SEPTEMBER 2020

PERSPECTIVE ON THE Rx PIPELINE

Understanding changes in the medication market and their impact on cost and care.

elixir
CRAFTED Rx SOLUTIONS

Perspective on the Rx Pipeline

Elixir continuously monitors the drug pipeline. As treatment options change, we evaluate and share our perspective on the clinical benefits, cost-effectiveness and overall impact to payers and patients. Our Perspective on the Rx Pipeline report provides ongoing actionable insights from our team of clinical experts and the steps we are taking to protect and improve plan performance.

INCLUDED IN THIS EDITION:

The Quest for a COVID-19 Vaccine:
Updates on the Vaccine Pipeline

COVID-19 VACCINE

The Quest for a COVID-19 Vaccine: Updates on the Vaccine Pipeline

PIPELINE STAGE

TIMING

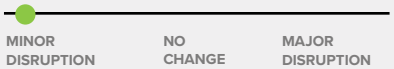
When will payers be impacted?

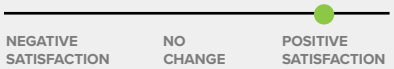
CLINICAL EFFECTIVENESS

Compared to available options, is this drug better for treatment?

MEMBER EXPERIENCE

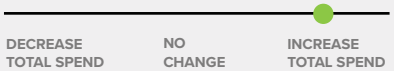
Will this positively or negatively impact members?





PAYER IMPACT

How will this influence Rx spend?



Note: It is unknown if the government will supplement coverage

Situation Summary

COVID-19 is a household term in 2020. It has impacted every aspect of daily life. As of September 8, 2020, there are 27.1 million confirmed cases of coronavirus accounting for over 889,981 deaths worldwide, with the United States accounting for 188,603 deaths and 6.2 million cases. While the number of new cases are declining across the U.S., numbers continue to rise around the world, leaving people desperate for a solution.[1] Current efforts have been guided toward prevention through enhanced precautions of self-quarantine, mask requirements and social distancing.[2] Additionally, international and national research is being conducted to develop a safe and effective vaccination to create immunity from contracting the virus. Vaccine immunization would allow the immune system to be exposed to an inactivated form of the virus, which would create antibodies to protect against infection.

Traditional Vaccine Development Process: The usual course for vaccine development is lengthy and rigorous.[3-5]

- **Research** - Two to four years detailed laboratory research on the proposed immunization.
- **Pre-Clinical Period** - Promising vaccine candidates move on to a pre-clinical period, lasting between one to two years, where laboratory animals are used to establish safety and efficacy.
- **Phase 1 Clinical Trials** - A small group of healthy participants are chosen to take part in the first clinical phase to determine the safety profile, appropriate dose and ability to produce an immune response in humans.
- **Phase 2 Clinical Trials** - Eligible vaccines move into second phase trials where they are then compared against a placebo to further assess the safety and efficacy of the vaccine in a wider population of hundreds of participants over two to three years.
- **Phase 3 Clinical Trials** - The final phase of clinical trials, prior to approval, includes thousands of participants randomized to receive the vaccine or a placebo in a blinded fashion and can take up to five years. Again, the purpose is to establish safety and effectiveness, but with a larger population, a more robust side effect profile can be identified.
- **Biologics License Application (BLA)** - After the conclusion of clinical trials, a BLA is submitted to the Food and Drug Administration (FDA) and, upon approval, the vaccine can be manufactured on a mass scale.

COVID-19 VACCINE

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COVID-19 Vaccine Development Process: In the event of a pandemic or disease outbreak such as this, the normal process for vaccine development is modified. Although all the same steps are taken throughout development, the timeline is reduced significantly.

Research

At the start of the pandemic, researchers began trying to decipher the SARS-COV-2 genome (the genome that produces COVID-19) in order to develop a vaccine. Researchers were also able to use data that was previously collected from the SARS outbreak in the early 2000s to apply to developing a COVID-19 vaccine.

Pre-Clinical Period

Limited research time is followed by shortened pre-clinical trials.

Combined Multi-Phase Clinical Trials

Clinical trial phases are often combined to further speed up the process.[6,7] For example, phase 1/2 trials can measure safety, efficacy and appropriate dose in hundreds of patients over just a few months. Another consideration is the number of people that are available to participate in clinical trials during this global pandemic.

Manufacturing

Additionally, mass manufacturing starts early, prior to formal approval. This introduces a significant financial risk to the companies developing the vaccines, as well as their investors.[6] Because of the financial uncertainties involved with manufacturing a large amount of a vaccine that is not yet approved, a recent government program known as Operation Warp Speed (OWS) has been developed. OWS provides funding to vaccine developers to encourage rapid manufacturing of a safe and effective COVID-19 vaccine. The goal of OWS is to deliver 300 million doses of safe, effective vaccines for COVID-19 by January 2021.[8] Some researchers believe it is optimistic to think that Americans will have access to vaccines as early as January 2021.

Safety Concerns: With such a short development timeline, concerns have been raised for the safety of potential vaccines. It is important to know that the FDA still requires vaccines to meet quality standards in the midst of a pandemic. A vaccine will not be approved until complete safety and efficacy data are available.[9] Based on the FDA's guidance, vaccines would have to have a greater than 50% infection benefit, meaning approved vaccines would need to reduce the risk of COVID-19 by 50%. More data than antibody levels alone is needed to determine the infection benefit since researchers do not know what level of antibodies prevent infection.

As of September 8, 2020, nine drugmakers had their chief executives sign a pledge promising not to file for regulatory approval or authorization of their experiemental COVID-19 vaccines until the vaccinations have shown to work safely through late-stage clinical testing.

Additionally, vaccines, like any drug, have post-marketing follow-up to monitor for potential long-term side effects through the FDA-driven Vaccine Adverse Event Reporting System (VAERS). Through VAERS, anyone with a safety concern following the administration of a vaccine can submit a report for documentation and review.[10]

Summary of Top COVID-19 Vaccine Candidates[11]: As of early September, the World Health Organization (WHO) accounts for 165 COVID-19 vaccines being developed worldwide, with 34 entering human trials. Multiple vaccine mechanisms are in the pipeline to determine if one vaccine mechanism is more successful with infection reduction than others.

Internationally, two vaccines have been approved for use in their respective countries. In China, CoronaVac by Sinovac was given emergency approval for limited use in July. Russia moved Gamaleya Research Institute's product, Gam-Covid-Vac (Sputnik-V), into phase 3 trials two weeks after the vaccine received a Russian conditional registration certificate, which depends on positive results from the phase 3 trials. Note that these drugs are still being studied for approval and use in the United States.

With a number of manufacturers in the U.S. racing to be the first safe and effective vaccine to market, the FDA is planning an advisory panel meeting on October 22, 2020, to discuss COVID-19 vaccine development. At that time, large-scale clinical trials of the leading candidates from Moderna, Pfizer and AstraZeneca will be well into phase 3 trials. The FDA will make approval decisions separately from the advisory committee, but the advisory committee was formed to support transparency for vaccine development in the U.S.[12]

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Phase 3 Vaccine Candidates[11]

Pipeline Name Manufacturer National Clinical Trial (NCT)	Vaccine Mechanism*	Status	Study Population	Methods	Primary Outcomes	Estimated Study Completion
mRNA-1273 **Moderna** **NCT 04470427**	Genetic	Recruiting	30,000 healthy or at-risk adults	• Randomized, parallel assignment, blinded, placebo-controlled trial • **Intervention**: 2 doses intramuscular (IM) injection of 100 mcg vaccine on days 1 and 29 • **Comparator**: 2 IM normal saline (NS) injections	• Number of patients with first occurrence of COVID-19 beginning 2 weeks after second dose up to 2 years after second dose • Number of patients with adverse events leading to withdrawal up to 2 years after second dose • Number of patients with local and systemic adverse reactions up to 7 days after the first and second dose • Number of patients with adverse events up to 28 days after each dose	October 27, 2022
AZD1222 **AstraZenica/ Oxford** **NCT 04516746**	Viral vector	Not yet recruiting	30,000 stable, at-risk adults	• Randomized, parallel assignment, double blind, placebo-controlled trial, with 2:1 randomization • **Intervention**: 2 IM doses 4 weeks apart • **Comparator**: 2 IM doses of placebo (NS) 4 weeks apart	• Efficacy of 2 IM doses of vaccine compared to placebo to prevent COVID-19 measured ≥15 days after second dose for 1 year • Safety and tolerability of vaccine compared to placebo from day 1 through day 730, and 28 days after each dose	October 5, 2022
BNT162b2 **BioNTech/ Pfizer** **NCT 04368728**	Genetic	Recruiting	29,481 healthy adults	• Phase 1/2/3 randomized, placebo-controlled, single-blind study • Dose-finding, vaccine candidate-selection and efficacy study • **Intervention**: 2 multi-arm mid-doses, separated by 21 days • **Comparator**: 2 placebo doses, separated by 21 days	• Percentage of patients reporting adverse events from first dose through 1 month after last dose • Percentage of serious event reports from first dose to 6 months after last dose • Confirmed COVID-19 cases without evidence of previous infection from 7 days after last dose up to 2 years after last dose • Confirmed COVID-19 cases with and without evidence of previous infection from 7 days after last dose up to 2 years after last dose	November 11, 2022

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Phase 3 Vaccine Candidates[11] *Continued*

Pipeline Name Manufacturer National Clinical Trial (NCT)	Vaccine Mechanism*	Status	Study Population	Methods	Primary Outcomes	Estimated Study Completion
Ad5-nCoV CanSino/ Beijing NCT 04526990	Viral vector	Not yet recruiting	40,000 healthy adults	• Randomized, parallel assignment, double-blind, placebo-controlled trial, with 1:1 randomization • **Intervention**: Single IM injection • **Comparator**: Single IM injection of placebo	• Incidence of COVID-19 cases from day 28 to 12 months after vaccination • Incidence of severe adverse events within 12 months of vaccination	January 30, 2022
Gam-COVID-Vac Gamaleya NCT 04530396	Viral vector	Not yet recruiting	40,000 healthy adults	• Randomized, double-blind, placebo-controlled trial, with 3:1 randomization • **Intervention**: 2 IM doses given on days 1 and 21 • **Comparator**: 2 IM doses of placebo given on days 1 and 21	• Percentage of patients with COVID-19 developing within 6 months after first dose	May 1, 2021
CoronaVac Sinovac NCT 04456595	Inactivated	Recruiting	8,870 healthy adult healthcare professionals	• Randomized, double-blind, placebo-controlled trial • **Intervention**: 2 IM doses separated by 2 weeks • **Comparator**: 2 IM doses of placebo separated by 2 weeks	• Incidence of COVID-19 cases 2 weeks after complete immunization up to 1 year after first dose • Adverse events up to 7 days after each dose	October 2021

**Genetic Vaccines: Vaccines that use one or more of coronavirus' own gene to provoke immune response. Viral Vector Vaccines: Vaccines that use a virus to deliver coronavirus genes into cells. The cells make viral proteins, provoking an immune response, but the virus cannot replicate.*

Note: If studies see adequate results, they can move forward in the approval process before the study is complete.

Vaccine Dissemination: Vaccine campaigns are still being developed to ensure widespread dissemination of a vaccine, once approved, and adequate supply. Draft guidance was released by the National Academies Sciences, Engineering and Medicine recommending a four-phase approach for equitable allocation. The first phase, or "jumpstart" phase, would target frontline health workers, first responders and people at serious risk of infection for vaccination. The panel has also advised that officials should ensure vaccines are available to everyone, no matter their social and economic resources, employment, immigration or insurance status.[13]

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PAYER ACTION PLAN

- **Continue Social Distancing**
  Payers and their members should continue to follow current prevention guidance of social distancing, wearing masks and self-quarantine.
- **Influenza Vaccination**
  Members should be encouraged to get an influenza vaccination as an additional defense against illness.

Impact to the Pharmacy Care Experience

Pipeline Monitoring and Pharmacy & Therapeutics Review: Elixir's Pharmacy & Therapeutics (P&T) committee continues to monitor the drug pipeline and FDA approvals. The P&T committee will review the safety and efficacy of a new vaccine once FDA approval is granted. After review, more information will be provided about accessibility and coverage.

In the meantime, we are entering flu season. An additional defense against illness is getting an influenza vaccine. Since the COVID-19 vaccine will most likely not be available to the general public until 2021, there should be no concern of overlap of vaccination for influenza and COVID-19. For more information about flu vaccines and the importance of getting vaccinated, click here.

Sources

[1] Covid19.who.int. 2020. WHO Coronavirus Disease (COVID-19) Dashboard. [online] Available at: <https://covid19.who.int/> [Accessed 26 August 2020].

[2] Centers for Disease Control and Prevention. 2020. Coronavirus Disease 2019 (COVID-19) – Prevention & Treatment. [online] Available at: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html> [Accessed 26 August 2020].

[3] Historyofvaccines.org. 2018. Vaccine Development, Testing, And Regulation | History Of Vaccines. [online] Available at: <https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation> [Accessed 26 August 2020].

[4] Ifpma.org. 2020. [online] Available at: <https://www.ifpma.org/wp-content/uploads/2019/07/IFPMA-ComplexJourney-2019_FINAL.pdf> [Accessed 26 August 2020].

[5] Cdc.gov. 2014. Vaccine Testing And Approval Process | CDC. [online] Available at: <https://www.cdc.gov/vaccines/basics/test-approve.html> [Accessed 26 August 2020].

[6] Lurie, N., Saville, M., Hatchett, R. and Halton, J., 2020. Developing Covid-19 Vaccines at Pandemic Speed. New England Journal of Medicine, 382(21), pp.1969-1973.

[7] Modernatx.com. 2020. Moderna's Work On A COVID-19 Vaccine Candidate | Moderna, Inc.. [online] Available at: <https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19> [Accessed 26 August 2020].

[8] HHS.gov. 2020. Fact Sheet: Explaining Operation Warp Speed. [online] Available at: <https://www.hhs.gov/coronavirus/explaining-operation-warp-speed/index.html> [Accessed 26 August 2020].

[9] U.S. Food and Drug Administration. 2020. Development And Licensure Of Vaccines To Prevent COVID-19. [online] Available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19> [Accessed 27 August 2020].

[10] U.S. Food and Drug Administration. 2020. Vaccine Adverse Events. [online] Available at: <https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/vaccine-adverse-events#:~:text=The%20Vaccine%20Adverse%20Event%20Reporting,adverse%20events%20associated%20with%20vaccines.> [Accessed 27 August 2020].

[11] Who.int. 2020. Draft landscape of COVID-19 candidate vaccines. [online] Available at: <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines> [Accessed 8 September 2020].

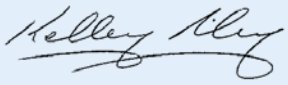
[12] U.S. Food and Drug Administration. 2020. Coronavirus (COVID-19) Update: FDA Announces Advisory Committee Meeting to Discuss COVID-19 Vaccines. [online] Available at: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-announces-advisory-committee-meeting-discuss-covid-19-vaccines> [Accessed 8 September 2020].

[13] Nationalacademies.org. 2020. Draft Frameworks for Equitable Allocation of a COVID-19 Vaccine. [online] Available at: <https://www.nationalacademies.org/news/2020/09/national-academies-release-draft-framework-for-equitable-allocation-of-a-covid-19-vaccine-seek-public-comment> [Accessed 8 September 2020].

Our Clinical Steering Committee

The Elixir Clinical Steering Committee brings together leaders from across our national pharmacy care company to monitor the drug landscape, provide recommendations on how to address changes, and to ensure our clients and patients are prepared—in advance.

With any new development, we partner with our Pharmacy & Therapeutics (P&T) committee and consult with our best-in-class specialty pharmacy, to provide a balanced perspective on the clinical effectiveness of all available options, the cost impact to our plan sponsors and patients, and the impact on the overall patient experience.



Kel Riley, MD
Chief Medical Officer

More ways to improve member and plan outcomes

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