

Network modeling and text-mining are both algorithm-based discovery tools that utilize a network structure to uncover possible drug-target interactions. These networks are often constructed of nodes that represent an element or idea such as a drug, virus, gene, or disease, which are connected by edges representing relationships between the nodes. Networks can be built from existing large-scale datasets, including those from transcriptomic, proteomic, metabolomic studies, as well as non-molecular datasets such as drug-indication lists [38]. Databases and knowledgebases with diverse categories of datasets such as PharmGKB [39], DrugBank, DrugCentral [40], UniProt [41], ChEMBL [42], and ViPR [43, 44] can be important resources for network building. Once a network is constructed, one simply needs to select a node to interrogate and retrieve all neighboring nodes to find potential drug-virus interactions.

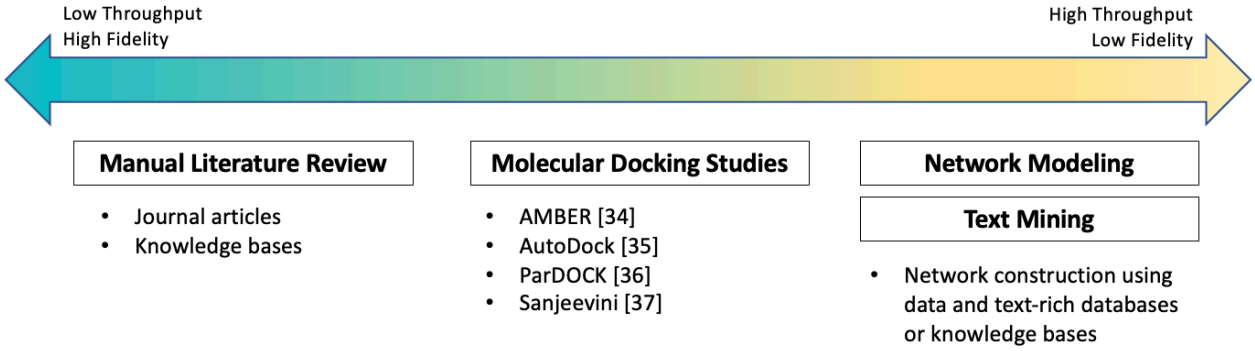

Figure 2. Common methods of *in silico* screening. Manual literature review requires synthesizing reported data from published journal articles and other scientific resources to form a hypothesis about potential drug candidates. Molecular docking relies on algorithms to calculate the level of interaction between a potential drug and drug target, allowing researchers to target combinations with the highest affinity for experimental validation. Network modeling and text mining both rely on construction of networks that map broad relationships between elements or ideas.

However, if the data required for the network cannot be extracted from existing databases, text mining can also be used to uncover associations between preselected nodes [45]. These text mining-based networks consist of pre-selected nodes such as a list of drugs, proteins, side effects, and symptoms, and connect these nodes based on their concurrent appearance in the same document or text entry. These techniques take advantage of documents in text repositories and text-rich knowledgebases, such as UniProt, Wikipedia, Proteopedia [46], MEDLINE, PubMed Central, and ViralZone [47]. Publicly available online tools used for text mining include PolySearch [48], DrugQuest [40], KinderMiner [49], and BEST [50]. Once text mined networks are constructed, they can be interrogated like any other network model for potential associations.

Once a list of compounds has been narrowed down for a specific virus, experimental screening must occur to determine the actual antiviral activity of each drug-virus relationship. Initial screening experiments are usually done in cell lines, due to their rapid growth and relative ease of maintenance. The measure of a compound's potential as an antiviral is often expressed through its selectivity index (SI) value. This value is derived from a compound's half maximal inhibitory value (EC50), denoting the concentration of a compound needed to inhibit viral

replication by half its original value; divided by a compound's half cytotoxic concentration (CC50), denoting the concentration of a compound needed to kill 50% of cells in culture (Equation 1).

$$\textit{Equation 1} \qquad \text{SI (Selectivity Index)} = \frac{\text{CC50}}{\text{EC50}}$$

Thus, a high SI value indicates that a compound has potent antiviral properties relative to its toxicity and thus high potential as an antiviral candidate, while a low SI value indicates that a compound is less likely to succeed as an antiviral. EC50 values can be experimentally determined by measuring the level of viral infection for varying concentrations of a drug and plotting the dose response curve. This can either be measured using direct detection of viral particles through immunoassays, RT-PCR, RNA-Seq, microarrays, or fluorescent viral particles; or indirectly detected with the use of reporter systems [51-65]. Similarly, CC50 values can be experimentally determined by measuring cell viability using a variety of experimental techniques, such as reducible dyes, exclusion dyes, metabolic assays, or apoptosis-related assays.

1.4 Validation of antiviral activity and further stages of BSAA development

Once the antiviral drug candidates have been identified, they pass on to experimental validation steps (Figure 3). These include *in vitro* testing in primary cells, differentiated induced pluripotent stem cells (iPSCs), 3D cell cultures, and organoids, as well as *in vivo* testing of the drug against viral infections in an animal model. Antiviral testing in primary cells often takes place immediately following initial experimental screening, likely due to the relative ease of procuring and growing primary cells compared to other *in vitro* alternatives [66-69]. However, primary cells offer the advantage of having enhanced biological similarities to their donors, which can provide more accurate insights into antiviral response and viral infection [70, 71]. Alternatively, induced pluripotent stem cells (iPSCs) could be differentiated into the required tissue type needed for viral infection, especially if the tissue type is difficult to obtain from donors [72-74].

To further mimic biological conditions *in situ*, these tests can be conducted in 3D culture or iPSC-derived organoids [75-77]. While these techniques require more labor and time to

generate than normal primary cell culture, they offer the advantage of mimicking the physiology of the tissues and organs involved in viral infections. Organoids are particularly useful for studying viral infections that attack entire organ systems, such as Zika virus on the brain and Rotavirus on the intestines [73, 78-84].

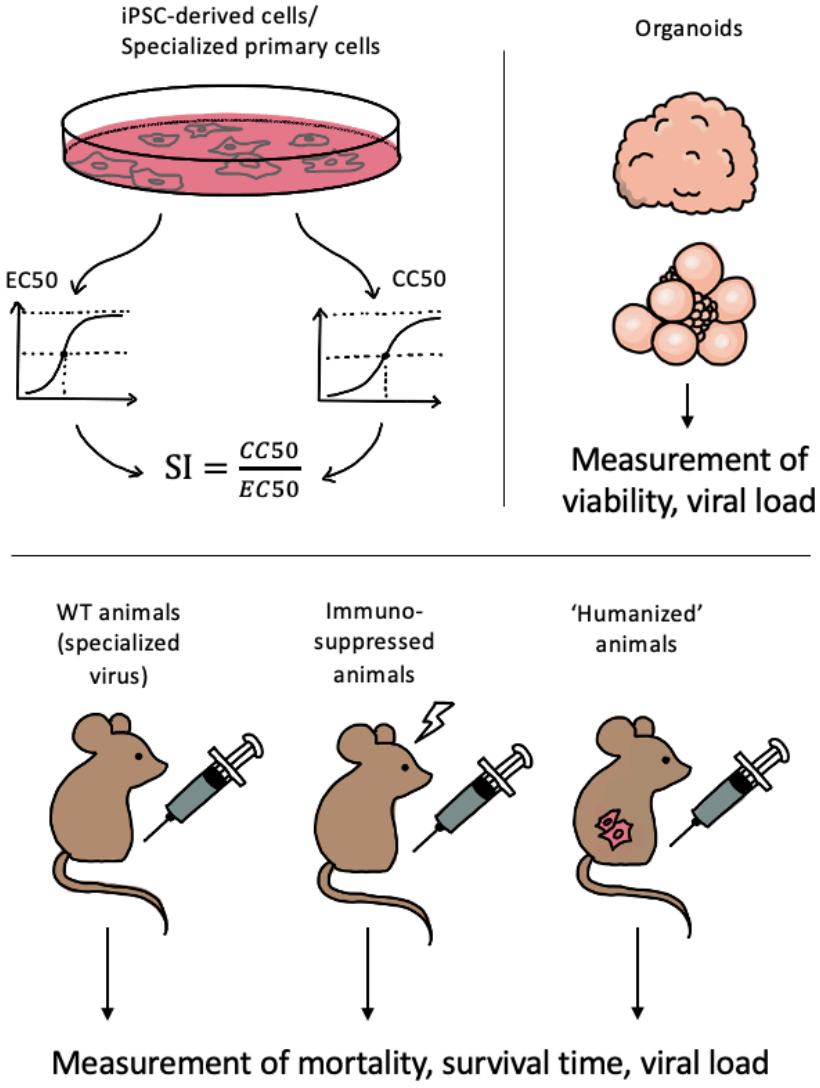

Figure 3. Experimental validation of antiviral activity. Following experimental screening, antiviral compounds can further be validated by testing in tissue-specific primary cells or tissue-specific iPSC-derived cells, complex cellular organoids, or animal models. Most animal models must be modified slightly to become permissive to infection by the virus being studied.

Another form of validation is testing on animal models. *In vivo* animal testing offers some advantages over *in vitro* testing due to its ability to discern antiviral effects on a complete set of organ systems. This adds another level of resolution when it comes to measuring antiviral activity; however, because animal models are non-human, information obtained from them may diverge from true human responses. Moreover, although some viruses are able to infect non-human species, animals often lack the same host factors present on humans and therefore can be less susceptible to human-infecting viruses. Several methods can be used to clear this hurdle. For example, immune systems of certain animals can be impaired by genetic or chemical means to allow for easier viral infection [85]. Alternatively, animals can be surgically transplanted with human tissue or genetically augmented to become more 'humanized', and therefore more likely to be susceptible to the human viral infection [86]. Finally, if the development of a new animal model isn't feasible, viruses can also be genetically customized to infect the desired animal species [87, 88]. Because *in vitro* and *in vivo* testing offer separate advantages and shortcomings, it is often necessary to validate a BSAA's activity with both methods before continuing on to further studies.

Preclinical studies are the first drug development step that may be bypassed during drug repurposing. These studies normally begin after validation of antiviral activity, but prior to clinical testing. Similar to antiviral validation tests, preclinical tests are both done *in vitro* and *in vivo*. However, they place focus on drug characterization instead of the potency of antiviral activity. During this stage, pharmacokinetic (PK) studies identify how a drug candidate is processed and removed by an organism and often includes tests for adsorption, distribution, metabolism, and excretion (ADME); pharmacodynamic (PD) studies identify the physiological and biochemical effect of the drug candidate on an organism; and toxicology studies identify the negative biological impact of the drug candidate on organismal health. Because preclinical characterization must be completed prior to clinical testing, the ability to skip this step during the drug repurposing process allows many repurposed drugs to proceed directly to clinical trials.

The last steps of drug development are clinical trials. The first step constitutes the first time a drug candidate is tested in humans. Phase 1 clinical trials involve few human subjects and aim to establish both general safety and safe dosage. Because this phase of clinical testing

unspecific to an indication, it can also be skipped by many drug repurposing studies if this phase has been successfully completed by the same drug candidate in the past. Phase 2 trials last longer and have more participants than Phase 1 and have the purpose of further evaluating safety, as well as examining side effects and efficacy. While it may have some indication-specific endpoints, Phase 2 trials may still be skipped depending on the extent of previous safety characterization of a repurposed drug. Phase 3 involves even more time and participants than Phase 2, which allow for the monitoring of possible long-term side effects and higher-resolution characterization of efficacy. Generally, Phase 3 trials cannot be skipped in the BSAA development process due to its focus on efficacy for a specific indication. However, drug candidates that have not passed Phase 3 trials due to lack of efficacy for an original indication are often sourced as good candidates for drug repurposing as BSAAs because of their well-established safety profile. Finally, a drug can be approved once it has passed Phase 3 clinical trials. However, these drugs still must undergo continuous monitoring for very long-term side effects in a Phase 4 trial and may still be withdrawn if Phase 4 trials are not passed.

2 Aims of the Project

Much like the invention of antibiotics which has greatly reduced the impact of infectious bacterial infections on public health, the increasing popularity of BSAA development can change our current relationship with viral diseases. The surfacing of SARS-CoV-2, along with its resultant COVID-19 global pandemic in March 2020, has highlighted the need for having a well-developed BSAA arsenal to prepare ourselves for unknown future outbreaks. Additionally, the economic and psychological toll of the year-long lockdown exposed the urgency of finding a reliable cure and led to the clinical testing of many repurposed drugs such as hydroxychloroquine, remdesivir, lopinavir/ritonavir, camostat, famotidine, umifenovir, nitazoxanide, and ivermectin.

However, while the volume of BSAA and antiviral research has skyrocketed following the emergence of the pandemic, the collective data obtained in this process has become unwieldy and difficult to manage. Few public online resources existed for antiviral drug discovery prior to January 2020, and among these, none focused on aggregation of antiviral research data or BSAA discovery and development.

To bolster *in silico* drug discovery of BSAAs and allow antiviral researchers with limited knowledge of algorithmic screening techniques or bioinformatics to easily begin experimental BSAA screenings, I endeavored to generate a publicly accessible online database that provides a complete and succinct summary of existing data pertaining to BSAA discovery. The information presented in this database was intended as a guide for basic and translational researchers to investigate certain antiviral compounds with high potential for BSAA activity. It was also meant to be used internally as a guide for experimental antiviral assays in the Kainov Laboratory. Therefore, to streamline research and maximize efficiency, the database would only collect data on drugs with established safety profiles that have passed Phase 1 clinical trials and can therefore be quickly redeveloped and repurposed as BSAAs. Additionally, drugs would only be included if they already demonstrate BSAA activity by inhibiting members of at least two viral families. The progress of drug development for each drug-virus combination would be tracked through cell line screening, primary cell culture validation, and *in vivo* validation stages of research, as well as

Phase 1, Phase 2, Phase 3, and Phase 4 clinical trials to prevent time- and resource draining repeat experiments.

In light of the rapidly developing and disorganized scientific news that appeared in the wake of the COVID-19 pandemic, I also aimed to curate a public online resource that tracks and summarizes relevant, peer-reviewed scientific information relating to SARS-CoV-2 research, as well as updated information on clinical research for potential treatments, prophylaxes, and diagnoses as it comes out. This resource would be intended for virology and medical researchers, as well as laypeople who were interested in staying informed with the latest medical information. Therefore, while all the information would be science-oriented, layman's terms would be used as far as is possible. Because of our interest in drug repositioning for BSAA development, it would also be a method to track the repurposing of existing drugs against SARS-CoV-2, to monitor the development speed and efficacy of BSAA repurposing in a real-world, pandemic situation.

Therefore, this thesis will address:

- The population and expansion of a freely accessible BSAA database by manual curation of peer-reviewed scientific literature

- The development of a fast-response website that disseminates information relating to treatment, diagnosis and prevention of SARS-CoV-2; scientific news relating to SARS-CoV-2 research; and public health information necessary for curbing the spread of the pandemic.

3 Materials and Methods

3.1 Manual Curation of a BSAA Database, DrugVirus.info

3.1.1 Initial population of the DrugVirus database

An initial list of 155 drugs that were categorized as antiviral agents were sourced from the DrugBank database (DrugBank category DBCAT000066). Of these, drugs that are either approved, investigational, nutraceutical, or withdrawn were selected as the initial drug list for population of the database. Experimental, illicit, and exclusively veterinary drugs were not included in our database due to their unknown safety profile in humans. Each of the 140 resulting antiviral drug terms in this initial list were queried on PubMed and ClinicalTrials.org, in combination with the terms 'virus', 'antiviral', or one of the 130 known human viruses obtained from ViralZone. The returned results were examined to determine if antiviral activity has been demonstrated between the drug and two or more viruses of different viral families. If antiviral activity could be established in more than 2 viral families, then all such drug-virus combinations would be recorded.

3.1.2 Ongoing expansion of the DrugVirus database

The complete list of available drugs was downloaded from the DrugBank database. All drugs annotated with approved, investigational, nutraceutical, or withdrawn statuses were selected and queried on PubMed and Clinical Trials.org in combination with the terms 'virus', 'antiviral', or one of the 130 known human viruses obtained from ViralZone. The drug-virus combinations would be recorded as new entries if antiviral activity was demonstrated against two or more viruses of different families. Novel BSAAs discovered through this method were also continually tracked and updated in the case of further antiviral development.

Weekly PubMed and Google alerts were created for the term "Broad Spectrum Antiviral" to find novel research on newly identified BSAAs. Additional weekly PubMed and Google alerts were created for each drug name on the unique drug term list in combination with the term 'antiviral' or 'virus'. Novel antiviral activity uncovered through these weekly search alerts were entered into the database on a weekly or biweekly basis.

3.1.3 Qualification of antiviral activity

To make the database as extensive and inclusive as possible, broad inclusion criteria were set. A drug was considered to have antiviral activity against a virus in cell culture if it produced an SI value greater than one (if the EC50 value is greater than the CC50 value). If a paper does not report EC50, CC50, or SI values, the authors' interpretation of the results were used as confirmation or rejection of antiviral activity. In organoids and animal models, a drug was considered to have antiviral activity if viral load, proportion of deaths within the test population, or symptoms attributed to viral infection were significantly decreased between treatment and non-treatment groups. Similarly, a significant increase in survival time between treatment and non-treatment groups also constituted qualifying antiviral activity.

Drugs registered in recruiting, enrolling by invitation, active, or completed clinical trials are considered to be 'in' their respective trial phases. Positive results for a certain clinical trial phase were not required for a drug to be qualified as having successfully reached that phase. Clinical trials that had not begun recruiting or have been withdrawn, terminated, and suspended were not included in the results.

3.1.4 Information curation

For each unique drug entry in the DrugVirus database, the drug name, DrugBank ID, PubChem ID, InChI key, primary indication, mode of action, and potential targets were recorded. For each unique virus entry, the virus name, virus abbreviation, Baltimore classification, virus family, and associated disease were recorded. For each drug-virus interaction, that phase of development and up to two most recent sources were recorded. All data was written and saved in CSV format.

3.2 Development of a COVID-19 information aggregator and tracker, SARS-coronavirus-2.info

3.2.1 Sources for Treatment, Prevention, and Diagnostics trackers

Clinical research data was used as the main source of information in tracking the development of prevention and treatment options against SARS-CoV-2. ClinicalTrials.org and the dataset from

the International Clinical Trials Registry Platform (ICTRP) were used as sources. ICTRP includes data from 17 primary clinical trial registries from around the world, including the Australian New Zealand Clinical Trials Registry (ANZCTR), Brazilian Clinical Trials Registry (ReBec), Chinese Clinical Trials Register (ChiCTR), Clinical Research Information Service (CRiS – Korea), Clinical Trials Registry India (CTRI), Cuban Public Registry of Clinical Trials (RPCEC), EU Clinical Trials Register (EU-CTR), German Clinical Trials Register (DRKS), Iranian Registry of Clinical Trials (IRCT), IRSCTN, Japan Primary Registries Network (JPRN), Lebanese Clinical Trials Registry (LBCTR), Thai Clinical Trials Registry (TCTR), The Netherlands National Clinical Trials Register (NTR), Pan African Clinical Trials Register (PACTR), Peruvian Clinical Trials Registry (REPEC), and Sri Lanka Clinical Trials Registry (SLCTR).

Information about SARS-CoV-2 diagnostics development was initially gathered from web searches, press releases, and news reports. Subsequent updates and diagnostic additions were sourced from FindDX.org [89].

3.2.2 Inclusion criteria for Treatment Aggregator and Tracker

Therapeutic agents that were being clinically tested as a treatment against SARS-CoV-2 infection, or as a treatment of direct symptoms of SARS-CoV-2 infection, were the subject of this treatment tracker. Thus, aggregation of clinical trial data focused only on small-molecule drugs, biologicals, or dietary supplementation, while ignoring other therapeutic methods that may be included in clinical trial data such as surgery, ventilation procedures, rehabilitation exercises, or use of medical devices. Similarly, tools that aimed to improve public health, treatments of comorbidities or co-infections of SARS-CoV-2 (such as cancer or HIV), or treatment of health complications arising from stress or isolation caused by the COVID-19 pandemic were excluded from the tracker.

Information was recorded about potential treatments and the associated clinical trial details, including the treatment or treatments being tested, clinical trial phase, primary trial sponsor, projected completion date, registry identifier, primary registry source, trial acronym, and a link to the source. Because this tracker focused only on tracking the progress of potential drugs to combat SARS-CoV-2, information on placebo treatments and standard treatment

comparators were excluded from the tracker. If a trial was conducted to compare two non-standard treatments with each other, both would be included and listed in the tracker.

3.2.3 Inclusion criteria for Prevention Tracker

The prevention tracker included clinical trials of either novel developments in vaccines or prophylactic drugs to prevent COVID-19. Prophylactic measures were only considered if they were being tested against prophylaxis of viral infection and were excluded if only being tested for prophylaxis of certain symptoms of the COVID-19 disease, such as thrombosis or anoxia. Clinical trials of existing repurposed vaccines, trials of novel adjuvants with old vaccines, and herbal/dietary supplementation were also included in the list. Information recorded about preventative agents were the name of the vaccine or prophylactic drug, type of preventative measure (mRNA vaccine, DNA vaccine, inactivated virus vaccine, live attenuated virus vaccine, subunit vaccine, cell-based vaccine, or chemoprophylaxis drug), trial phase, vaccine or drug developer, estimated completion date, registry identifier, primary registry source, and a link to the source.

3.2.4 Inclusion criteria for Diagnostics Tracker

Initially, the diagnostics tracker included all commercially available kits that could detect SARS-CoV-2. However, due to the large quantity of detection kits that were rapidly being developed in the wake of the SARS-CoV-2 pandemic, the lack of supporting data available for many of these tests, and the existence of a similar diagnostics tracker at FindDX.org, it was shifted to only include test kits that have been approved or accepted by emergency use authorization by at least one governing body. Diagnostic tests that were being tested in in clinical trials were also included in the tracker. Information gathered for the tracker included the name of the diagnostic test, developer of the test, type of detection used (nucleic acid test, antigen-based immunoassay, or antibody-based immunoassay), intended setting for the test (manual assay, automated assay, or point-of-care/rapid diagnostic test), and the type of approval it has.

4 Results

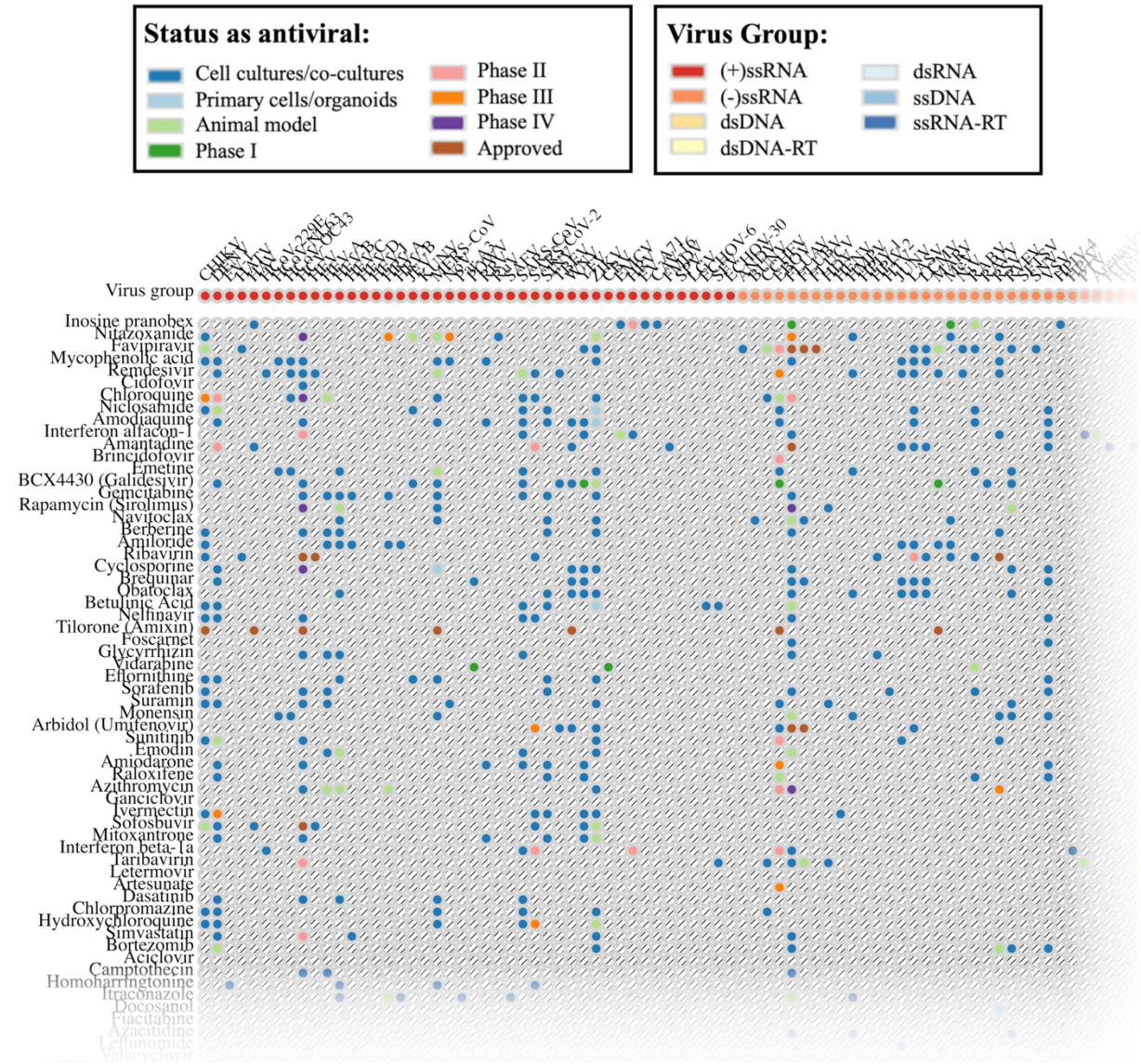

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Figure 4. Heatmap presentation of the data listed on DrugVirus.info. Unique drugs are listed along the vertical axis while unique viruses are listed along the horizontal axis. The Baltimore group of the viruses are indicated by color. The existence of demonstrated antiviral activity is denoted by a solid dot with a color corresponding to the level of development. Grey shaded dots indicate that there is no proven antiviral activity between the drug/virus combination.

4.1 DrugVirus.info: A manually curated database of known BSAAs

4.1.1 Website description and functionality

The information on the DrugVirus.info database is presented as a heatmap plot, with viruses listed on the horizontal axis and BSAAs listed on the vertical axis (Figure 4). Individual drug-virus interactions are denoted by a shaded dot where the virus and drug intersect, and is color-coded based on the stage of translational or clinical research that the interaction has been demonstrated in. The colored dots differentiate between antiviral activity demonstrated in cell lines, primary cells or organoids, animal models, as well as those that have completed Phases 1 through 4 clinical trials. The heatmap plot also indicates the drug-virus combinations that have already been approved for use.

To optimize information presentation on the website, users also have the option to select and display only the viruses and drugs that are of interest to them, thereby reducing the noisiness of data presentation and providing a more focused view. Users who require raw data for independent analysis may also download the entire contents of the database in CSV format.

4.1.2 Breadth of curated data

The DrugVirus.info database contains information about 164 unique drugs which been deemed to be safe for human investigation, are widely used herbal or nutritional supplementation, or have been approved for use for another indication. Of these drugs, 136 have been approved for use for humans in at least one indication, meaning that immediate off-label use for these drugs is possible without the need for further development. The antiviral activity of each drug has been tracked against 109 species of viruses across 24 different viral families and all 7 Baltimore groups. As of December 2020, a total of 1084 unique and efficacious drug-virus combinations have been recorded in our database (Table S1), with 16,792 interactions that have yet to be documented or have previously been shown to be ineffective. The breadth of the information included in the DrugVirus database is illustrated in Figure 5a.

Of these interactions, 76.8% (833 interactions) have been demonstrated in preclinical studies, while 13.4% (145 interactions) have been tested in clinical trials and 9.8% (106

interactions) have already been approved for the drug-virus combination in question. Of the 833 drug-virus interactions that have only been demonstrated in preclinical studies, 85.0% (708 interactions) have been shown in cell lines, 3.1% (26 interactions) have been shown in primary cell or organoid cultures, and 11.9% (99 interactions) have been shown in animal models. Of the 145 interactions that are being investigated in clinical trials, 31.0% (45 interactions) are in Phase 1, 35.2% (51 interactions) are in Phase 2, 20.0% (29 interactions) are in Phase 3, and 13.8% (20 interactions) are in Phase 4. A detailed distribution of the research progress for all drug-virus combinations included in DrugVirus.info is illustrated in Figure 5b.

4.1.3 Host-targeting and virus-targeting BSAAs have similar broad-spectrum potential

By assembling all drug-virus interactions that demonstrate antiviral activity, we were able to interrogate the comparative efficacies of different antiviral strategies utilized by different BSAAs. The BSAAs listed in the DrugVirus database were approximately evenly distributed between host-targeted and virus-targeted agents, with 73 drugs most likely to preferentially target host factors and 78 drugs most likely to target virus factors. Additionally, 13 of the drugs in the database have mechanisms of action which are unknown or unclear in the context of preventing viral infection. Drugs that target host factors and drugs that target viral factors appear to have comparable potential for broad-spectrum antiviral activity, with host-targeting BSAAs having demonstrated efficacy against an average of 6.8 viruses and virus-targeting BSAAs having demonstrated efficacy against 5.8 viruses on average (two-tailed t test, $p = 0.098$). However, this observation may be inexact due to the limited information available about antiviral mechanism of action for many BSAAs that have been repurposed from other primary indications.

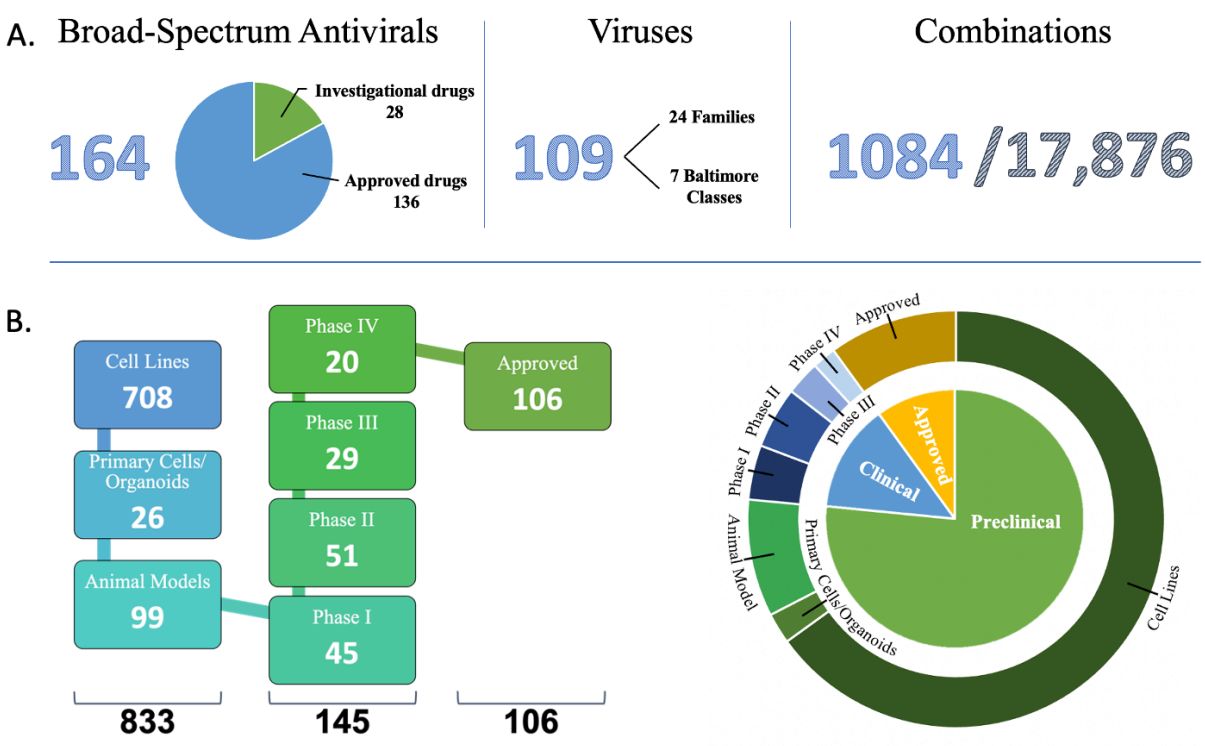

Figure 5. Summary of information available on the DrugVirus database. (A) The breadth of data coverage on DrugVirus.info. The database covers the activity of 164 unique approved and investigational BSAAs against 109 viruses from 24 families and all 7 Baltimore classes. 1084 out of 17,876 possible antiviral interactions are recorded. (B) The drug development progress of drug-virus combinations in the database. The majority (833) interactions are demonstrated only in pre-clinical models, while a small proportion (145) are in clinical trials. 106 of the drug-virus combinations listed are already approved.

4.1.4 Website impact

As of December 2020, the DrugVirus.info website is the first and only database that collects and summarized information on investigational or approved BSAAs. In light of the COVID-19 pandemic, such resources that provide widely accessible and rapidly actionable information on antiviral drug development could be of interest to the wider scientific community. Indeed, this interest has been reflected in our website statistics. Since its launch in January 2020, DrugVirus.info has received 26,000 visits from 166 countries around the world, with most website visits being accessed from the United States of America (19.6% of visits), France (10.8% of visits), Germany (9.3% of visits), and Russia (8.0% of visits). Considering the low-budget and small-scale nature of our project and niche nature of our focus, we believe that the size and breadth of our

usage reflects tremendous interest in and need for drug repurposing resources such as this, and that further development of such resources would be justified.

4.2 SARS-Coronavirus-2.info: A fast-moving tracker of aggregated medical research information

4.2.1 Website description and functionality

The SARS-Coronavirus-2.info website was constructed with the goal of serving two main purposes: (1) Dissemination of general educational content at the beginning of the pandemic, and (2) tracking the development of treatments, diagnostics, and preventative measures in real-time as they progress. To fulfill these purposes, the main page of the website contains basic scientific information about the SARS-CoV-2 virus itself, as well as primers that explain potential treatments, diagnostics, and preventative measures written in language intended for a layperson audience. The main page also includes a stream of manually curated scientific news relating to SARS-CoV-2 research, with links to source material. There is also an interactive world map which reports the number of cases, deaths, and recovered cases by country. To ensure the widest accessibility possible for our website, the sections of the website described above were presented in several language options, including English, Russian, Spanish, Ukrainian, Estonian, Chinese, Lithuanian, Polish, Tagalog, and Norwegian.

Users can toggle available trackers in the top menu bar for the clinical development progress of COVID-19 treatments, diagnostic tests, and prevention. These trackers are presented as tables that appear as a pop-up window over the main page and can be sorted by various categories such as the name of the treatment, diagnostic, or preventative agent in question, the main developer of the product, or the clinical phase of development. While these trackers were easily navigable at the outset of the pandemic, the number of entries for each tracker has grown considerably as more clinical trials have been registered and more diagnostic tests have been validated. Thus, trackers may also be queried to return entries with specific terms to provide a more focused view of development progress.

4.2.2 Description of data in SARS-CoV-2 trackers

As of December 2020, the SARS-Coronavirus-2.info website is tracking a total of 2080 clinical trials for treatments to combat SARS-CoV-2 infection or to treat fatal symptoms that may arise from development of COVID-19. These clinical trials feature testing of various doses, routes of administration, and combinations of 797 unique therapeutic agents, including small-molecule drugs, biologicals, and herbal or dietary supplements. Of the 797 treatments being tested, only 35 are newly developed treatments made to specifically combat SARS-CoV-2 or COVID-19, while 762 being tested in drug repurposing studies (Figure 6a).

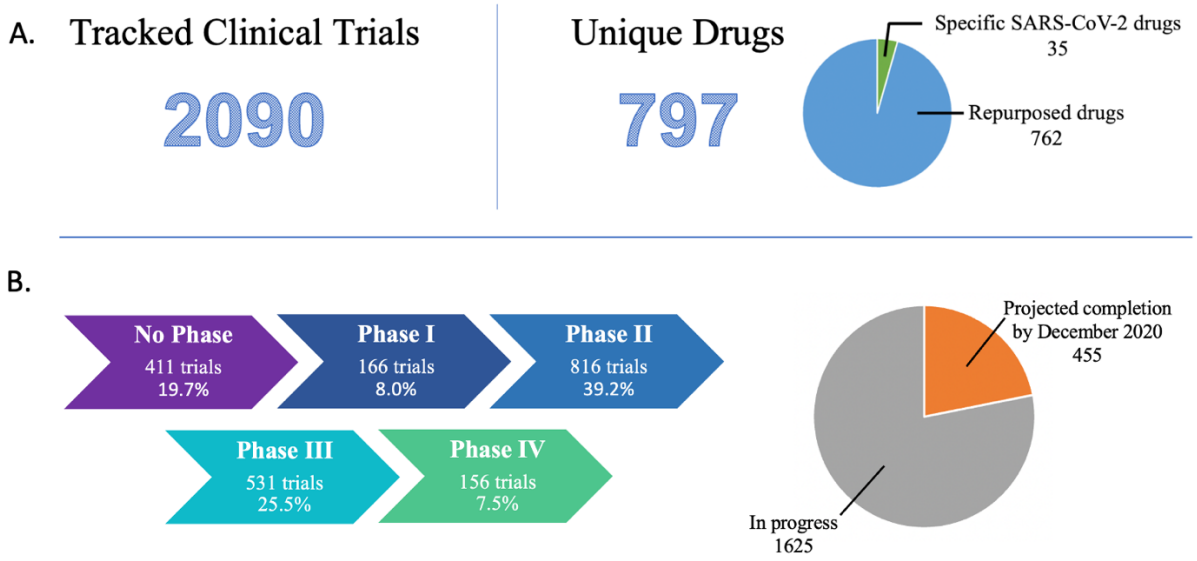

Figure 6. Summary of information available on the SARS-CoV-2 Treatment Tracker. (A) The breadth of information available on the SARS-CoV-2 Treatment Tracker. The tracker contains information on 2080 clinical trials which test the efficacy of 797 unique drugs, biologicals, or supplementation. Overwhelmingly, the majority of treatments (762 drugs) tested are repurposed treatments, while only 35 have been specifically developed for SARS-CoV-2. (B) The progress of clinical trials of treatments against SARS-CoV-2 as of December 2020. Of the clinical trials listed, 166 are in Phase 1, 816 are in Phase 2, 531 are in Phase 3, 156 are in Phase 4, and 411 have no phase listed. As of December 2020, 455 of the 2080 trials are projected to have already been completed.

Out of the 2080 clinical trials listed in the SARS-CoV-2 treatment tracker, 8.0% (166 trials) are in Phase 1, 39.2% (816 trials) are in Phase 2, 25.5% (531 trials) are in Phase 3, and 7.5% (156 trials) are in Phase 4. An additional 411 trials did not have an applicable trial phase included in their registry data. A total of 455 (21.9%) trials listed in the treatment tracker is expected to have

been completed by December 2020. Because an estimated trial completion date is not requisite information for most clinical trial registries, this information is not included for the majority of clinical trial data, and the actual proportion of completed trials should be assumed to be higher. A summary of the current statuses in our treatment tracker is shown in Figure 6b.

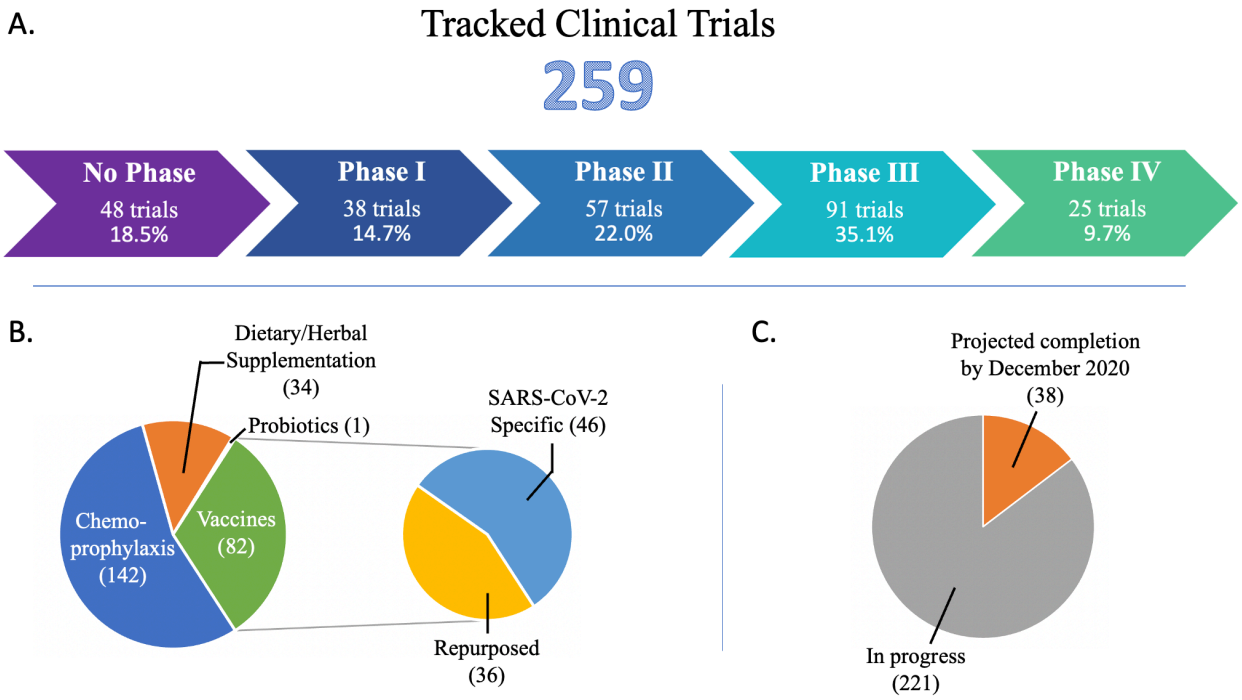

Figure 7. Summary of information available on the SARS-CoV-2 Prevention Tracker. (A) Distribution of phases of clinical trials listed on the SARS-CoV-2 Prevention tracker. (B) The different prevention methods being tested against SARS-CoV-2. The majority of trials test the chemoprophylactic potential of repurposed drugs, while trials of vaccines are second most abundant. Approximately half of the vaccines under clinical trials have been repurposed from other diseases. (C) Of the tracked clinical trials, 38 were projected to have been completed by December 2020.

The prevention and diagnostic trackers on the SARS-Coronavirus-2.info website are much more limited in entries when compared with the treatment tracker, likely due to the fact that drug repurposing features appreciably less in the development of both vaccines and diagnostic tests. The prevent tracker currently lists 259 clinical trials of preventative measures against SARS-CoV-2 infection. Out of these, 14.7% (38 trials) are in Phase 1, 22.0% (57 trials) are in Phase 2, 35.1% (91 trials) are in Phase 3, and 9.7% (25 trials) are in Phase 4, while 18.5% (48 trials) have

no phase listed. The majority of the trials listed are testing for the effectiveness of chemoprophylactic agents (54.8% of trials), likely due to the fact that they can more readily be repurposed than vaccines and are therefore able to enter clinical trials sooner. Vaccines represent the next-most popular prevention strategy being tested, accounting for 31.7% of the trials listed (82 trials). Interestingly, of these vaccine trials, almost half (43.9%; 36 trials) investigate the efficacy of repurposed vaccines, while the rest (56.1%; 46 trials) are investigating vaccines specifically developed for SARS-CoV-2. Other, less common strategies being tested are herbal or dietary supplementation, traditional medicines or homeopathy, and the conferring of passive immunity through administration of antibodies or convalescent serum. Of the 259 trials, 14.7% (38 trials) are expected to be completed by December 2020. However, due to the lack of estimated completion date data available on most clinical trial registries discussed above, this number should be assumed to be much higher. A full summary of the clinical trials in our prevention tracker is shown in Figure 7.

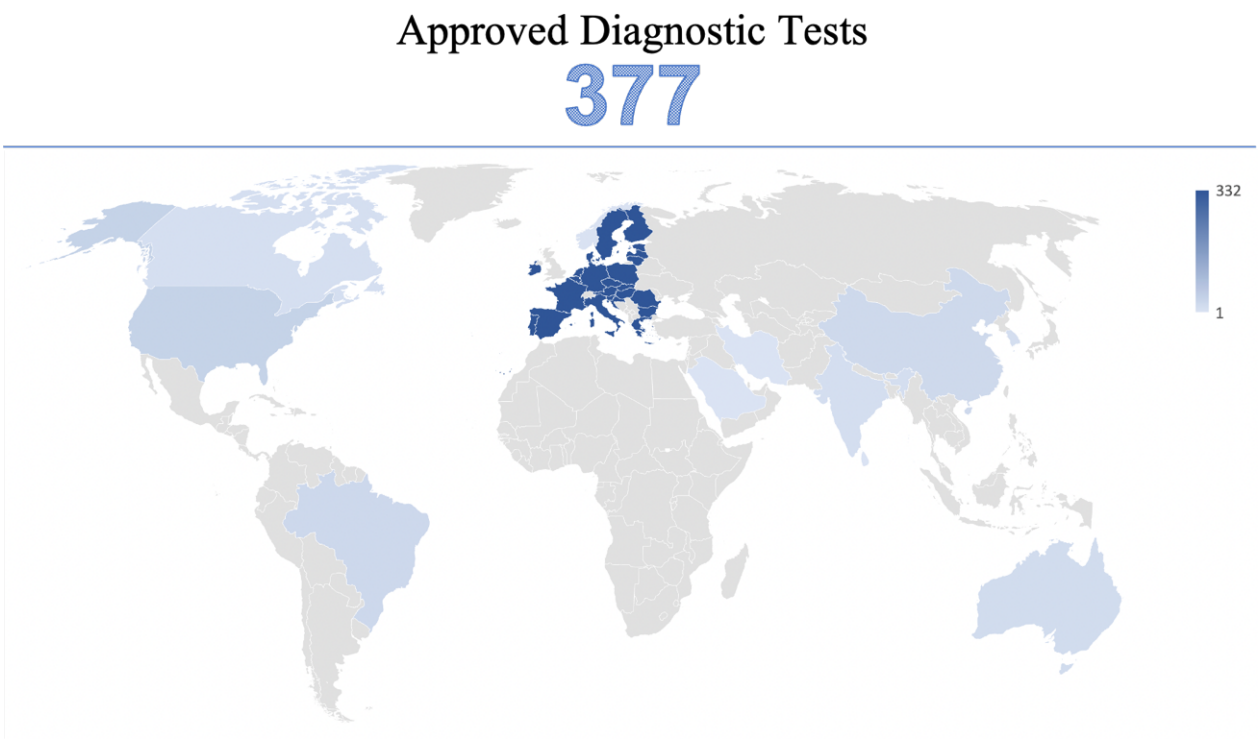

Figure 8. Status of approved SARS-CoV-2 diagnostic methods around the world. A total of 332 tests have been authorized for diagnostic use in the European Union, 36 tests have been authorized in the United States, and a total of 94 have been granted authorization elsewhere.

In general, completion of clinical trials is not necessary for the development of diagnostic tests. Therefore, authorization status served as a substitute for phase numbers in the SARS-CoV-2 diagnostic tracker. A total of 377 diagnostic tests that have been approved for laboratory use by at least one governing body. Of these 36 have been granted authorization for use in the United States of America, 332 have been granted authorization for use in Europe, and 94 have been granted authorization for use elsewhere (Figure 8).

4.2.3 Website impact

When it was first launched in April 2020, the SARS-Coronavirus-2.info website was the largest aggregator of COVID-19 treatments in clinical trials, the second largest aggregator of diagnostic tests, and the only aggregator of COVID-19 vaccines in clinical trials. However, as the pandemic progressed and development of treatment, prevention, and diagnostic options against COVID-19 became the subject of public focus, other resources emerged that provided similar aggregation and tracking services. Despite this, as of December 2020, SARS-Coronavirus-2.info remains the only aggregator of COVID-19 clinical trial information that focuses only on treatments specifically intended to impair replication or entry of the SARS-CoV-2 virus or treat the direct and fatal symptoms of COVID-19, while cutting out studies that focuses on other symptoms of infection or other indirect consequences of the pandemic.

To make these efforts available to the broadest audience possible, most of the information on the website was translated into 10 different languages by volunteer effort. These languages include English, Russian, Spanish, Ukrainian, Estonian, Chinese, Lithuanian, Polish, Tagalog, and Norwegian. This was a crucial aspect in the effort to improve the accessibility of our website to people around the world who do not necessarily have a professional scientific background or strong English comprehension. From April 2020 to December 2020, SARS-Coronavirus-2.info has received over 7,500 visits by users from 85 countries. Of note, the countries from which the website registered most visits were Norway, the United States, Ukraine, Russia, and Poland, which are all countries in which were likely able to take advantage of our translation efforts.

4.3 Large overlap of drugs being tested against SARS-CoV-2 and previously discovered BSAAs

Of the 797 unique COVID-19 treatments listed in our SARS-Coronavirus-2 treatment tracker, 467 are officially recognized as drugs by the DrugBank database, with the remaining 330 treatments falling into the category of traditional, herbal, or alternative medicines. Of the 467 recognized drugs being tested against SARS-CoV-2 infection, 17.1% (80 drugs) are BSAAs that can be found in our DrugVirus.info database. Many of these BSAAs had already shown antiviral activity toward other coronaviruses prior to the emergence of the COVID-19 pandemic, suggesting that they were specifically targeted as treatment candidates for that reason. Moreover, the only drug that is currently approved by the FDA for treatment of COVID-19 is remdesivir, which itself is a repurposed BSAA listed in the DrugVirus database. Taken together, these observations indicate the great necessity for identification of BSAAs prior to viral emergence and illustrate the efficiency that this may impart to the drug development process.

5 Discussion

Development of a BSAA database, DrugVirus.info began long before the outset of the COVID-19 pandemic. However, the emergence of SARS-CoV-2 and COVID-19 at the beginning of 2020 brought the importance of this research under an urgent spotlight. The heavy interest in this antiviral development work by scientists and laypeople alike spurred our group to launch the second open-access online project, SARS-Coronavirus-2.info. While one was meant to act as a drug development and translational science resource for scientists and pharmaceutical industry professionals, the other was meant as a general information dissemination tool that provides up-to-date information to the general public from a virology and molecular biological perspective.

Throughout the course of the pandemic, engagement with and impact of both resources fluctuated. As rates of COVID-19 skyrocketed globally in April 2020, both DrugVirus.info and SARS-Coronavirus-2.info were access from around the world with heavy traffic. However, this

initial heavy engagement only lasted several months, and traffic was reduced to only a small fraction of what it had been in April 2020. This is not unexpected, because the beginning of the global COVID-19 pandemic and the resulting international response was unprecedented for almost every living person, and was certain to have caused widespread feelings of uncertainty, unease, and panic. It is therefore expected for people to make the initiative to seek out informational resources of all kinds to better equip themselves for an unprecedented, unforeseen time. However, as SARS-CoV-2 infection rates leveled off and eventually plummeted for the summer months, it is expected for user engagement to naturally drop as lives regained some degrees of normalcy, and the fear of the unknown gradually wore off.

The high traffic received by the two websites, underscores the importance of using technology as a resource for rapid information dissemination in rapidly evolving situations like the COVID-19 pandemic. Both websites achieved an unexpectedly broad audience, especially when considering geographical location. In terms of the SARS-Coronavirus-2 website, this is in part due to the great effort put into translating the information presented into different languages. However, it is also notable that the websites' reach extended to further corners of the world, including Romania, Suriname Zimbabwe, Palestine, and many other countries where the official language was not included in our translations. An even broader geographical audience was achieved by DrugVirus.info, which had no translations associated with it, but was presented graphically with minimal text to achieve ease of understanding.

Interestingly, while the resource we meant to reach a broader audience (SARS-Coronavirus-2.info) received very little traffic after the initial surge of the pandemic, the more scientifically driven resource (DrugVirus.info) continues to maintain a steady level of traffic to this day. This like likely due to the fact that several months into the pandemic, many other general resources concerning the SARS-CoV-2 virus were also created to serve the same purpose of general information dissemination, while many others were created with the purpose of tracking the development of tools to combat the COVID-19 pandemic [89-94]. Moreover, much of the public health and layperson-directed information presented on our website soon became common knowledge as the pandemic continued to spread.

In contrast, the DrugVirus.info database retained its relevance as time progressed, likely due to its ability to help direct drug development in response to the COVID-19 epidemic, which is a slower process that is still ongoing to this day. BSAA resources similar to DrugVirus.info have been demonstrated to be important to pandemic response, as evidenced by the large quantities of repurposed BSAAs from the DrugVirus database that is currently undergoing clinical trials against SARS-CoV-2, as reported by the treatment tracker on SARS-Coronavirus-2.info. Additionally, the emergence of the COVID-19 pandemic demonstrated the necessity for research in preparation for future emergent viruses, illustrating the potential for the DrugVirus database to continue to have utility well past the resolution of the current pandemic.

Contrary to only being a drain on resources, the pandemic actually also greatly helped the field of BSAA development by stimulating research into drug repurposing and BSAA development. At the beginning of the pandemic, many researchers were compelled to investigate the antiviral efficacy of repurposed drugs, for the simple reason that specific anti-SARS-CoV-2 treatments did not yet exist. Because of the high volume of testing that took place for various existing drugs and compounds against SARS-CoV-2, several repurposed drugs may potentially be discovered to have previously undiscovered antiviral activity. These drugs, if caught and recorded by the DrugVirus database, could then be tested against a library of other disease-causing viruses and could be brought forward as a candidate for BSAA development, if initial experimental results were promising. Thus, this system of BSAA tracking and development could not only be a valuable tool in combating future pandemics, but may also be strengthened by them as they occur.

Although both DrugVirus.info and SARS-Coronavirus-2.info have undergone regular development over the course of the past year, both have significant limitations associated with them. The most salient of these is the redundancy of information presented by the SARS-Coronavirus-2.info website. While it started off as one of the few tracking websites for the rapidly evolving situation surrounding the COVID-19 epidemic, it was quickly overshadowed by several other online resources that spread the same information. It became increasingly more impractical at spreading layperson information as time passed and the virus became more famous. This was reflected in the relatively low traffic to the website as the pandemic progressed.

Therefore, although SARS-Coronavirus-2 will continue to update its treatment, prevention, and diagnosis trackers as new developments emerge, it will likely stop being updated once vaccines are made widely available to the general public and the pandemic begins to decline.

On the other hand, the DrugVirus database is likely to remain a useful resource with capacity for further development and growth, despite the progression of the pandemic. However, several changes are proposed in order to maintain the website's optimal functionality and relevance. Firstly, the DrugVirus database was mainly assembled using manual curation techniques. While this was the easiest way to ensure the most conservatively accurate entries, the efforts of one master's student over the course of one year would naturally have very low coverage. Therefore, it cannot be compared with other manually curated databases that may employ teams of full-time manual curators. Further work on the database should either employ a larger team to carry out manual curation or incorporate techniques such as text mining or network building to broaden the scope of the database. In the latter case, future versions of the database may include information on *in silico* connections as well as experimental ones that have been manually curated.

Another current limitation of the DrugVirus database lies in the fact that the level of scientific rigor required for an entry to be included is very low. This decision was made in part because DrugVirus.info was the first database of its kind, and therefore had the goal of creating the broadest dataset possible. Therefore, for the purposes of our database, a drug was considered to have antiviral activity against as long as it was demonstrated to have an SI value of over 1. This is extremely liberal inclusion criteria, especially when published antiviral research often tends to focus on drugs with SI values in the hundreds, or even in the thousands [95-97]. While it is indeed important to include less selective antiviral activity in the DrugVirus database to guide the direction of further studies, future versions should have more stringent inclusion criteria, such as SI > 5, and have a standardized system to indicate the degree of selectivity observed for each drug-virus combination.

Finally, the DrugVirus database has limited functionality because it currently does not report negative results. There is currently no system to record and report studies that may demonstrate the *lack* of antiviral activity of a drug-virus combination. Although the paucity of

negative result publishing has been an ongoing dilemma in the scientific community, clear negative results do exist in the literature. For example, a research group may publish that out of a library of drugs tested, only one or two demonstrated sufficient antiviral activity while the rest had negligible effect. Otherwise, some drugs may have been demonstrated to have moderate *in vitro* efficacy in one model but fail to show efficacy in a further stage of development. In addition, the Kainov Lab at NTNU routinely conducts studies to fill in knowledge gaps and validate data presented by the DrugVirus database [98, 99]. The inclusion of negative results generated internally, as well as any that have been published, could be a valuable addition to the database and prevent many unnecessary repeat experiments that could drain resources from other research.

6 Conclusion

Drug repurposing for BSAA development remains an effective, quick-response option for dealing with pandemic-causing emergent viruses such as SARS-CoV-2. Here, we have highlighted two projects that help to shed light on this fact: DrugVirus.info, a database of known BSAAs that was used for drug repurposing in the wake of the COVID-19 pandemic and SARS-Coronavirus-2.info, a website that tracked treatments, prevention, and diagnostics related to COVID-19 while providing a basic scientific understanding of the virus to a general audience. Both websites have been accessed thousands of times from countries all over the world over the course of the pandemic and continue to welcome visitors today. While work on SARS-Coronavirus-2.info is beginning to wind down as vaccines are being administered, the DrugVirus database is in its infancy, requiring further development and addition of features. Going forward, further *in silico* and experimental work would be needed to flesh out our understanding of BSAAs.

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Appendix

Table S1. All Drug-Virus combinations recorded on the DrugVirus.info database as of December 2020

Drug	Virus	Status
Acetylsalicylic acid	FLUAV	Cell Lines
Acetylsalicylic acid	HCV	Cell Lines
Acetylsalicylic acid	HSV-1	Phase I
Acetylsalicylic acid	ZIKV	Cell Lines
Aciclovir	CMV	Cell Lines
Aciclovir	EBV	Cell Lines
Aciclovir	HHV-6	Cell Lines
Aciclovir	HPV	Phase II
Aciclovir	HSV-1	Approved
Aciclovir	HSV-2	Approved
Aciclovir	VZV	Approved
Adefovir	CRPV	Animal Model
Adefovir	FLUAV	Animal Model
Adefovir	HDV	Phase I
Adefovir	HIV-1	Phase II
Adefovir	HSV-1	Animal Model
Adefovir dipivoxil	CPXV	Cell Lines
Adefovir dipivoxil	HBV	Approved
Adefovir dipivoxil	VACV	Cell Lines
Alisporivir	HCoV-229E	Cell Lines
Alisporivir	HCV	Phase III
Alisporivir	HIV-1	Cell Lines
Alisporivir	MERS-CoV	Cell Lines
Alisporivir	SARS-CoV	Cell Lines
Alpha-lipoic acid	HIV-1	Primary Cells
Alpha-lipoic acid	VACV	Cell Lines
Amantadine	DENV	Phase II
Amantadine	FLUAV	Approved
Amantadine	FMDV	Cell Lines
Amantadine	HAV	Cell Lines
Amantadine	HBV	Animal Model
Amantadine	HTNV	Cell Lines
Amantadine	JUNV	Cell Lines
Amantadine	LASV	Cell Lines
Amantadine	LCMV	Cell Lines
Amantadine	MOPV	Cell Lines
Amantadine	PICV	Cell Lines
Amantadine	SARS-CoV-2	Phase II
Amantadine	VSV	Cell Lines
Amantadine	WNV	Cell Lines
Amiloride	CHIKV	Cell Lines
Amiloride	EBOV	Cell Lines
Amiloride	HEV-A	Cell Lines
Amiloride	HEV-B	Cell Lines
Amiloride	HEV-C	Cell Lines
Amiloride	HRV-A	Cell Lines
Amiloride	HRV-B	Cell Lines
Amiloride	HSV-1	Cell Lines
Amiloride	JUNV	Cell Lines
Amiloride	KSHV	Cell Lines
Amiloride	LASV	Cell Lines
Amiloride	MARV	Cell Lines
Amiloride	MeV	Cell Lines
Amiodarone	DENV	Cell Lines
Amiodarone	EBOV	Phase III
Amiodarone	HCV	Cell Lines
Amiodarone	HSV-1	Cell Lines
Amiodarone	RRV	Cell Lines
Amiodarone	SARS-CoV	Cell Lines
Amiodarone	SINV	Cell Lines
Amiodarone	VSV	Cell Lines
Amiodarone	YFV	Cell Lines
Amodiaquine	DENV	Cell Lines
Amodiaquine	EBOV	Cell Lines
Amodiaquine	HCV	Cell Lines
Amodiaquine	HSV-1	Cell Lines
Amodiaquine	LASV	Cell Lines
Amodiaquine	MERS-CoV	Cell Lines
Amodiaquine	RABV	Cell Lines
Amodiaquine	RRV	Cell Lines
Amodiaquine	SARS-CoV	Cell Lines
Amodiaquine	SINV	Cell Lines
Amodiaquine	VSV	Cell Lines
Amodiaquine	WNV	Cell Lines
Amodiaquine	YFV	Cell Lines
Amodiaquine	ZIKV	Primary Cells
Amprenavir	HIV-1	Approved
Amprenavir	SARS-CoV-2	Cell Lines
Anisomycin	DENV	Cell Lines
Anisomycin	JEV	Cell Lines
Anisomycin	MERS-CoV	Cell Lines
Anisomycin	SARS-CoV	Cell Lines
Anisomycin	ZIKV	Cell Lines
Aprotinin	DENV	Cell Lines
Aprotinin	FLUAV	Cell Lines
Aprotinin	FLUBV	Cell Lines
Aprotinin	RV	Animal Model
Aprotinin	SINV	Animal Model
Aprotinin	WNV	Cell Lines
Artesunate	BKV	Cell Lines
Artesunate	CMV	Phase III
Artesunate	EBOV	Phase III
Artesunate	EBV	Cell Lines
Artesunate	HHV-6	Cell Lines
Artesunate	HPV	Phase II
Artesunate	JCV	Cell Lines
Atazanavir	HIV-1	Approved
Atazanavir	SARS-CoV-2	Cell Lines
Atovaquone	CHIKV	Cell Lines
Atovaquone	ZIKV	Primary Cells
Azacitidine	ADV	Cell Lines
Azacitidine	FLUAV	Cell Lines
Azacitidine	HIV-1	Cell Lines
Azacitidine	HIV-2	Cell Lines
Azacitidine	HMPV	Cell Lines

Azacitidine	RVFV	Cell Lines
Azithromycin	EBOV	Phase II
Azithromycin	FLUAV	Phase IV
Azithromycin	HCV	Cell Lines
Azithromycin	HEV-A	Animal Model
Azithromycin	HEV-B	Animal Model
Azithromycin	HIV-1	Phase I
Azithromycin	HRV-A	Animal Model
Azithromycin	RSV	Phase III
Azithromycin	ZIKV	Cell Lines
Baloxavir marboxil	BUNV	Cell Lines
Baloxavir marboxil	FLUAV	Approved
Baloxavir marboxil	FLUBV	Approved
Baloxavir marboxil	HTNV	Cell Lines
Baloxavir marboxil	LACV	Cell Lines
Beclabuvir	HCV	Phase II
Beclabuvir	LGV	Cell Lines
Beclabuvir	NoV	Cell Lines
Beclabuvir	SPV	Cell Lines
Benztropine	EBOV	Cell Lines
Benztropine	HCV	Cell Lines
Benztropine	MARV	Cell Lines
Benztropine	MERS-CoV	Cell Lines
Benztropine	SARS-CoV	Cell Lines
Bepridil	DENV	Cell Lines
Bepridil	EBOV	Cell Lines
Bepridil	MARV	Animal Model
Berberine	CHIKV	Cell Lines
Berberine	CMV	Cell Lines
Berberine	FLUAV	Cell Lines
Berberine	HCV	Cell Lines
Berberine	HEV-A	Cell Lines
Berberine	HEV-B	Cell Lines
Berberine	HIV-1	Cell Lines
Berberine	HPV	Cell Lines
Berberine	HSV-1	Cell Lines
Berberine	RSV	Cell Lines
Berberine	SINV	Cell Lines
Berberine	ZIKV	Cell Lines
Betulinic Acid	CHIKV	Cell Lines
Betulinic Acid	DENV	Cell Lines
Betulinic Acid	ECHOV-6	Cell Lines
Betulinic Acid	FLUAV	Animal Model
Betulinic Acid	HIV-1	Cell Lines
Betulinic Acid	HPV	Phase II
Betulinic Acid	HSV-1	Cell Lines
Betulinic Acid	HSV-2	Cell Lines
Betulinic Acid	SARS-CoV	Cell Lines
Betulinic Acid	SFV	Cell Lines
Betulinic Acid	SINV	Cell Lines
Betulinic Acid	ZIKV	Primary Cells
Bithionol	BKV	Cell Lines
Bithionol	SV40	Cell Lines
Bithionol	ZIKV	Cell Lines
Boceprevir	HCV	Approved
Boceprevir	SARS-CoV-2	Cell Lines
Bortezomib	DENV	Animal Model
Bortezomib	FLUAV	Cell Lines
Bortezomib	HBV	Animal Model
Bortezomib	RSV	Animal Model
Bortezomib	RVFV	Cell Lines
Bortezomib	VSV	Cell Lines
Bortezomib	ZIKV	Cell Lines
Brequinar	DENV	Cell Lines
Brequinar	FLUAV	Cell Lines
Brequinar	FLUBV	Cell Lines
Brequinar	HIV-1	Cell Lines
Brequinar	JUNV	Cell Lines
Brequinar	LASV	Cell Lines
Brequinar	LCMV	Cell Lines
Brequinar	POWV	Cell Lines
Brequinar	RV	Primary Cells
Brequinar	VSV	Cell Lines
Brequinar	WNV	Cell Lines
Brequinar	YFV	Cell Lines
Brincidofovir	ADV	Phase III
Brincidofovir	B19V	Cell Lines
Brincidofovir	BKV	Phase III
Brincidofovir	CMV	Phase III
Brincidofovir	EBOV	Phase II
Brincidofovir	EBV	Phase III
Brincidofovir	HHV-6	Phase III
Brincidofovir	HSV-1	Phase III
Brincidofovir	JCV	Cell Lines
Brincidofovir	KSHV	Cell Lines
Brincidofovir	VACV	Phase III
Brincidofovir	VARV	Phase III
Brincidofovir	VZV	Cell Lines
Brivudine	CPXV	Cell Lines
Brivudine	HPV	Animal Model
Brivudine	HSV-1	Animal Model
Brivudine	HSV-2	Cell Lines
Brivudine	VACV	Cell Lines
Brivudine	VZV	Approved
Caffeine	FLUAV	Cell Lines
Caffeine	HCV	Phase I
Caffeine	HSV-1	Cell Lines
Caffeine	JUNV	Cell Lines
Caffeine	VZV	Cell Lines
Calanolide A	CMV	Cell Lines
Calanolide A	HIV-1	Approved
Camostat	FLUAV	Cell Lines
Camostat	FLUBV	Cell Lines
Camostat	MERS-CoV	Cell Lines
Camostat	SARS-CoV	Cell Lines
Camptothecin	EBV	Cell Lines
Camptothecin	FLUAV	Cell Lines
Camptothecin	HCV	Cell Lines
Camptothecin	HEV-A	Cell Lines
Camptothecin	HIV-1	Cell Lines
Camptothecin	HSV-1	Cell Lines
Camptothecin	KSHV	Cell Lines
Cenicriviroc	HCV	Cell Lines
Cenicriviroc	HIV-1	Phase II

Cenicriviroc	HIV-2	Primary Cells
Cenicriviroc	SARS-CoV-2	Cell Lines
Cepharanthine	HCoV-OC43	Cell Lines
Cepharanthine	HIV-1	Cell Lines
Cepharanthine	HSV-1	Cell Lines
Cepharanthine	SARS-CoV	Cell Lines
Cepharanthine	SARS-CoV-2	Cell Lines
Chloroquine	CCHFV	Cell Lines
Chloroquine	CHIKV	Phase III
Chloroquine	DENV	Phase II
Chloroquine	EBOV	Animal Model
Chloroquine	FLUAV	Phase II
Chloroquine	HCoV-OC43	Cell Lines
Chloroquine	HCV	Phase IV
Chloroquine	HEV-A	Animal Model
Chloroquine	HIV-1	Phase III
Chloroquine	KSHV	Cell Lines
Chloroquine	MERS-CoV	Cell Lines
Chloroquine	SARS-CoV	Cell Lines
Chloroquine	SARS-CoV-2	Cell Lines
Chloroquine	ZIKV	Cell Lines
Chlorpromazine	CCHFV	Cell Lines
Chlorpromazine	CHIKV	Cell Lines
Chlorpromazine	DENV	Cell Lines
Chlorpromazine	EBV	Primary Cells
Chlorpromazine	MERS-CoV	Cell Lines
Chlorpromazine	SARS-CoV	Cell Lines
Chlorpromazine	ZIKV	Cell Lines
Cidofovir	ADV	Cell Lines
Cidofovir	B19V	Cell Lines
Cidofovir	BKV	Phase II
Cidofovir	CMV	Approved
Cidofovir	EBV	Cell Lines
Cidofovir	HCV	Cell Lines
Cidofovir	HHV-6	Cell Lines
Cidofovir	HPV	Phase II
Cidofovir	HSV-1	Phase II
Cidofovir	HSV-2	Phase II
Cidofovir	JCV	Cell Lines
Cidofovir	KSHV	Cell Lines
Cidofovir	MCV	Cell Lines
Cidofovir	VZV	Cell Lines
Clomipramine	EBOV	Cell Lines
Clomipramine	MERS-CoV	Cell Lines
Clomipramine	SARS-CoV	Cell Lines
Cyclosporine	CMV	Phase IV
Cyclosporine	DENV	Cell Lines
Cyclosporine	FLUAV	Cell Lines
Cyclosporine	HCV	Phase IV
Cyclosporine	HIV-1	Phase IV
Cyclosporine	MERS-CoV	Primary Cells
Cyclosporine	RVFV	Cell Lines
Cyclosporine	VACV	Cell Lines
Cyclosporine	VSV	Cell Lines
Cyclosporine	WNV	Cell Lines
Cyclosporine	YFV	Cell Lines
Cyclosporine	ZIKV	Cell Lines

CYT107	HBV	Phase II
CYT107	HCV	Phase II
CYT107	HIV-1	Phase II
Daclatasvir	HCV	Approved
Daclatasvir	SARS-CoV-2	Phase I
Dalbavancin	EBOV	Cell Lines
Dalbavancin	HEV-B	Cell Lines
Dalbavancin	MERS-CoV	Cell Lines
Dalbavancin	SARS-CoV	Cell Lines
Dalbavancin	ZIKV	Cell Lines
Dapivirine	FLUAV	Cell Lines
Dapivirine	FLUBV	Cell Lines
Dapivirine	HIV-1	Cell Lines
Darunavir	HIV-1	Approved
Darunavir	SARS-CoV-2	Cell Lines
Dasabuvir	HCV	Approved
Dasabuvir	TBEV	Cell Lines
Dasabuvir	WNV	Cell Lines
Dasabuvir	ZIKV	Cell Lines
Dasatinib	BKV	Cell Lines
Dasatinib	DENV	Cell Lines
Dasatinib	HCV	Cell Lines
Dasatinib	HEV-B	Cell Lines
Dasatinib	HIV-1	Cell Lines
Dasatinib	MERS-CoV	Cell Lines
Dasatinib	SARS-CoV	Cell Lines
Dexelvucitabine	HBV	Animal Model
Dexelvucitabine	HIV-1	Phase I
Dibucaine	HCV	Cell Lines
Dibucaine	HEV-A	Cell Lines
Dibucaine	HEV-B	Cell Lines
Dibucaine	HEV-D	Cell Lines
Didanosine	HIV-1	Approved
Didanosine	HSV-1	Cell Lines
Docosanol	CMV	Cell Lines
Docosanol	HHV-6	Cell Lines
Docosanol	HIV-1	Primary Cells
Docosanol	HSV-1	Approved
Docosanol	HSV-2	Approved
Docosanol	KSHV	Phase II
Docosanol	RSV	Primary Cells
Doxycycline	CHIKV	Animal Model
Doxycycline	DENV	Cell Lines
Doxycycline	VSV	Cell Lines
Efavirenz	HIV-1	Approved
Efavirenz	ZIKV	Primary Cells
Eflornithine	CHIKV	Cell Lines
Eflornithine	CMV	Cell Lines
Eflornithine	DENV	Cell Lines
Eflornithine	HEV-B	Cell Lines
Eflornithine	HSV-1	Cell Lines
Eflornithine	JEV	Cell Lines
Eflornithine	MERS-CoV	Cell Lines
Eflornithine	SINV	Cell Lines
Eflornithine	VSV	Cell Lines
Eflornithine	ZIKV	Cell Lines
Elvucitabine	HBV	Animal Model

Elvucitabine	HIV-1	Phase I
Emetine	CMV	Animal Model
Emetine	EBOV	Cell Lines
Emetine	HCoV-NL63	Cell Lines
Emetine	HCoV-OC43	Cell Lines
Emetine	HEV-B	Cell Lines
Emetine	HIV-1	Cell Lines
Emetine	HMPV	Cell Lines
Emetine	HSV-2	Cell Lines
Emetine	MERS-CoV	Animal Model
Emetine	RABV	Cell Lines
Emetine	RVFV	Cell Lines
Emetine	SARS-CoV	Cell Lines
Emetine	ZIKV	Cell Lines
Emodin	CMV	Cell Lines
Emodin	EBV	Cell Lines
Emodin	FLUAV	Animal Model
Emodin	HBV	Animal Model
Emodin	HEV-A	Cell Lines
Emodin	HEV-B	Animal Model
Emodin	HSV-1	Cell Lines
Emodin	SARS-CoV	Cell Lines
Emodin	ZIKV	Cell Lines
Erlotinib	BKV	Cell Lines
Erlotinib	DENV	Animal Model
Erlotinib	EBOV	Phase II
Erlotinib	HCV	Phase II
Etravirine	HIV-1	Approved
Etravirine	ZIKV	Cell Lines
Ezetimibe	HBV	Cell Lines
Ezetimibe	HCV	Phase IV
Ezetimibe	HDV	Phase II
Ezetimibe	HIV-1	Phase I
Ezetimibe	RVFV	Cell Lines
Ezetimibe	ZIKV	Cell Lines
Famciclovir	HBV	Phase I
Famciclovir	HHV-8	Phase II
Famciclovir	HSV-1	Approved
Famciclovir	HSV-2	Approved
Famciclovir	VZV	Approved
Favipiravir	ANDV	Cell Lines
Favipiravir	CCHFV	Animal Model
Favipiravir	CHIKV	Animal Model
Favipiravir	EBOV	Phase II
Favipiravir	FLUAV	Approved
Favipiravir	FLUBV	Approved
Favipiravir	FLUCV	Approved
Favipiravir	HATV	Cell Lines
Favipiravir	LASV	Cell Lines
Favipiravir	LCMV	Cell Lines
Favipiravir	MARV	Animal Model
Favipiravir	NiV	Cell Lines
Favipiravir	RABV	Cell Lines
Favipiravir	RVFV	Cell Lines
Favipiravir	SNV	Cell Lines
Favipiravir	YFV	Cell Lines
Favipiravir	ZIKV	Cell Lines

Fenretinide	DENV	Animal Model
Fenretinide	HCV	Cell Lines
Fenretinide	HIV-1	Cell Lines
Fenretinide	RSV	Cell Lines
Fenretinide	WNV	Cell Lines
Fenretinide	ZIKV	Cell Lines
Fiacitabine	CMV	Animal Model
Fiacitabine	EBV	Cell Lines
Fiacitabine	HBV	Animal Model
Fiacitabine	HSV-1	Animal Model
Fiacitabine	HSV-2	Animal Model
Fiacitabine	KSHV	Cell Lines
Fiacitabine	VZV	Phase II
Filociclovir	ADV	Cell Lines
Filociclovir	CMV	Phase I
Filociclovir	EBV	Cell Lines
Filociclovir	HHV-6	Cell Lines
Filociclovir	KSHV	Cell Lines
Flavopiridol	ADV	Cell Lines
Flavopiridol	FLUAV	Animal Model
Flavopiridol	HSV-1	Cell Lines
Fluoxetine	DENV	Cell Lines
Fluoxetine	HCV	Cell Lines
Fluoxetine	HEV-B	Cell Lines
Fluoxetine	HEV-C	Cell Lines
Fluvastatin	DENV	Cell Lines
Fluvastatin	FLUAV	Cell Lines
Fluvastatin	HCV	Phase I
Fluvastatin	ZIKV	Cell Lines
Formoterol	HEV-A	Cell Lines
Formoterol	HEV-B	Cell Lines
Formoterol	HEV-C	Cell Lines
Formoterol	HEV-D	Cell Lines
Foscarnet	CMV	Approved
Foscarnet	EBV	Cell Lines
Foscarnet	FLUAV	Cell Lines
Foscarnet	HBV	Animal Model
Foscarnet	HHV-6	Cell Lines
Foscarnet	HSV-1	Approved
Foscarnet	HSV-2	Approved
Foscarnet	KSHV	Cell Lines
Foscarnet	RoV	Cell Lines
Foscarnet	VSV	Cell Lines
Foscarnet	VZV	Phase IV
Galidesivir	DENV	Cell Lines
Galidesivir	EBOV	Phase I
Galidesivir	HCV	Cell Lines
Galidesivir	JEV	Cell Lines
Galidesivir	MARV	Phase I
Galidesivir	MERS-CoV	Cell Lines
Galidesivir	RAVV	Cell Lines
Galidesivir	RVFV	Cell Lines
Galidesivir	SARS-CoV	Cell Lines
Galidesivir	TBEV	Cell Lines
Galidesivir	WNV	Cell Lines
Galidesivir	YFV	Phase I
Galidesivir	ZIKV	Animal Model

Ganciclovir	ADV	Phase IV
Ganciclovir	CMV	Approved
Ganciclovir	EBV	Cell Lines
Ganciclovir	HBV	Phase I
Ganciclovir	HSV-1	Cell Lines
Ganciclovir	HSV-2	Cell Lines
Ganciclovir	VACV	Cell Lines
Ganciclovir	VZV	Phase II
Gefitinib	BKV	Cell Lines
Gefitinib	CMV	Animal Model
Gefitinib	HCV	Cell Lines
Gefitinib	VACV	Cell Lines
Gemcitabine	FLUAV	Cell Lines
Gemcitabine	HCV	Cell Lines
Gemcitabine	HEV-A	Cell Lines
Gemcitabine	HEV-B	Cell Lines
Gemcitabine	HEV-C	Cell Lines
Gemcitabine	HIV-1	Cell Lines
Gemcitabine	HRV-A	Cell Lines
Gemcitabine	HSV-1	Cell Lines
Gemcitabine	MERS-CoV	Cell Lines
Gemcitabine	SARS-CoV	Cell Lines
Gemcitabine	SINV	Cell Lines
Gemcitabine	VACV	Cell Lines
Gemcitabine	ZIKV	Cell Lines
Glycyrrhizin	EBV	Cell Lines
Glycyrrhizin	FLUAV	Cell Lines
Glycyrrhizin	HCV	Cell Lines
Glycyrrhizin	HEV-A	Cell Lines
Glycyrrhizin	HEV-B	Cell Lines
Glycyrrhizin	HIV-1	Cell Lines
Glycyrrhizin	HPIV-2	Cell Lines
Glycyrrhizin	HSV-1	Cell Lines
Glycyrrhizin	KSHV	Cell Lines
Glycyrrhizin	RV	Cell Lines
Glycyrrhizin	SARS-CoV	Cell Lines
Hexachlorophene	BKV	Cell Lines
Hexachlorophene	MERS-CoV	Cell Lines
Hexachlorophene	SFTSV	Cell Lines
Hexachlorophene	SV40	Cell Lines
Homoharringtonine	EV-1	Cell Lines
Homoharringtonine	HBV	Cell Lines
Homoharringtonine	HEV-B	Cell Lines
Homoharringtonine	HSV-1	Cell Lines
Homoharringtonine	MERS-CoV	Cell Lines
Homoharringtonine	SARS-CoV-2	Cell Lines
Homoharringtonine	VZV	Cell Lines
Hydroxychloroquine	CHIKV	Cell Lines
Hydroxychloroquine	DENV	Cell Lines
Hydroxychloroquine	HIV-1	Phase II
Hydroxychloroquine	MERS-CoV	Cell Lines
Hydroxychloroquine	SARS-CoV	Cell Lines
Hydroxychloroquine	SARS-CoV-2	Phase III
Hydroxychloroquine	ZIKV	Animal Model
Idoxuridine	HPV	Phase II
Idoxuridine	HSV-1	Approved
Idoxuridine	HSV-2	Approved
Idoxuridine	ORFV	Phase I
Idoxuridine	PyV	Animal Model
Idoxuridine	VACV	Animal Model
Imatinib	BKV	Cell Lines
Imatinib	HCV	Cell Lines
Imatinib	MERS-CoV	Cell Lines
Imatinib	SARS-CoV	Cell Lines
Indinavir	HIV-1	Approved
Indinavir	HPV	Cell Lines
Indomethacin	HIV-1	Cell Lines
Indomethacin	HSV-1	Cell Lines
Indomethacin	SARS-CoV	Cell Lines
Indomethacin	VSV	Cell Lines
Ingavirin	FLUAV	Phase II
Ingavirin	FLUBV	Animal Model
Ingavirin	HAdV	Animal Model
Ingavirin	HMPV	Cell Lines
Ingavirin	HPIV	Animal Model
Inosine pranobex	CAV-16	Cell Lines
Inosine pranobex	EMCV	Cell Lines
Inosine pranobex	EV-A71	Cell Lines
Inosine pranobex	FLUAV	Phase I
Inosine pranobex	HAdV-2	Cell Lines
Inosine pranobex	HAdV-5	Cell Lines
Inosine pranobex	HAV	Cell Lines
Inosine pranobex	HBV	Phase I
Inosine pranobex	HIV-1	Phase III
Inosine pranobex	HPIV-4	Cell Lines
Inosine pranobex	HPV	Approved
Inosine pranobex	HRV	Phase II
Inosine pranobex	HSV-1	Approved
Inosine pranobex	HSV-2	Approved
Inosine pranobex	MeV	Phase I
Inosine pranobex	RABV	Animal Model
Inosine pranobex	RoV	Cell Lines
Inosine pranobex	VACV	Phase I
Inosine pranobex	VZV	Phase I
Interferon alfa-n1	HCV	Phase III
Interferon alfa-n1	HPV	Approved
Interferon alfacon-1	Arenavirus	Animal Model
Interferon alfacon-1	CMV	Cell Lines
Interferon alfacon-1	EMCV	Animal Model
Interferon alfacon-1	FLUAV	Cell Lines
Interferon alfacon-1	HBV	Phase II
Interferon alfacon-1	HCV	Phase II
Interferon alfacon-1	HRV	Cell Lines
Interferon alfacon-1	HSV-1	Cell Lines
Interferon alfacon-1	HSV-2	Cell Lines
Interferon alfacon-1	PTV	Cell Lines
Interferon alfacon-1	RSV	Cell Lines
Interferon alfacon-1	SARS-CoV	Cell Lines
Interferon alfacon-1	VSV	Cell Lines
Interferon alfacon-1	YFV	Cell Lines
Interferon beta-1a	EBOV	Phase II
Interferon beta-1a	FLUAV	Cell Lines
Interferon beta-1a	HCoV-229E	Cell Lines
Interferon beta-1a	HIV	Cell Lines

Interferon beta-1a	HPIV	Cell Lines
Interferon beta-1a	HRV	Phase II
Interferon beta-1a	SARS-CoV	Cell Lines
Interferon beta-1a	SARS-CoV-2	Phase II
Irbesartan	HBV	Cell Lines
Irbesartan	HDV	Cell Lines
Isolanid	CHIKV	Cell Lines
Isolanid	DENV	Cell Lines
Isolanid	HEV-B	Cell Lines
Isolanid	KUNV	Cell Lines
Isolanid	SINV	Cell Lines
Itraconazole	FLUAV	Animal Model
Itraconazole	HEV-B	Cell Lines
Itraconazole	HMPV	Cell Lines
Itraconazole	HRV-A	Animal Model
Itraconazole	HRV-B	Cell Lines
Itraconazole	Par-A3	Cell Lines
Itraconazole	SAFV	Cell Lines
Ivermectin	CHIKV	Cell Lines
Ivermectin	DENV	Phase III
Ivermectin	HENV	Cell Lines
Ivermectin	HIV-1	Cell Lines
Ivermectin	SARS-CoV-2	Cell Lines
Ivermectin	SINV	Cell Lines
Ivermectin	YFV	Cell Lines
Ivermectin	ZIKV	Cell Lines
Kasugamycin	FLUAV	Animal Model
Kasugamycin	HSV-2	Animal Model
Kasugamycin	ZIKV	Animal Model
Lamivudine	HBV	Approved
Lamivudine	HIV-1	Approved
Lamivudine	HIV-2	Approved
Lapachone	HIV-1	Cell Lines
Lapachone	JCV	Primary Cells
Leflunomide	BKV	Cell Lines
Leflunomide	CMV	Cell Lines
Leflunomide	EBV	Animal Model
Leflunomide	HSV-1	Cell Lines
Leflunomide	JUNV	Cell Lines
Leflunomide	RV	Primary Cells
Letermovir	ADV	Cell Lines
Letermovir	CMV	Approved
Letermovir	EBV	Cell Lines
Letermovir	HHV-6	Cell Lines
Letermovir	HSV-1	Cell Lines
Letermovir	HSV-2	Cell Lines
Letermovir	VZV	Cell Lines
Lobucavir	CMV	Phase I
Lobucavir	HBV	Cell Lines
Lobucavir	HIV-1	Phase I
Lobucavir	HSV-1	Cell Lines
Lopinavir	HIV-1	Approved
Lopinavir	HIV-2	Approved
Lopinavir	HMPV	Cell Lines
Lopinavir	MERS-CoV	Phase III
Lopinavir	SARS-CoV-2	Cell Lines
Lopinavir	ZIKV	Animal Model
Lovastatin	DENV	Animal Model
Lovastatin	EBOV	Cell Lines
Lovastatin	HPIV-1	Cell Lines
Lovastatin	RSV	Animal Model
Lovastatin	ZIKV	Cell Lines
Manidipine	CMV	Cell Lines
Manidipine	DENV	Cell Lines
Manidipine	JEV	Animal Model
Manidipine	WNV	Cell Lines
Manidipine	ZIKV	Cell Lines
Maraviroc	HIV-1	Approved
Maraviroc	SARS-CoV-2	Cell Lines
Mefloquine	JCV	Cell Lines
Mefloquine	MERS-CoV	Cell Lines
Mefloquine	SARS-CoV	Cell Lines
Mefloquine	SARS-CoV-2	Cell Lines
Mefloquine	ZIKV	Cell Lines
Memantine	FLUAV	Cell Lines
Memantine	HCoV-OC43	Animal Model
Memantine	HIV-1	Phase II
Memantine	ZIKV	Animal Model
Metformin	DENV	Cell Lines
Metformin	FLUAV	Animal Model
Metformin	HBV	Cell Lines
Metformin	HEV-B	Cell Lines
Metformin	KSHV	Cell Lines
Minocycline	DENV	Animal Model
Minocycline	HCV	Cell Lines
Minocycline	HIV-1	Animal Model
Minocycline	RVFV	Cell Lines
Minocycline	WNV	Animal Model
Mitoxantrone	DENV	Cell Lines
Mitoxantrone	HCV	Cell Lines
Mitoxantrone	HSV-1	Cell Lines
Mitoxantrone	KSHV	Phase II
Mitoxantrone	RRV	Cell Lines
Mitoxantrone	SINV	Cell Lines
Mitoxantrone	YFV	Cell Lines
Mitoxantrone	ZIKV	Animal Model
Monensin	CMV	Cell Lines
Monensin	FLUAV	Animal Model
Monensin	HCoV-NL63	Cell Lines
Monensin	HCoV-OC43	Cell Lines
Monensin	HMPV	Cell Lines
Monensin	HSV-1	Cell Lines
Monensin	MERS-CoV	Cell Lines
Monensin	RSV	Cell Lines
Monensin	RVFV	Cell Lines
Monensin	VSV	Cell Lines
Mycophenolic acid	BKV	Phase IV
Mycophenolic acid	CHIKV	Cell Lines
Mycophenolic acid	DENV	Cell Lines
Mycophenolic acid	FLUAV	Cell Lines
Mycophenolic acid	HCoV-NL63	Cell Lines
Mycophenolic acid	HCoV-OC43	Cell Lines
Mycophenolic acid	HCV	Cell Lines
Mycophenolic acid	JUNV	Cell Lines

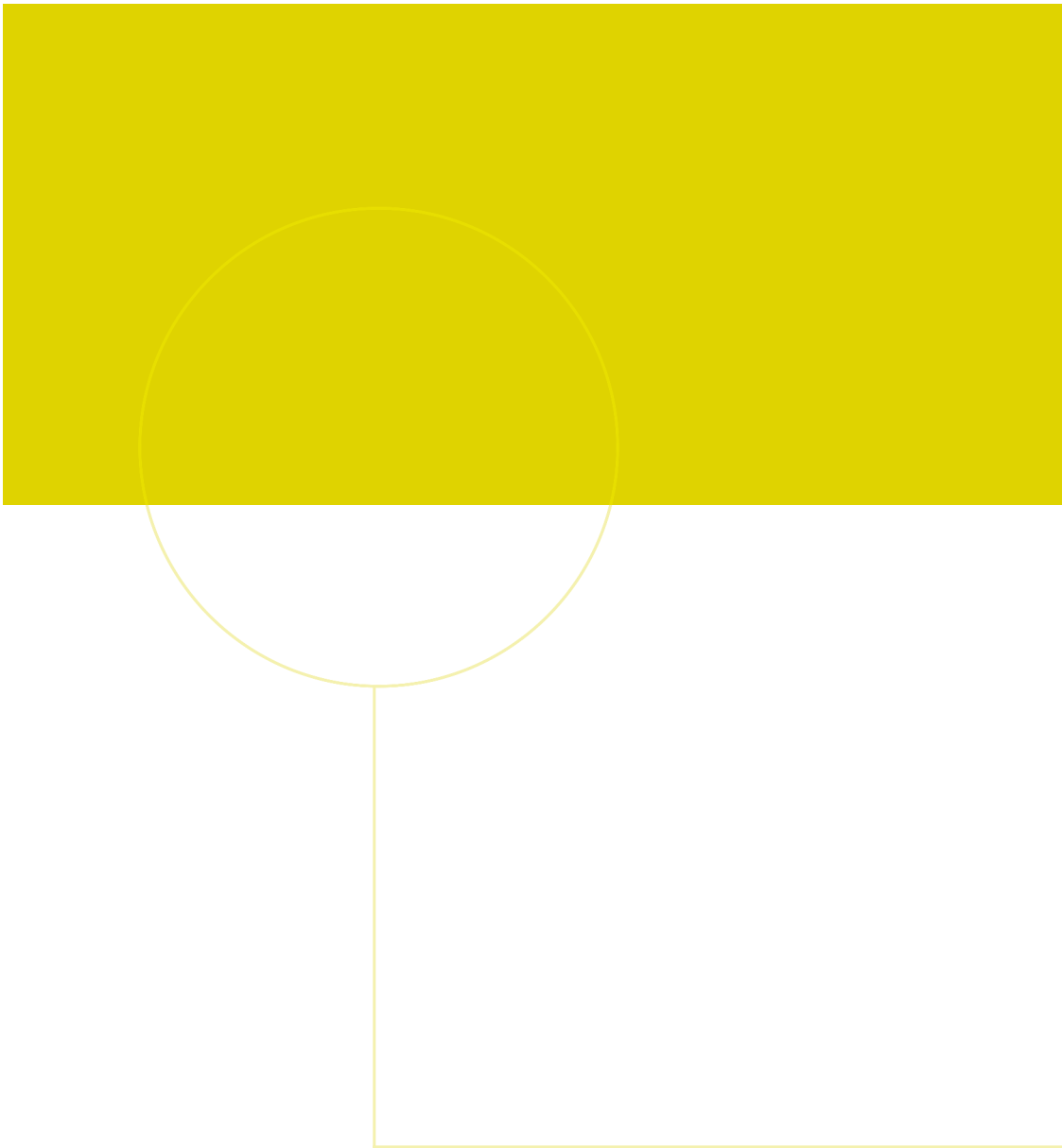
Mycophenolic acid	LASV	Cell Lines
Mycophenolic acid	LCMV	Cell Lines
Mycophenolic acid	MERS-CoV	Cell Lines
Mycophenolic acid	NoV	Cell Lines
Mycophenolic acid	RRV	Cell Lines
Mycophenolic acid	RSV	Cell Lines
Mycophenolic acid	RV	Primary Cells
Mycophenolic acid	ZIKV	Cell Lines
N-MCT	EBV	Cell Lines
N-MCT	HSV-1	Cell Lines
N-MCT	HSV-2	Phase I
N-MCT	KSHV	Cell Lines
N-MCT	VZV	Cell Lines
Nafamostat	EBOV	Cell Lines
Nafamostat	FLUAV	Cell Lines
Nafamostat	FLUBV	Cell Lines
Nafamostat	MERS-CoV	Cell Lines
Navitoclax	BUNV	Cell Lines
Navitoclax	FLUAV	Animal Model
Navitoclax	FLUBV	Cell Lines
Navitoclax	HBV	Cell Lines
Navitoclax	HEV-B	Cell Lines
Navitoclax	HIV-1	Cell Lines
Navitoclax	HSV-1	Cell Lines
Navitoclax	HSV-2	Cell Lines
Navitoclax	MERS-CoV	Cell Lines
Navitoclax	MeV	Cell Lines
Navitoclax	SINV	Cell Lines
Navitoclax	ZIKV	Cell Lines
Nelfinavir	CHIKV	Cell Lines
Nelfinavir	DENV	Cell Lines
Nelfinavir	FLUAV	Cell Lines
Nelfinavir	HAdV	Cell Lines
Nelfinavir	HCV	Cell Lines
Nelfinavir	HIV-1	Approved
Nelfinavir	HSV-1	Cell Lines
Nelfinavir	KSHV	Primary Cells
Nelfinavir	SARS-CoV	Cell Lines
Nelfinavir	SARS-CoV-2	Cell Lines
Nelfinavir	VSV	Cell Lines
Niclosamide	CHIKV	Cell Lines
Niclosamide	DENV	Animal Model
Niclosamide	EBOV	Cell Lines
Niclosamide	EBV	Cell Lines
Niclosamide	HSV-1	Cell Lines
Niclosamide	HSV-2	Cell Lines
Niclosamide	JEV	Cell Lines
Niclosamide	LASV	Cell Lines
Niclosamide	RABV	Cell Lines
Niclosamide	SARS-CoV	Cell Lines
Niclosamide	SINV	Cell Lines
Niclosamide	VACV	Cell Lines
Niclosamide	VSV	Cell Lines
Niclosamide	ZIKV	Cell Lines
Niclosamide	ZIKV	Primary Cells
Nitazoxanide	ADV	Phase III
Nitazoxanide	CHIKV	Cell Lines
Nitazoxanide	FLUAV	Phase III
Nitazoxanide	HBV	Phase II
Nitazoxanide	HCV	Phase IV
Nitazoxanide	HIV-1	Phase II
Nitazoxanide	HMPV	Cell Lines
Nitazoxanide	HRV-A	Phase III
Nitazoxanide	JEV	Animal Model
Nitazoxanide	MERS-CoV	Animal Model
Nitazoxanide	MeV	Cell Lines
Nitazoxanide	NoV	Phase III
Nitazoxanide	RSV	Cell Lines
Nitazoxanide	RuV	Cell Lines
Nitazoxanide	RV	Cell Lines
Nitazoxanide	RV	Phase III
Nitazoxanide	VACV	Cell Lines
Nitazoxanide	ZIKV	Animal Model
Novobiocin	EBV	Cell Lines
Novobiocin	HSV-1	Animal Model
Novobiocin	JEV	Cell Lines
Novobiocin	KSHV	Cell Lines
Novobiocin	VACV	Cell Lines
Novobiocin	ZIKV	Animal Model
Obatoclax	FLUAV	Cell Lines
Obatoclax	HEV-B	Cell Lines
Obatoclax	HMPV	Cell Lines
Obatoclax	HSV-2	Cell Lines
Obatoclax	JUNV	Cell Lines
Obatoclax	LASV	Cell Lines
Obatoclax	LCMV	Cell Lines
Obatoclax	RVFV	Cell Lines
Obatoclax	SINV	Cell Lines
Obatoclax	WNV	Cell Lines
Obatoclax	YFV	Cell Lines
Obatoclax	ZIKV	Cell Lines
Oritavancin	EBOV	Cell Lines
Oritavancin	HCV	Cell Lines
Oritavancin	HMPV	Cell Lines
Oritavancin	MERS-CoV	Cell Lines
Oritavancin	RVFV	Cell Lines
Oritavancin	SARS-CoV	Cell Lines
Oseltamivir	EV-A71	Primary Cells
Oseltamivir	FLUAV	Approved
Oseltamivir	FLUBV	Approved
Peginterferon alfa-2a	HBV	Approved
Peginterferon alfa-2a	HCV	Approved
Peginterferon alfa-2a	HEV	Phase I
Peginterferon alfa-2a	HPV	Phase I
Peginterferon alfa-2a	SARS-CoV	Primary Cells
Peginterferon alfa-2b	HBV	Phase IV
Peginterferon alfa-2b	HCV	Approved
Peginterferon alfa-2b	HEV	Phase I
Peginterferon alfa-2b	HPV	Phase I
Peginterferon alfa-2b	MERS-CoV	Phase II
Peginterferon alfa-2b	SARS-CoV	Primary Cells
Penciclovir	HBV	Cell Lines
Penciclovir	HSV-1	Approved
Penciclovir	HSV-2	Approved

Pentosan polysulfate	FLUAV	Cell Lines
Pentosan polysulfate	HEV-A	Cell Lines
Pentosan polysulfate	HEV-B	Cell Lines
Pentosan polysulfate	HHV-7	Cell Lines
Pentosan polysulfate	HIV-1	Cell Lines
Pentosan polysulfate	RRV	Animal Model
Pirlindole	HCV	Cell Lines
Pirlindole	HEV-A	Cell Lines
Pirlindole	HEV-B	Cell Lines
Pirlindole	HEV-D	Cell Lines
Pleconaril	HEV-D	Phase IV
Pleconaril	HEV-J	Phase IV
Pleconaril	HRV-A	Phase IV
Pleconaril	HRV-B	Phase IV
Podofilox	CMV	Cell Lines
Podofilox	FLUAV	Cell Lines
Podofilox	HPV	Approved
Podofilox	HSV-1	Cell Lines
Podofilox	MCV	Phase I
Podofilox	VSV	Cell Lines
Posaconazole	DENV	Cell Lines
Posaconazole	EBOV	Cell Lines
Posaconazole	Par-A3	Cell Lines
Posaconazole	ZIKV	Cell Lines
Promethazine	EBV	Primary Cells
Promethazine	MERS-CoV	Cell Lines
Promethazine	SARS-CoV	Cell Lines
Quinacrine	DENV	Cell Lines
Quinacrine	EBOV	Primary Cells
Quinacrine	HEV-A	Cell Lines
Quinacrine	ZIKV	Cell Lines
Quinine	DENV	Cell Lines
Quinine	FLUAV	Cell Lines
Quinine	HSV-1	Cell Lines
Racivir	HBV	Cell Lines
Racivir	HIV-1	Phase II
Raloxifene	DENV	Cell Lines
Raloxifene	EBOV	Animal Model
Raloxifene	HIV-1	Cell Lines
Raloxifene	HSV-1	Cell Lines
Raloxifene	RABV	Cell Lines
Raloxifene	SINV	Cell Lines
Raloxifene	VACV	Cell Lines
Raloxifene	VSV	Cell Lines
Raloxifene	YFV	Cell Lines
Rapamycin	BKV	Phase IV
Rapamycin	CMV	Phase IV
Rapamycin	FLUAV	Phase IV
Rapamycin	HBV	Cell Lines
Rapamycin	HCV	Phase IV
Rapamycin	HDV	Cell Lines
Rapamycin	HEV-B	Animal Model
Rapamycin	HIV-1	Phase IV
Rapamycin	KSHV	Phase II
Rapamycin	MERS-CoV	Cell Lines
Rapamycin	RV	Primary Cells
Rapamycin	RVFV	Animal Model

Regorafenib	FLUAV	Cell Lines
Regorafenib	HSV-1	Cell Lines
Regorafenib	HTV	Cell Lines
Regorafenib	SFTSV	Cell Lines
Regorafenib	VSV	Cell Lines
Remdesivir	DENV	Cell Lines
Remdesivir	EBOV	Phase III
Remdesivir	HCoV-229E	Cell Lines
Remdesivir	HCoV-OC43	Cell Lines
Remdesivir	HCV	Cell Lines
Remdesivir	HEV	Cell Lines
Remdesivir	HMPV	Cell Lines
Remdesivir	JUNV	Cell Lines
Remdesivir	LASV	Cell Lines
Remdesivir	MARV	Cell Lines
Remdesivir	MERS-CoV	Animal Model
Remdesivir	NiV	Cell Lines
Remdesivir	RSV	Cell Lines
Remdesivir	SARS-CoV	Animal Model
Remdesivir	SARS-CoV-2	Cell Lines
Remdesivir	TBEV	Cell Lines
Ribavirin	CHIKV	Cell Lines
Ribavirin	HATV	Cell Lines
Ribavirin	HCV	Approved
Ribavirin	HEV	Approved
Ribavirin	HPIV-2	Cell Lines
Ribavirin	LASV	Phase II
Ribavirin	LCMV	Cell Lines
Ribavirin	MeV	Cell Lines
Ribavirin	RABV	Cell Lines
Ribavirin	RSV	Approved
Ribavirin	RV	Primary Cells
Ribavirin	SARS-CoV-2	Cell Lines
Rilpivirine	HIV-1	Approved
Rilpivirine	ZIKV	Animal Model
Rimantadine	FLUAV	Approved
Rimantadine	PyV	Phase I
Ritonavir	EBOV	Animal Model
Ritonavir	HIV-1	Approved
Ritonavir	HIV-2	Approved
Ritonavir	MERS-CoV	Phase III
Ritonavir	RVFV	Cell Lines
Ritonavir	SARS-CoV-2	Phase II
Roscovitine	EBV	Cell Lines
Roscovitine	HIV-1	Cell Lines
Roscovitine	HSV-1	Cell Lines
Roscovitine	JCV	Cell Lines
Roscovitine	VZV	Animal Model
Rupintrivir	ECHOV-30	Cell Lines
Rupintrivir	EV-A71	Cell Lines
Rupintrivir	HRV	Primary Cells
Rupintrivir	NoV	Cell Lines
Rupintrivir	SARS-CoV-2	Cell Lines
Salinomycin	CMV	Cell Lines
Salinomycin	FLUAV	Animal Model
Salinomycin	RSV	Cell Lines
Saquinavir	FLUAV	Cell Lines

Saquinavir	HIV-1	Approved
Saquinavir	SARS-CoV-2	Cell Lines
Saquinavir	VSV	Cell Lines
Saracatinib	CMV	Phase I
Saracatinib	DENV	Cell Lines
Saracatinib	MERS-CoV	Cell Lines
Simeprevir	EV-A71	Cell Lines
Simeprevir	HCV	Approved
Simeprevir	HSV-1	Cell Lines
Simeprevir	SARS-CoV-2	Phase I
Simeprevir	ZIKV	Cell Lines
Simvastatin	CMV	Cell Lines
Simvastatin	DENV	Cell Lines
Simvastatin	FLUAV	Cell Lines
Simvastatin	HBV	Phase I
Simvastatin	HCV	Phase II
Simvastatin	HEV-C	Cell Lines
Simvastatin	ZIKV	Cell Lines
Sofosbuvir	CHIKV	Animal Model
Sofosbuvir	DENV	Cell Lines
Sofosbuvir	HAV	Cell Lines
Sofosbuvir	HCV	Approved
Sofosbuvir	HEV	Cell Lines
Sofosbuvir	SARS-CoV-2	Cell Lines
Sofosbuvir	YFV	Cell Lines
Sofosbuvir	ZIKV	Animal Model
Sorafenib	CHIKV	Cell Lines
Sorafenib	FLUAV	Cell Lines
Sorafenib	HCV	Cell Lines
Sorafenib	HEV-A	Cell Lines
Sorafenib	HSV-1	Cell Lines
Sorafenib	HTV	Cell Lines
Sorafenib	KSHV	Phase I
Sorafenib	RABV	Cell Lines
Sorafenib	SINV	Cell Lines
Sorafenib	VSV	Cell Lines
Stavudine	HAdV-5	Cell Lines
Stavudine	HIV-1	Approved
Stavudine	HSV-1	Cell Lines
Sunitinib	BKV	Cell Lines
Sunitinib	CHIKV	Cell Lines
Sunitinib	DENV	Animal Model
Sunitinib	EBOV	Phase II
Sunitinib	HCV	Cell Lines
Sunitinib	HIV-1	Cell Lines
Sunitinib	JUNV	Cell Lines
Sunitinib	RSV	Cell Lines
Sunitinib	ZIKV	Cell Lines
Suramin	CHIKV	Cell Lines
Suramin	DENV	Cell Lines
Suramin	EBOV	Cell Lines
Suramin	HCV	Cell Lines
Suramin	HDV	Cell Lines
Suramin	HEV-A	Cell Lines
Suramin	HIV-1	Cell Lines
Suramin	NoV	Cell Lines
Suramin	RVFV	Cell Lines
Suramin	ZIKV	Cell Lines
Tamoxifen	EBOV	Animal Model
Tamoxifen	HCV	Phase I
Tamoxifen	HIV-1	Phase I
Tamoxifen	HSV-1	Cell Lines
Tamoxifen	MERS-CoV	Cell Lines
Tamoxifen	SARS-CoV	Cell Lines
Taribavirin	CCHFV	Cell Lines
Taribavirin	FLUAV	Cell Lines
Taribavirin	FLUBV	Animal Model
Taribavirin	HCV	Phase II
Taribavirin	HDV	Cell Lines
Taribavirin	PICV	Animal Model
Taribavirin	PTV	Animal Model
Taribavirin	SFV	Cell Lines
Teicoplanin	EBOV	Cell Lines
Teicoplanin	FLUAV	Cell Lines
Teicoplanin	FLUBV	Cell Lines
Teicoplanin	MERS-CoV	Cell Lines
Teicoplanin	SARS-CoV	Cell Lines
Telavancin	EBOV	Cell Lines
Telavancin	MERS-CoV	Cell Lines
Telavancin	SARS-CoV	Cell Lines
Telbivudine	B19V	Primary Cells
Telbivudine	HBV	Approved
Telbivudine	HIV-1	Phase I
Tenofovir	HBV	Approved
Tenofovir	HIV-1	Approved
Tenofovir	HIV-2	Approved
Tenofovir	HSV-2	Phase III
Tenofovir alafenamide	HBV	Approved
Tenofovir alafenamide	HIV-1	Approved
Tenofovir disoproxil	HBV	Approved
Tenofovir disoproxil	HIV-1	Approved
Teriflunomide	EBOV	Cell Lines
Teriflunomide	EBV	Cell Lines
Teriflunomide	FLUAV	Cell Lines
Teriflunomide	ZIKV	Cell Lines
Thymalfasin	HBV	Approved
Thymalfasin	HCV	Approved
Thymalfasin	HIV-1	Phase I
Tilorone	CHIKV	Approved
Tilorone	CMV	Approved
Tilorone	EBOV	Approved
Tilorone	HAV	Approved
Tilorone	HBV	Approved
Tilorone	HCV	Approved
Tilorone	HSV-1	Approved
Tilorone	HSV-2	Cell Lines
Tilorone	MARV	Approved
Tilorone	MERS-CoV	Approved
Tilorone	WNV	Approved
Tipranavir	HIV-1	Approved
Tipranavir	TBEV	Cell Lines
Tipranavir	WNV	Cell Lines
Tipranavir	ZIKV	Cell Lines
Topotecan	DENV	Cell Lines

Topotecan	EBOV	Animal Model
Topotecan	FLUAV	Cell Lines
Topotecan	HCV	Cell Lines
Topotecan	HIV-1	Phase II
Topotecan	JCV	Cell Lines
Toremifene	EBOV	Cell Lines
Toremifene	MERS-CoV	Cell Lines
Toremifene	SARS-CoV	Cell Lines
Trametinib	FLUAV	Cell Lines
Trametinib	HIV-1	Cell Lines
Trametinib	MERS-CoV	Cell Lines
Trifluridine	HAdV	Cell Lines
Trifluridine	HSV-1	Approved
Trifluridine	HSV-2	Approved
Trifluridine	VACV	Animal Model
Umifenovir	EBOV	Cell Lines
Umifenovir	FLUAV	Approved
Umifenovir	FLUBV	Approved
Umifenovir	HSV-1	Cell Lines
Umifenovir	HSV-2	Animal Model
Umifenovir	LASV	Cell Lines
Umifenovir	SARS-CoV-2	Phase III
Umifenovir	TBEV	Cell Lines
Umifenovir	WNV	Cell Lines
Umifenovir	ZIKV	Cell Lines
Valacyclovir	CMV	Approved
Valacyclovir	EBV	Approved
Valacyclovir	HBV	Approved
Valacyclovir	HCV	Phase II
Valacyclovir	HSV-1	Approved
Valacyclovir	HSV-2	Approved
Valacyclovir	VZV	Approved
Valganciclovir	CMV	Approved
Valganciclovir	HAdV-5	Animal Model
Valganciclovir	HHV-8	Phase I
Verapamil	CMV	Cell Lines
Verapamil	EBOV	Animal Model
Verapamil	FLUAV	Cell Lines
Verapamil	HRV-A	Cell Lines
Vesatolimod	EV-A71	Animal Model
Vesatolimod	HBV	Phase I
Vesatolimod	HIV-1	Primary Cells
Vesatolimod	NoV	Cell Lines
Vidarabine	BKV	Phase I
Vidarabine	CBV	Phase I
Vidarabine	HAdV	Phase I
Vidarabine	HPV	Phase II
Vidarabine	HSV-1	Approved
Vidarabine	HSV-2	Approved
Vidarabine	POWV	Phase I
Vidarabine	PyV	Phase I
Vidarabine	RABV	Animal Model
Vidarabine	VARV	Animal Model
Vidarabine	VZV	Approved
Zalcitabine	HAdV-19	Animal Model
Zalcitabine	HIV-1	Approved
Zanamivir	FLUAV	Approved
Zanamivir	FLUAV	Approved
Zanamivir	FLUBV	Approved
Zanamivir	FLUBV	Approved
Zanamivir	HPIV-3	Cell Lines
Zanamivir	Par-A3	Cell Lines
Zidovudine	EBOV	Cell Lines
Zidovudine	EBV	Cell Lines
Zidovudine	HIV-1	Approved
Zidovudine	HSV-1	Cell Lines
Zidovudine	HTNV	Cell Lines



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