COVID-19 Vaccine Research and Development Landscape: Supplementary Download

Developed by L.E.K.'s Global Healthcare Insights Center (HIC)

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Contents of these materials:

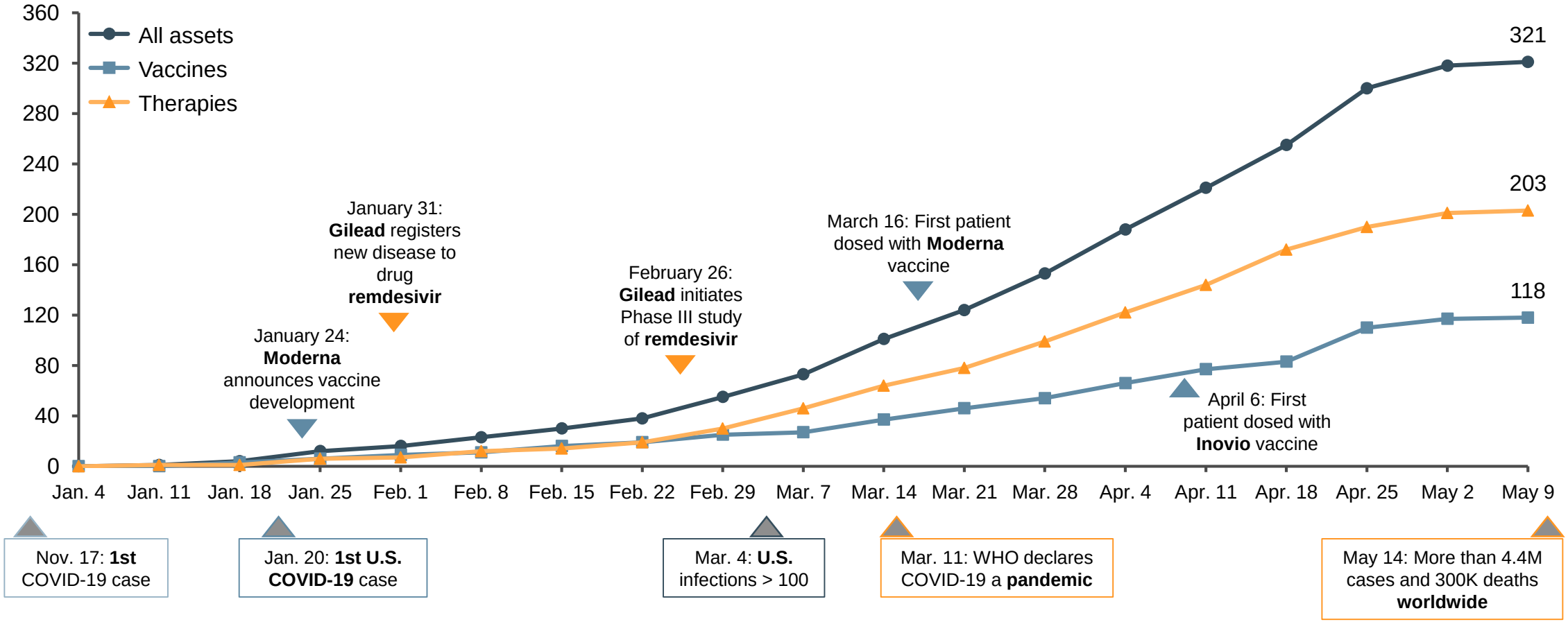
- COVID-19's impact is first and foremost a global humanitarian crisis that has thrown us into uncharted territory. We at L.E.K. Consulting extend our heartfelt sympathies to all who are affected by this crisis around the world

- These materials provide additional asset-by-asset information on the vaccine candidates in development for COVID-19 as a supplement to the *Executive Insights* published on our webpage; the pipeline is continually evolving as new trends and data emerge

- The research and development (R&D) pipeline is evolving, with new assets in development and both scientific and anecdotal data being refreshed on a daily basis; hence, certain perspectives herein may be out of date at the time of publishing

There are more than 300 individual assets in development for COVID-19 worldwide, demonstrating the wide-ranging manner in which the biopharma industry has mobilized its response

Worldwide timeline of COVID-19 asset development start*
Number of assets (2020)



*Denotes the date that a new drug was added or new license reported on Pharmaprojects; press release dates were used for select assets not in Pharmaprojects
Sources: Pharmaprojects pull as of 5/12/2020; company press releases; L.E.K. research and analysis

Case study: CanSino Biologics' Ad5-nCoV vaccine

In-clinic:
Phase II

R&D commencement: January 2020
Humans dosed: 500 (expected Phase II)
Funding disclosed: N/A
Vaccine type: Nonreplicating vector

Asset overview

- Ad5-nCov is a coronavirus vaccine developed by CanSinoBIO in partnership with the Beijing Institute of Technology and the Academy of Military Medical Sciences, a part of the Chinese military
- The vaccine is a nonreplicating adenoviral vector encoding the SARS-CoV-2 spike protein, which triggers immune response and generation of antibodies

Development timeline

- CanSinoBIO initiated a Phase I clinical trial in March 2020, with an expected completion date of December 2020
- CanSinoBIO began Phase II trials for its vaccine in mid-April 2020, with an expected completion date of January 2021

Reasons for optimism

- CanSinoBIO has produced one approved vaccine for the Ebola virus using the same platform, which was the first Ebola vaccine approved worldwide (2017, not FDA-approved), and has 16 additional vaccine candidates in its pipeline
- With Phase II trials already initiated, Ad5-nCoV is considered to be among the most advanced candidates of those currently in development

Sources: Pharmaprojects; BioSpace; BioWorld; L.E.K. research and analysis

Case study: The University of Oxford's ChAdOx1-nCov19 vaccine

UNIVERSITY OF OXFORD

In-clinic:
Phase II

R&D commencement: January 2020
Humans dosed: 6,100 (expected)
Funding disclosed: ~$25M
Vaccine type: Nonreplicating vector

Asset overview

- ChAdOx1-nCov19 is a coronavirus vaccine developed by the University of Oxford, leveraging a chimpanzee adenovirus from Vaccitech
- The adenovirus vector carries the DNA that produces the coronavirus spike protein in the host, triggering the production of antibodies
- The U.K. government has pledged funding to help support the University of Oxford's coronavirus vaccine program

Development timeline

- The University of Oxford is combining Phase I and Phase II clinical testing into a combined trial with numerous endpoints in an effort to aggressively pursue approval
- The University of Oxford is planning to combine Phase II and Phase III testing with a 5,000-person trial expected to begin in May 2020
- In late April, the University of Oxford announced a partnership with AstraZeneca to manufacture and distribute up to 100M doses of the vaccine by the end of 2020

Reasons for optimism

- AstraZeneca's partnership with the University of Oxford is a promising endorsement of the clinical viability and manufacturing scalability of the vaccine, while the group has previously worked on developing a MERS vaccine using the same adenovirus platform with favorable Phase I efficacy and safety profile
- Six rhesus macaques — among the closest to human relatives — were given single doses of the University of Oxford's vaccine and 28 days after exposure had not contracted COVID-19

Sources: *Financial Times*; Pharmaprojects; University of Oxford; *The New York Times*; L.E.K. research and analysis

Case study: Sinovac's PiCoVacc COVID-19 vaccine

SINOVAC

In-clinic:
Phase II

R&D commencement: January 2020
Humans dosed: 744 (expected Phase II)
Funding disclosed: N/A
Vaccine type: Inactivated vaccine

Asset overview

- PiCoVacc is a COVID-19 vaccine candidate based on a chemically inactivated formulation of the SARS-CoV-2 virus developed by Sinovac
- PiCoVacc uses a proven formulation that induces a SARS-CoV-2-specific neutralizing antibody response, conferring immunity
- Sinovac has partnered with Dynavax to use their CPG 1018 adjuvant, which boosts the immune response to inactivated vaccines (e.g., HEPLISAV-B)

Development timeline

- Sinovac announced the beginning of a combined Phase I/Phase II clinical trial on April 20, 2020
- Sinovac recently expanded its manufacturing capabilities by acquiring space and funding; over 70K square meters of land were acquired in addition to funding from the Bank of Beijing to prepare for scaled production

Reasons for optimism

- The antibodies generated by PiCoVacc appear to be effective against multiple known mutations of the virus, and have shown promise in trials on macaques
- No evidence of antibody-dependent enhancement, an occasional side effect in which some antibodies generated by a vaccine can be beneficial to the virus

Sources: *FiercePharma*; Pharmaprojects; Reuters; company websites; L.E.K. research and analysis

Case study: BNT162, BioNTech and Pfizer's vaccine collaboration

In clinic:
Phase II

R&D commencement: March 17, 2020
Humans dosed: 200 (expected)
Funding disclosed: $185M
Vaccine type: RNA

Asset overview

- Pfizer Inc. and BioNTech announced a collaboration to co-develop and distribute (outside of China) a potential mRNA-based coronavirus vaccine; Pfizer will pay BioNTech up to $748M to develop the drug
- The partnership aims to expedite the development of BioNTech's COVID-19 mRNA vaccine program, BNT162
- The collaboration builds on an existing relationship that began in 2018 to develop mRNA-based vaccines for influenza

Development timeline

- On April 29, BioNTech and Pfizer announced that the first cohort for their Phase I/Phase II clinical trial had been dosed with BNT162
- BioNTech and Pfizer will also conduct trials in the U.S. upon receiving regulatory approval (expected shortly, as of April 2020)
- The two companies aim to test thousands of patients by September 2020, and expect to be able to produce millions of doses by the end of 2020 and hundreds of millions in 2021

Reasons for optimism

- BioNTech's proprietary mRNA vaccine platforms combined with Pfizer's deep experience in vaccine R&D, regulatory capabilities and global presence create an opportunity to combine BioNTech's agile research team with Pfizer's scaled-up manufacturing and distribution operations

Sources: Pharmaprojects; *Pharmatimes*; Biopharmadive; company websites; L.E.K. research and analysis

Case study: Sinopharm/Wuhan Institute of Virology's inactivated vaccine candidate

SINOPHARM

中國科學院武漢病毒研究所
WUHAN INSTITUTE OF VIROLOGY, CAS

In-clinic:
Phase II

R&D commencement: Q1 2020
Humans dosed: 96 (expected Phase II)
Funding disclosed: $141M
Vaccine type: Inactivated vaccine

Asset overview

- The COVID-19 vaccine candidate developed by Sinopharm/Wuhan Institute of Virology is based on an inactivated formulation of the SARS-CoV-2 virus
- Chinese state-owned pharmaceutical group Sinopharm has partnered with the Wuhan Institute of Virology to co-develop their first inactivated vaccine, which induces a SARS-CoV-2-specific neutralizing antibody response

Development timeline

- First and second phases of the trial for the vaccine candidate were launched in April 2020, with trial participants from the first phase still under observation
- Chairman of Sinopharm, Liu Jingzhen, stated that a fund of 1B yuan (~$141M) has been set up to support vaccine R&D efforts
- Sinopharm intends to conduct the third phase of the trial and expects that the safety and efficacy study will take one year to complete all three phases

Reasons for optimism

- Phase I of trials for the vaccine candidate has demonstrated a strong safety profile so far
- Sinopharm's inactivated vaccine is the third COVID-19 vaccine candidate to be approved in China; once successfully synthesized, inactivated vaccines can be produced on a large scale while other types of vaccines developed using new technologies are limited due to a lack of production capacity

Sources: Pharmaprojects; *China Daily*; company websites; L.E.K. research and analysis

Case study: Sinopharm/Beijing Biological Products' inactivated vaccine candidate

SINOPHARM

北京天坛生物制品股份有限公司
Beijing Tiantan Biological Products Co., Ltd.

In-clinic:
Phase II

R&D commencement: April 2020
Humans dosed: N/A
Funding disclosed: N/A
Vaccine type: Inactivated vaccine

Asset overview

- The COVID-19 vaccine candidate is based on an inactivated formulation of the SARS-CoV-2 virus (specifically using Vero cells)
- Chinese state-owned pharmaceutical group Sinopharm has partnered with Beijing Tiantan Biological Products to co-develop this inactivated vaccine (in addition to the vaccine developed in partnership with Wuhan Institute)

Development timeline

- There is little information on the Sinopharm/Beijing Tiantan vaccine partnership; according to the Chinese Clinical Trial Registry, the study registration was filed at the end of April
- However, Sinopharm has been actively working on other COVID-19 vaccines that can potentially be leveraged for this project

Reasons for optimism

- Sinopharm already has two potential vaccines in the pipeline through partnerships with other institutes in China

Sources: Chinese Clinical Trial Registry; *The New York Times*; L.E.K. research and analysis

Case study: Inovio's INO-4800 vaccine

inovio

In-clinic: Phase I

R&D commencement: January 2020
Humans dosed: 40 (expected)
Funding disclosed: $14M
Vaccine type: DNA

Asset overview

- Inovio scientists reportedly designed the INO-4800 vaccine hours after the Chinese government released data about the coronavirus strain
- A plasmid is injected into a patient such that the patient's cells produce a desired, targeted antibody to fight off a specific infection; this work is based on a previous candidate vaccine for MERS that showed promising results after a Phase I study
- The asset has attracted $5M in funding from the Bill and Melinda Gates Foundation and $9M from the Coalition for Epidemic Preparedness Innovations (CEPI)

Development timeline

- Since January, Inovio has rapidly scaled development and production of its INO-4800 vaccine in order to support Phases I and II trials, initiating its first human dose on April 6
- Inovio completed enrollment of 40 healthy volunteers to its Phase I U.S. trial of INO-4800, with results expected in June 2020
- Phase I of Inovio's clinical trial plans to include 40 healthy adult volunteers, with results expected in the fall; a quick turnaround to initiate further trials is expected

Reasons for optimism

- The speed of Inovio's candidate vaccine development, backing by large players including the U.S. Department of Defense and CEPI, and its unique mechanism of action make INO-4800 a promising candidate
- Inovio is the only company with a Phase II vaccine for a related coronavirus that causes MERS

Sources: Pharmaprojects; *Science* magazine; company websites; L.E.K. research and analysis

Case study: Moderna's mRNA-1273 vaccine

moderna™
messenger therapeutics

In-clinic:
Phase I

R&D commencement: January 13, 2020
Humans dosed: 45 (expected)
Funding disclosed: $483 million
Vaccine type: RNA

Asset overview

- mRNA-1273 is an messenger RNA (mRNA) vaccine coding for a stabilized form of the SARS-CoV-2 spike protein, developed by Moderna and the U.S. National Institutes of Health (NIH); the sequence was finalized on January 13
- The vaccine, mRNA-1273, is built on Moderna's mRNA platform and encodes COVID-19's spike protein to elicit an immune response
- Funding for this batch of the mRNA vaccine was provided by CEPI

Development timeline

- The first clinical batch of vials, including fill-finish form, was completed on February 7, just 25 days after the sequence was finalized; FDA's review of the IND application was completed on March 4
- The first participant in Phase I was dosed on March 16; expected enrollment is 45 healthy adult volunteers aged 18 to 55 years over approximately six weeks
- Moderna expects the vaccine to be available for emergency use in fall 2020, though a commercially available vaccine is not likely until 2021
- Received fast-track designation from FDA on May 12

Reasons for optimism

- WHO and several other organizations have identified Moderna's mRNA-1273 vaccine as a frontrunner due to the speed of its development and potential of the mRNA platform
- The U.S. has allocated up to $483M in funding via the Biomedical Advanced Research Development Authority (BARDA) to accelerate and support the development of the vaccine
- Early data from Phase I trials may indicate that the vaccine generates an immune response, though the data set released was very limited (N=8)

Sources: Pharmaprojects; CNBS; *Fierce Biotech*; L.E.K. research and analysis

Case study: Novavax's NVX-CoV2373 vaccine candidate

NOVAVAX
Creating Tomorrow's Vaccines Today

In-clinic:
Phase I

R&D commencement: April 2020
Humans dosed: ~130 (expected Phase I)
Funding disclosed: $388M
Vaccine type: Protein subunit

Asset overview

- NVX-CoV2373 is a vaccine candidate based on a prefusion protein developed using Novavax's proprietary nanoparticle technology
- Novavax will incorporate its proprietary adjuvant, Matrix-M, with NVX-CoV2373 to enhance immune responses and activate neutralizing antibodies
- Received $388M in funding via CEPI to support clinical development efforts

Development timeline

- Novavax announced plans to begin Phase I clinical trials in mid-May with preliminary immunogenicity and safety results by July 2020
- In March 2020, Novavax secured initial funding of $4M from CEPI to support vaccine development efforts
- Novavax also entered into an agreement with Emergent BioSolutions in March to receive GMP vaccine product for use in clinical trials

Reasons for optimism

- NVX-CoV2373 has demonstrated high immunogenicity in spike protein-specific antibodies, which block binding of the spike protein to the receptor and wild-type virus-neutralizing antibodies
- The candidate's positive early results and preliminary CEPI funding has enabled Novavax to initiate a Phase I trial earlier than originally scheduled

Sources: *FiercePharma*; Pharmaprojects; Clinical Trials Arena; company website; L.E.K. research and analysis

Case study: Johnson & Johnson's Ad26 vector vaccine

Janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

Preclinical

R&D commencement: January 2020
Humans dosed: N/A
Funding disclosed: $1B
Vaccine type: Non-replicating vector

Asset overview

- Janssen initiated research on several vaccine candidates in January 2020, identifying a lead candidate for further development on March 30: Ad26 SARS-CoV-2, an engineered version of the adenovirus 26 vector to prevent virus replication
- J&J partnered with BARDA to devote a combined $912M to coronavirus vaccine R&D and clinical testing
- The vaccine uses Janssen's AdVac and PER.C6 technologies employed in its investigational Ebola vaccine

Development timeline

- J&J expects to initiate human clinical studies of its lead vaccine candidate by September 2020; the first batch of vaccines for emergency use is anticipated to be available by early 2021
- The company currently has a manufacturing capacity of ~300M vaccines annually, and has committed to scale this up to ~1B doses annually in 2021 through the addition of manufacturing plants

Reasons for optimism

- Scientific optimism that adenovirus 26 may neutralize the ability of the virus to infect cells, coupled with an accelerated development timeline and substantial public and private funding, will provide tailwinds for AD26
- J&J has preexisting robust testing resources and infrastructure that can facilitate a quick turnaround between Phases I, II and III clinical testing

Sources: Pharmaprojects; *Science* magazine; company websites; L.E.K. research and analysis

Case study: COVID-19 S-Trimer vaccine by Clover Biopharmaceuticals, GSK and Dynavax

三叶草生物制药 Clover Biopharmaceuticals | gsk | DYNAVAX

Preclinical 

R&D commencement: January 28, 2020
Humans dosed: N/A
Funding disclosed: N/A
Vaccine type: Protein subunit

Asset overview

- COVID-19 S-Trimer is a novel protein-based coronavirus vaccine candidate
- The vaccine candidate is based on Clover Biopharmaceuticals' proprietary Trimer-Tag technology, which allows the production of recombinant 2019-nCOV S protein that leads to prophylactic functions in the human body
- GSK and Dynavax agreed on collaborations to evaluate the vaccine candidate with their vaccine adjuvant systems

Development timeline

- After initiating R&D on January 28, Clover successfully produced a vaccine candidate on February 10 via a mammalian cell expression system and validated it using serum antibodies from fully recovered COVID-19 patients
- On February 28, GSK announced its collaboration with Clover by providing its pandemic adjuvant system for evaluation of the vaccine candidate; on March 24, Dynavax announced its agreement to allow Clover to use its CpG1018 vaccine adjuvant
- On April 28, Linear Clinical was awarded the clinical trials, and the clinical research firm expects to begin enrollment in the next two months

Reasons for optimism

- Clover owns the novel recombinant protein technology that has been under testing in clinical trials for other indications; it is now in collaboration with GSK, an experienced vaccine developer, and Dynavax to facilitate its development
- Clover is among the first responders to develop a vaccine for COVID-19; it had early access to patient samples during the original pandemic in China, which has provided a competitive advantage

Sources: Pharmaprojects; *FiercePharma*; GSK website; Clover website; MarketWatch; L.E.K. research and analysis

Case study: GSK and Sanofi's vaccine collaboration

Preclinical

R&D commencement: April 16, 2020
Humans dosed: N/A
Funding disclosed: N/A
Vaccine type: Protein subunit

Asset overview

- Sanofi will contribute its S-protein COVID-19 antigen, which is based on recombinant DNA technology, while GSK will contribute its proven pandemic adjuvant technology, which is designed to boost the immune response to a vaccine
- The project is being supported through funding and collaboration with BARDA

Development timeline

- R&D was initiated in early April 2020, with initial human trials expected to begin in the second half of 2020
- If human trials prove successful, the vaccine is expected to complete development required for regulatory approval by the second half of 2021
- The companies estimate production of up to 600M doses of its coronavirus vaccine next year, if the outlined timeline is met

Reasons for optimism

- Asset is the product of an unprecedented collaboration between two vaccine giants with proven technology, and further support from the U.S. government, demonstrating substantive stakeholder support
- Backing by pharmaceutical companies with reserves of capital and significant production capabilities is particularly promising for the subsequent challenge in worldwide-scale production occurring in 2021

Sources: Pharmaprojects; *Pharmatimes*; Biopharmadive; company websites; L.E.K. research and analysis

Case study: Imperial College's RNA vaccine candidate

Imperial College London

Preclinical

R&D commencement: February 2020
Humans dosed: N/A
Funding disclosed: $28M
Vaccine type: RNA

Asset overview

- Imperial College is developing a self-amplifying RNA vaccine, which works by injecting new genetic code into a muscle and then produces a protein found on the surface of the coronavirus and effectively triggers an immune response

Development timeline

- The lead for the research team developing the vaccine, Professor Robin Shattock, stated it could become available in 2021
- Human clinical trials are expected to begin in June 2020
- On April 27, Imperial College announced a collaboration with TriLink Biotechnologies to manufacture the self-amplifying RNA

Reasons for optimism

- Early findings demonstrate that animals are able to produce neutralizing antibodies against COVID-19 once given the vaccine
- The U.K. government awarded $28.33M to the Imperial COVID-19 vaccine team on April 22 to support future Phase II clinical trials and subsequent large Phase III trials

Sources: *FiercePharma*; Pharmaprojects; Reuters; company websites; L.E.K. research and analysis

Case study: CureVac's mRNA vaccine candidate

Preclinical

R&D commencement: January 2020
Humans dosed: N/A
Funding disclosed: ~$80M
Vaccine type: mRNA

Asset overview

- CureVac's vaccine introduces to the body an mRNA sequence coded for a COVID-19 antigen, which prepares the immune system for the real disease
- The vaccine is being developed in partnership with CEPI as a follow-on from an existing partnership that began in 2019, which provided CureVac with funding to develop facilities to print mRNA vaccines

Development timeline

- CureVac expects to enter clinical trials with the vaccine in June 2020
- The board of the European Investment Bank approved a 75M euros investment in CureVac to scale vaccine production, in response to concerns that the U.S. government was attempting to buy exclusive rights to the vaccine

Reasons for optimism

- CureVac recently announced successful results in its rabies vaccination program, which relies on two doses of only 1 microgram; CureVac's success with this dosage is encouraging with regard to meeting the global supply requirements for addressing the COVID-19 pandemic

Sources: BioSpace; *Politico*; PharmaProjects; company website; L.E.K. research and analysis

Case study: Vaxart's adenovirus vaccine candidate

Preclinical

R&D commencement: January 2020
Humans dosed: N/A
Funding disclosed: N/A
Vaccine type: Non-replicating vector

Asset overview

- Vaxart's COVID-19 candidate is based on its oral vaccines platform, which relies on the adenovirus type 5 as the mechanism of action
- Vaxart is particularly interested in vaccines that generate mucosal immune responses in addition to an antibody response

Development timeline

- Vaxart has obtained positive preclinical results in animal trials and is expected to start Phase I trials in the second half of 2020
- Vaxart entered into an agreement with Emergent BioSolutions for development solutions to prepare for production of the COVID-19 vaccine

Reasons for optimism

- Vaxart's oral vaccine could be highly effective due to the mucosal immune response, which acts as a first line of defense against respiratory infection

Sources: Pharmaprojects; WHO; company website; L.E.K. research and analysis

Case study: Altimmune's AdCOVID vaccine candidate

altimmune

Preclinical

R&D commencement: January 2020
Humans dosed: N/A
Funding disclosed: N/A
Vaccine type: Non-replicating vector

Asset overview

- Altimmune is developing an adenovirus-based intranasal vaccine
- Altimmune's COVID-19 vaccine is based on its proprietary intranasal vaccine technology, which has demonstrated mucosal and cellular immune responses in addition to an antibody response

Development timeline

- Altimmune is working with the University of Alabama Birmingham to conduct preclinical trials and is aiming to initiate Phase 1 trials in 3Q 2020

Reasons for optimism

- Altimmune has developed a number of other intranasal vaccines for respiratory diseases, including the NasoVAX candidate on which the COVID-19 vaccine is based

Sources: WHO; company website; L.E.K. research and analysis

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