



## JUST THE FACTS

MORE THAN

**2.8 M**

ANTIBIOTIC-RESISTANT INFECTIONS OCCUR IN THE U.S. EACH YEAR<sup>1</sup>

MORE THAN

**35,000**

PEOPLE DIE EACH YEAR OF ANTIBIOTIC-RESISTANT INFECTIONS IN THE U.S.<sup>1</sup>

HIV/AIDS DEATH RATE DROPPED

**NEARLY 90%**

SINCE THE INTRODUCTION OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)<sup>2</sup>

**167%**

INCREASE IN WORKER PRODUCTIVITY FOR PATIENTS WITH HEPATITIS C DUE TO NEW INNOVATIVE TREATMENTS<sup>3</sup>

## MEDICINES IN DEVELOPMENT | 2020 REPORT

# INFECTIOUS DISEASES

## More Than **400** Medicines and Vaccines in Development to Tackle Infectious Diseases

Throughout history, infectious diseases have taken a devastating toll on the lives and security of people around the world. With the ongoing COVID-19 pandemic (caused by the coronavirus SARS-CoV-2) gripping the world, we are experiencing an overwhelming situation that we haven't seen since the influenza pandemic of 1918-1919, when a third of the world's population became infected with the virus and about 675,000 Americans died from the disease.<sup>4</sup>

Infectious diseases, caused when pathogens such as bacteria or viruses enter the body and multiply, haven't been a leading cause of death in the United States since the 1920s, due to improved sanitation and hygiene, the discovery of antibiotics and the advent of childhood immunization programs.<sup>5</sup> Since then, vaccines and treatments for infectious diseases have continued to be developed and proven safe and effective. Despite that progress, infectious diseases still pose a very serious threat to patients. The current COVID-19 pandemic underscores the critical role that medicines and vaccines play in fighting these pathogens and how the industry is uniquely positioned to combat public health threats.

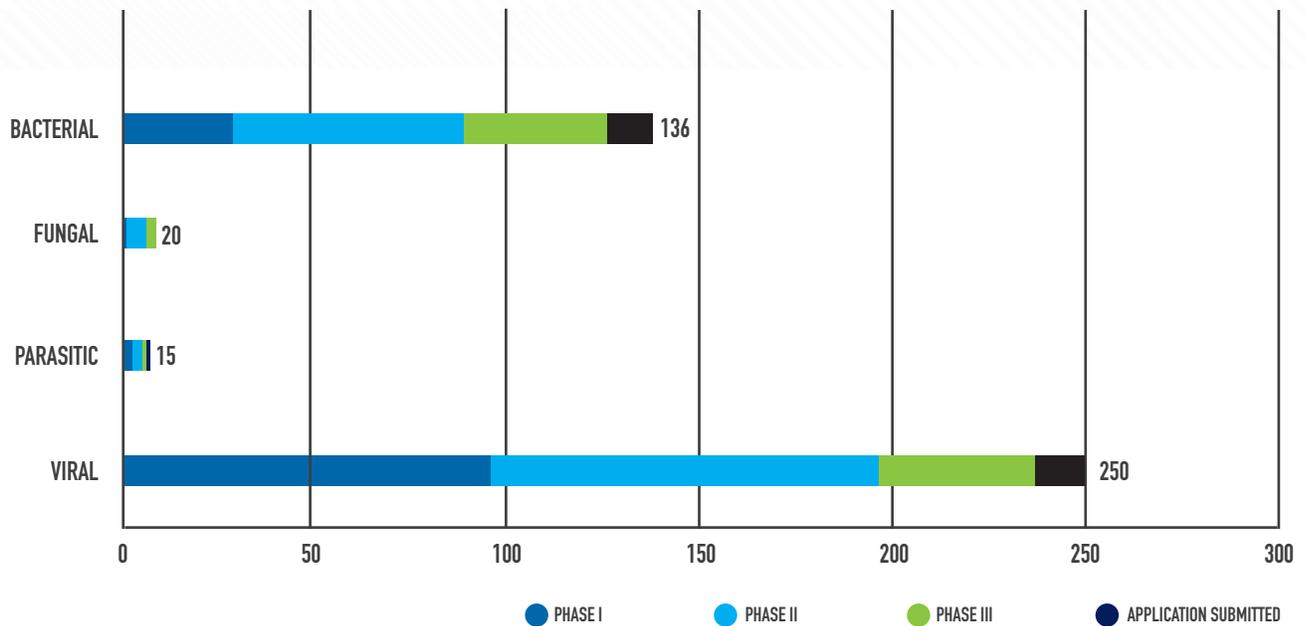
But the novel coronavirus isn't the only infectious pathogen threatening public health today; many pathogens, including bacteria such as *Pseudomonas* and *Staphylococcus aureus*, have become resistant to available treatments. And, diseases once considered defeated or substantially abated, such as tuberculosis and measles, have reemerged as growing health threats.

While vaccines can help prevent some infectious diseases, antibiotics also play an important role in public health. Effective antibiotics are needed to treat infected people and people with weakened immune systems, including to protect patients already fighting an infection from contracting a secondary bacterial infection. Antibiotics are also important for patients receiving cancer treatment or dialysis who are at a higher risk of contracting serious infectious diseases.

To try and tackle these issues, America’s biopharmaceutical research companies are developing 421 medicines and vaccines<sup>6</sup> to fight the many threats posed by infectious diseases. Each of these medicines and vaccines in development is either in clinical trials or under review by the U.S. Food and Drug Administration (FDA).

While many infectious diseases may never be fully eradicated, with expanded scientific knowledge, new technologies, and the commitment of America’s biopharmaceutical research companies, we can help meet the continuing—and ever-changing—threat from infectious diseases. cancer, and many more in development.

## Medicines and Vaccines in Development for Infectious Diseases



## Innovative Medicines and Vaccines in the Pipeline for Infectious Disease

Biopharmaceutical research companies have 421 medicines and vaccines in development to treat or prevent fungal, bacterial and viral infections that cause diseases such as COVID-19, influenza, meningitis, urinary tract infections and other infectious disease. Among the candidates in development are:

-  A broad-spectrum antiviral medicine, with in vitro activity against Ebola, Middle Eastern respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), is being studied as a treatment for the **COVID-19 infections**. The medicine blocks the RNA polymerase (an enzyme that is responsible for duplicating the virus’s RNA) of the virus and prevents its replication.
-  Two messenger RNA (mRNA)-based vaccines are in development for the prevention of **COVID-19 infections**. The mRNA-based vaccines are designed to direct the body’s cells to produce proteins (intracellular, membrane or secreted proteins) that can have a preventative benefit against the virus.
-  A benzimidazole riboside compound is being developed for the treatment of **cytomegalovirus (CMV)** infections in transplant patients. By inhibiting the CMV protein kinase, the medicine could potentially affect several critical processes in CMV replication including viral DNA synthesis, viral gene expression, encapsidation and release of mature capsids from the nucleus of infected cells. The drug demonstrated in vitro activity against strains of CMV that are resistant to current CMV therapies.

- ☀️ A long-acting injectable capsid inhibitor is being developed as an anti-retroviral (ARV) treatment for **HIV infections**. The medicine inhibits HIV-1 replication in human peripheral blood cells by inhibiting capsid protein formation (the capsid protein is the shell around the virus containing genetic material). It is being studied in both heavily treatment-experienced patients with multi-drug resistance and treatment-naïve patients living with HIV.
- ☀️ A long-acting version of an oral integrase inhibitor is in development for **HIV pre-exposure prophylaxis (PrEP)**. PrEP is the use of antiviral medicines in uninfected people who have not been exposed to the virus to prevent infection. Long-acting, injectable medicines help with patient adherence to treatment for chronic illnesses.<sup>7</sup> Integrase inhibitors block the action of integrase, a viral enzyme that inserts the viral genome into the DNA of the host cell. This is a vital step in retroviral replication and it's believed that blocking it can halt further spread of the virus.
- ☀️ An antibacterial is being developed as an oral treatment for **drug-susceptible mycobacterium tuberculosis (MTB)**. It acts by suppressing protein synthesis in MTB by selectively inhibiting the enzyme Leucyl t-ribose nucleic acid (RNA) synthetase. By inhibiting the protein synthesis, the medicine prevents the formation of the MTB cell walls.

## Developing COVID-19 Vaccines and Treatments

The biopharmaceutical industry is responding rapidly to COVID-19 and has a long track record of developing solutions to combat a range of infectious diseases. Biopharmaceutical companies bring deep scientific expertise from decades of working with similar viruses such as Ebola, MERS, SARS, influenza, HIV and hepatitis C. Over the past several decades, PhRMA members have invested billions of dollars in building the advanced manufacturing infrastructure and developing critical scientific advances that will allow us to accelerate vaccine development, identify and rapidly advance promising treatment options and quickly manufacture new vaccines and treatments for patients.

As of July 6, 2020, there are more than 1,200 clinical trials testing COVID-19 treatments and vaccines worldwide.<sup>8</sup> Sponsors are trying a variety of approaches, including 413 unique therapies in clinical trials for COVID-19 treatments and 18 unique vaccines in clinical trials.<sup>8</sup> About 270 of these clinical trials are taking place in the United States with many of the trials being conducted in multiple countries simultaneously.

## Successes in Treatment and Prevention Against Infectious Diseases

**Ebola:** The first vaccine to protect against Ebola virus disease was approved in the U.S. in 2019. A second vaccine was approved by the European Medicines Agency (EMA) in July 2020.<sup>9</sup> Both vaccines were advanced in response to the West African Ebola crisis, and both were successfully deployed to help contain the current outbreak in the Democratic Republic of the Congo (DRC). Ebola is a lethal and highly contagious hemorrhagic fever with mortality rate ranging from 40-90%.<sup>10</sup> Though Ebola risk remains low in the U.S., the virus has caused more than 30 epidemic outbreaks in Africa since 1976.<sup>10</sup>

**Hepatitis C Virus (HCV):** Recent scientific advances are transforming treatment of hepatitis C and have led to a new era of treatments. Direct-acting antiviral (DAA) agents are taken orally and target HCV at each step of the virus's lifecycle. Today, DAAs with cure rates approaching 100% are available for patients with all known genotypes of the virus and can be taken over the course of 8-12 weeks. Currently there are several DAAs

approved for use in the United States. This stands in stark contrast to previously available medicines which were injected over 48 weeks, offered cure rates of just 41% and caused severe flu-like side effects in patients just a decade ago.<sup>11</sup>

**HIV Infection:** For more than 30 years, research advances in HIV/AIDS have transformed the treatment standard for many patients. HIV/AIDS was once a fatal illness and is now a manageable, chronic disease with close to normal life expectancy for those who have access to medications.<sup>12</sup> In the United States alone, death rates have fallen nearly 90% since the introduction of highly active antiretroviral therapy (HAART), which involves the combination of three treatments from different drug classes that work to suppress the replication of the virus through different mechanisms. Additionally, studies have shown pre-exposure prophylaxis (PrEP) can reduce the risk of getting HIV from sex by about 99% when taken daily.<sup>13</sup> Among people who inject drugs, PrEP reduces the risk of getting HIV by at least 74% when taken daily.<sup>13</sup> Progress against HIV/AIDS didn't happen through one single breakthrough, but through a series of incremental steps, marked by both the introduction of new treatment and prevention options and constant learning about their optimal use and clinical value.<sup>14</sup>

**Influenza:** At its pinnacle, influenza took the lives of hundreds of thousands of people every year, with about 675,000 people dying during the 1918-1919 flu pandemic. With the advent of effective antivirals and flu vaccines, we've seen significant declines in mortality. Today, about 55,000 Americans die each year from influenza and pneumonia combined. During the 20th century, U.S. mortality from seasonal influenza dramatically declined, from 10.2 per 100,000 in the 1940s and to 0.56 per 100,000 in the 1990s.<sup>15</sup> And, in 2018, a new first-in-class antiviral was approved as a one-time, single-dose treatment that blocks influenza virus proliferation.

**River Blindness:** River blindness (onchocerciasis) is an infection caused by a parasitic worm and spread by the bite of an infected black fly. It is mainly found in rural agricultural areas in sub-Saharan Africa. Symptoms in infected people can include severe itching, skin disfigurement and eye lesions which can lead to visual impairment and permanent blindness. A disease-specific drug donation program started more than 30 years ago has seen great success with several countries in Africa making significant progress towards elimination of the disease.<sup>16</sup> The World Health Organization (WHO) has included it on its list of neglected tropical diseases targeted for elimination. And the WHO estimates that from 1974 to 2002, the program along with insecticide spraying, successfully treated 40 million people, prevented blindness in 600,000 people and ensured that 18 million children were born free from the threat of the disease and its consequences.

## Preventative Vaccines: Positive Impact to Health and Society

Advances in science and technology are driving increases in survival and improved quality of life for people around the world. Vaccines represent some of the most impactful public health advances, helping to prevent the spread of many infectious diseases and, in many parts of the world, eliminating some of the most devastating conditions. This has protected millions of children and families from preventable illness.

The prevention of disease has an enormous impact on the health of individuals and communities overall, as well as a substantial impact on the economy by reducing health care costs and avoiding lost productivity. Preventative vaccines are given to individuals but see their greatest public health benefit when entire populations are immunized. When a high concentration of vaccination is attained in a community with an effective vaccine, disease transmission can be successfully disrupted. When disease transmission is disrupted, even those who were not vaccinated, or those who did not receive immunity from the vaccine, benefit from vaccination and can be protected from the disease. This is known as **herd immunity**—where immunization coverage is sufficient enough to prevent the transmission of a disease to the susceptible population. This is especially important for the young, the elderly and those with compromised immune systems.

# Vaccination for Prevention

Hepatitis A.....	now preventable
Hepatitis B.....	now preventable
HPV and Viral Hepatitis Driven Cancer.....	now preventable
Pneumococcal Pneumonia.....	now preventable
Rubella.....	eliminated in the U.S.
Measles.....	eliminated in the U.S.
Polio.....	eliminated in the U.S.
Smallpox.....	eradicated

Footnote: Smallpox is the only disease to be eradicated from the world. Elimination of an infectious disease means the prevention of community transmission due to vaccination. It is still possible for people who contract the disease outside the US to come in and start transmission.

## Antimicrobial Resistance (AMR)

Antimicrobial resistance (AMR) occurs when microorganisms such as bacteria, viruses, fungi and parasites change in ways that make the medicines used to treat the infections they cause ineffective. According to the U.S. Centers for Disease Control and Prevention (CDC), more than 2.8 million antibiotic-resistant infections occur in the U.S. every year and more than 35,000 people die as a result.<sup>1</sup> A United Nations 2019 report on drug-resistant infections estimates that unless action is taken, AMR could take up to 10 million lives worldwide annually by 2050.<sup>17</sup>

On its 2019 antibiotic resistance threats list, the Centers for Disease Control and Prevention (CDC) estimates just eight of the pathogens on the list represented \$5.75 billion in annual direct health care costs.<sup>1</sup> The 2019 list includes five urgent threat pathogens, 11 serious threats, two new threats and three pathogens to watch. Some examples of the urgent pathogen threats from the CDC report include:

-  Multi-drug resistant *Candida auris* is an emerging pathogen that is 90% resistant to at least one antifungal treatment and 30% resistant to at least two antifungal treatments.
-  *Clostridioides difficile* (C. Diff) caused nearly 223,900 people in the U.S. to require hospital care and at least 12,800 people to die in 2017.
-  *Neisseria gonorrhoeae*, the pathogen that causes gonorrhea, has quickly developed strains with resistance to all but one class of antibiotics, and half of all infections are resistant to at least one antibiotic.

## Impact of COVID-19 on AMR

While COVID-19 is a viral disease and not directly affected by antibiotics, there is early data that up to 90% of hospitalized patients are being treated with antibiotics to help against secondary infections.<sup>18</sup> This new increased use of antibiotics could intensify antibiotic resistance even faster. Additionally, there is concern that with research pivoting to COVID-19 treatments, research into new effective antibiotics could fall further behind.

AMR presents a national security concern and is a threat to global public health. In order to manage the growing threat that AMR presents, we need a robust and diverse pipeline of treatments. Unfortunately, the current pipeline is insufficient to deal with the coming AMR threat as many biopharmaceutical companies have abandoned research into new infectious disease treatments due to a difficult R&D and marketplace environment.<sup>19</sup>

The environment for developing and marketing AMR treatments is challenging and unattractive due to several factors. While antibiotics save lives, they are only taken for a short duration, and newer antibiotics often times reserved for limited clinical situations, with both factors limiting profitability. Companies need high volume sales to recoup R&D investment costs, but too often there is limited use of novel antibiotics, with current hospital payment systems incentivizing the utilization of low-cost generics over novel antibiotics.

To ensure there is a pipeline of new and effective AMR medicines, stakeholders are advocating for policies that can stabilize the current marketplace and incentivize a sustainable pipeline of innovative AMR medicines.

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