A Survey prepared for the Hever Group of Heads of R&D of Pharmaceutical companies by Carlos Castellijos COVID-19

Industry Response

March 26th, 2020

Vaccine Candidates:

Live-Attenuated Viruses (LAVs)

LAVs elicit strong cellular immune responses, which are critical to eradicate many intracellular pathogens. Nevertheless, the failures that are sometimes caused by inactivated vaccines are ascribed to mutation of the surface antigens of pathogens. Additional concerns about LAV applications include the potential to cause disease in immuno-compromised individuals and the possibility of reversion to a virulent form due to the back-mutation, the acquisition of compensatory mutations, or recombination with circulating transmissible wild-type strains.

Codagenix (with Serum Institute of India)

- Jointly developing a live-attenuated vaccine. Codagenix has already designed multiple nCoV vaccine candidate genomes using its proprietary deoptimization technology. The vaccine viruses will then be grown and tested in vivo by contracted laboratories suitable for containment, prior to testing in clinical trials. The Serum Institute of India, a vaccine manufacturer and distributor with a global footprint, will then scale-up the manufacture of the vaccine to ensure its availability to meet a critical public health need.
- The company is planning clinical trials in India and expects to be market ready by 2022. Universal Flu in Ph I, RSV, Zika, Dengue in preclinical

Nucleic acid-based vaccines:

- **Non-viral delivered mRNA**

Currently, two forms of mRNA vaccines have been developed: conventional mRNA vaccines and self-amplifying mRNA vaccines, which are derived from positive strand RNA viruses. After the purified RNA replicon is delivered into host cells as synthetically formulated RNA, it is translated extensively and amplified by its encoding RNA-dependent RNA polymerase. Compared with the rapid expression of conventional mRNAs, published results have shown that vaccination with self-amplifying mRNA vaccines results in higher antigen expression levels, although delayed in time, which persist for several days *in vivo*. Equivalent protection is conferred but at a much lower RNA dose. Due to the lack of viral structural proteins, the replicon does not produce infectious viral particles. Additionally, both conventional mRNA and self-amplifying mRNAs

cannot potentially integrate into the host genome and will be degraded naturally during the process of antigen expression.

Arcturus Therapeutics

- Using their novel self-replicating mRNA platform (RNA -STARR) and LUNAR LNP formulation technology, Arcturus collaborates with Duke National University of Singapore. The latter will deploy their platform for rapid screening of vaccines for effectiveness and safety

CureVac- AG

- CureVac has received an initial funding of $8.3m from CEPI to accelerate the development of a vaccine against nCoV-2019. The company will leverage its technology and mRNA platform to develop the new vaccine and begin testing within the next few months. The European Commission said it is offering Germany's CureVac 80 million euros to scale up the development and production of a COVID-19 virus vaccine

Moderna mRNA-1273

- Preclinical stage RNA-based vaccine candidate (CEPI funded). National Institute of Allergy and Infectious Diseases will be responsible for carrying out IND-enabling studies as well as a phase one clinical study in the US. Human tests started mid-March (45 patients for Phase 1 at Kaiser Permanente); study expected to conclude June 2021. Moderna could make the vaccine available to health care workers in autumn this year.

Pfizer (with BioNTech-Germany and Fosun Pharma-China) BNT162

- Working on an mRNA vaccine. The prophylactic candidate, BNT162, licensed to Fosun Pharma in China. Global clinical study in Europe, the U.S. and China is planned (aiming to start end of April). Due to the broad definition of mRNA vaccine by BioNTech, it is not excluded that (also) self-amplifying mRNA (saRNA) are investigated for this vaccine besides (un)modified mRNA.

Stermirna Therpeutics (with Shanghai East Hospital Tongji University)

- Co-development of an mRNA vaccine. ~ 45 days needed to manufacture the vaccine samples based on the new generation of mRNA technology and some preliminary procedures.

Recombinant DNA platforms

Although promising and with shown safety, well-tolerability and immunogenicity, DNA vaccines were characterized by suboptimal potency in early clinical trials. Enhanced delivery technologies, such as electroporation, have increased the efficacy of DNA vaccines in humans, but have not reduced the potential risk of integration of exogenous DNA into the host genome, which may cause severe mutagenesis and induced new diseases.

Inovio INO-4800

- Accelerating the testing of a proprietary smart device for intradermal delivery of a vaccine to treat the coronavirus. Preclinical stage DNA-based vaccine candidate (funded by CEPI and BMGF). Clinical study planned in April (US) and separate trials in China and South Korea. First results expected Fall 2020.

- **Virus-Like Particle (VLP) based vaccines**

Vectors (typically large virus) capable of carrying several vaccine antigens, expresses proteins that assemble into VLP immunogens within (*in vivo*) the person receiving the vaccine. The production of VLPs in the person being vaccinated mimics virus production in a natural infection, stimulating both the humoral and cellular arms of the immune system to recognize, prevent, and control the target infection. The GV-MVA-VLP™ derived vaccines can elicit durable immune responses in the host similar to a live-attenuated virus, while typically providing the safety characteristics of a non-replicating or replication-defective vector.

GeoVax Labs (with BravoVax)

- US-based pharma company, and BravoVax, a China-based pharma company, have announced plans to develop a coronavirus cure in the form of vaccine based on the former's MVA-VLP vaccine platform. The viral basis of vaccine vector (MVA) has >50 years of safety records and has been recently approved by the FDA for prevention of smallpox and monkeypox diseases.

- **Non-replicating Viral Vectors**

Replication incompetent viral vectors that carry one or more antigens. No production of viral (-like) particles in the host. Examples of such vectors are recombinant adenoviruses (Ad vectors) and modified vaccinia Ankara (MVA) vectors. Also non-replicating vectors of other viral systems are employed as vaccines in general

CanSino Biologics

- China's CanSino Biologics has developed a recombinant novel coronavirus vaccine that incorporates the adenovirus type 5 vector (Ad5). Study Design: A Phase 1 clinical trial of 108 participants between 18 and 60 years old who will receive low, medium, and high doses of Ad5-nCoV. Currently recruiting

J&J

- Expediting investigational coronavirus vaccine program via expanded BARDA and Beth Israel Deaconess Medical Center collaboration to support the development preventive vaccine candidate for COVID-19 using Janssen's AdVac® technology which was used to develop Janssen's investigational Ebola, RSV and HIV vaccines. Preclinical testing of multiple vaccine prospects has commenced, with the aim to identify a COVID-19 vaccine candidate for clinical trials by the end of the month. J&J hopes to start human trials for coronavirus vaccine in November.
- Submitted proposal for vaccine development to CEPI

Recombinant Nanoparticles

Genetically engineered three-dimensional nanostructures that incorporate recombinant proteins critical to disease pathogenesis.

Novavax

- Novavax created the COVID-19 vaccine candidates using its proprietary recombinant protein nanoparticle technology platform to generate antigens derived from the coronavirus spike (S) protein, optimal candidate for human testing, is expected to begin by the end of spring 2020.. Emergent BioSolutions will use its CDMO services to advance Novavax's COVID-19 vaccine candidate into clinical stage. Coalition for Epidemic Preparedness Innovations (CEPI) awarded an initial funding of $4 million to support Novavax' efforts to develop a COVID-19 vaccine. CEPI and Novavax are having ongoing discussions on additional funding from CEPI to address Novavax' costs through Phase 1.

UfoVax

- Spin-off vaccine company from Scripps Research, uses a proprietary *one component self-assembling protein nanoparticle* (1c-SA*p*NP) vaccine platform technology for a vaccine against the coronavirus SARS-CoV-2. The vaccine prototype features SARS-CoV-2 protein spikes protruding from a protein nanoparticle scaffold. As a virus-like particle (VLP), the nanoparticle vaccine would induce the immune system to rapidly generate antibodies to neutralize (deactivate) the coronavirus, offering a recipient protection against the real SARS-CoV-2 virus. Produced on CHO cells.

Peptide Vaccines

Subunit and peptide based vaccines have been developed thanks to advancements in molecular biology theory and technologies. Nevertheless, subunit and peptide vaccines are less effective at eliciting a robust $CD8^+$ immune response, which is important for intracellular pathogens, including viruses and some bacteria

Generex (with EpiVax) Ii-Key peptide COVID-19 vaccine

- Generex signs contract with EpiVax to develop Ii-key peptide vaccines. Generex will use EpiVax's computational tools, along with NuGenerex Immuno-Oncology's Ii-Key technology, to predict epitopes — the parts of antigens recognized by the immune system — that can be used to generate peptide vaccines against the novel coronavirus.

Sanofi Pasteur

- Leveraging previous development work for a SARS vaccine to possibly unlock fast path for developing a COVID-19 vaccine in collaboration with BARDA. Sanofi will use its recombinant DNA platform technology to produce an exact genetic match to proteins found on the surface of the virus. The DNA sequence encoding this antigen will be

combined into the DNA of the baculovirus expression platform, the basis of Sanofi's licensed recombinant influenza product, and used to rapidly produce large quantities of the coronavirus antigen to stimulate the immune system to protect against the virus. Vaccine candidate is in preclinical stage. Phase 1 planned in Q2/Q3 202

Adjuvants

GSK (with Sichuan Clover Biopharm)

- GSK and CEPI formed a new collaboration to develop a vaccine for the COVID-19. GSK will make its established pandemic vaccine adjuvant platform technology available to enhance the development of an effective vaccine. Preclinical stage AS03 Adjuvant, Chinese biotech Clover Biopharmaceuticals using adjuvant in combination with vaccine candidate (preclinical)

CSL Behring (with University of Queensland)

- Partnered with the University of Queensland's COVID-19 vaccine development program. Will provide technical expertise as well as a donation of Seqirus' proprietary adjuvant technology, MF59®, to their pre-clinical development program. Seqirus' adjuvant technology has a long history of use and a strong safety profile in both seasonal and pandemic influenza vaccines. The University of Queensland will use the adjuvant to test the CHO expressed viral protein they are developing with their molecular clamp technology.

Novavax

- Novavax expects to utilize its proprietary Matrix-M™ adjuvant with its COVID-19 vaccine candidate to enhance immune responses. Novavax' patented saponin-based Matrix-M adjuvant has demonstrated a potent and well-tolerated effect by stimulating the entry of antigen-presenting cells into the injection site and enhancing antigen presentation in local lymph nodes, boosting immune responses.

Manufacturing Platforms

J&J

- PER.C6® (& PER.C6-TetR) technology which were used to develop and manufacture Janssen's investigational Ebola vaccine. This platform provides the ability to rapidly upscale production of an optimal vaccine candidate.

iBio (with CC-Pharming)

- Partnership to develop a plant-derived coronavirus VLP vaccine based on the former's FastPharming System™, which has been previously used for producing antibody candidates for Ebola and Dengue fever viruses.

By Development Stage

Phase 1 vaccine candidates

Company: Moderna
Vaccine candidate: mRNA-1273
Details: Moderna is the Massachusetts-based biotech company behind mRNA-1273, a vaccine candidate developed using prior studies of related coronaviruses, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).
Study Design: A Phase 1, open-label, dose-ranging clinical trial of 45 healthy participants between 18-55 years old
Institution: Kaiser Permanente Washington Health Research Institute
Status: Recruiting completed 19 March 2020
ClinicalTrials.gov Identifier: NCT04283461
Funding: NIAID

Company: CanSino Biologics
Vaccine candidate: Ad5-nCoV
Details: China's CanSino Biologics has developed a recombinant novel coronavirus vaccine that incorporates the adenovirus type 5 vector (Ad5).
Study Design: A Phase 1 clinical trial of 108 participants between 18 and 60 years old who will receive low, medium, and high doses of Ad5-nCoV
Institution: Tongji Hospital; Wuhan, China
Status: Currently recruiting
Chinese Clinical Trial Registry Identifier: ChiCTR2000030906

Pre-clinical vaccine candidates

Companies: Pfizer and BioNTech
Vaccine candidate: BNT162
Details: Pfizer and BioNtech have announced an agreement to collaborate on developing an mRNA-based COVID-19 vaccine originally developed by BioNTech. The companies had previously agreed to develop an mRNA-based influenza vaccine in 2018.
Status: Clinical testing is expected to begin in April 2020

Company: Inovio Pharmaceuticals
Vaccine candidate: INO-4800
Details: Inovio is developing a DNA vaccine for SARS-CoV-2 that is in line with other DNA vaccines the company is developing, such as for the MERS coronavirus. The vaccine is injected intradermally through a device which Inovio plans to scale production of while they wait for results of INO-4800.
Status: Phase 1 clinical trials are expected to begin in April

Company: Novavax
Vaccine candidate: No name announced
Details: Biotech company Novavax announced in March that it has produced several recombinant nanoparticle vaccine candidates for COVID-19 and is vetting them in animal testing.
Status: Novravax hopes to begin clinical testing in late spring of 2020.

Company: CureVac
Vaccine candidate: No name announced
Details: CureVac announced they are developing an mRNA-based COVID-19 vaccine "within a few months," according to a press release.
Status: The company plans to start clinical trials in the summer and have identified two study centers.

Company: Generex Biotechnology
Vaccine candidate: Ii-Key peptide COVID-19 vaccine
Details: Biotech company Generex subsidiary NuGenerex Immuno-Oncology is spearheading a vaccine project to create an Ii-Key peptide vaccine against COVID-19.
Status: In a company press release dated 27 February, Generex said they wanted to produce a vaccine candidate that could be tested in humans "within 90 days."

Company: Vaxart
Vaccine candidate: Oral recombinant COVID-19 vaccine
Details: Vaxart announced their agreement with Emergent Biosolutions to develop and manufacture their oral recombinant vaccine candidate for COVID-19.
Status: The company plans to initiate a Phase 1 clinical study "early in the second half of 2020," according to a press release.

Company: Imperial College London
Vaccine candidate: Self-amplifying RNA vaccine
Details: Imperial College London researchers are developing a self-amplifying RNA vaccine for COVID-19. They developed a vaccine candidate within 14 days of receiving the sequence from China.
Status: Animal testing is underway; the researchers aim to begin clinical trials in the summer of 2020.

Company: Medicago
Vaccine candidate: Plant-based COVID-19 vaccine

Detaisl: Medicago, which recently developed a seasonal recombinant quadrivalent virus-like particle (VLP) influenza vaccine, reported they created a coronavirus VLP 20 days after working with the SARS-CoV-2s gene.
Status: The company says their vaccine is in the pre-clinical testing stage, and they expect to begin human testing in July or August of 2020.

Company: Takis Biotech
Vaccine candidate: DNA-based vaccine for COVID-19
Details: The partnership between Takis Biotech and Applied DNA Sciences has resulted in four DNA vaccine candidates for COVID-19.
Status: Takis expects preclinical testing results in April 2020; their final vaccine candidate could begin human testing by fall, according to a company press release.

Companies: Johnson & Johnson and BARDA
Vaccine candidate: No name announced
Details: Johnson & Johnson has announced their intention to develop a COVID-19 vaccine, using their AdVac and PER.C6 systems, which were also used to develop the company's Ebola vaccine.
Status: J&J says they plan to have a vaccine candidate by the end of March, with human trials starting in November 2020.

Company: Altimmune
Vaccine candidate: Intranasal COVID-19 vaccine
Details: Altimmune has developed a COVID-19 vaccine candidate using the same technology they used build their influenza vaccine, NasoVAX. The COVID-19 vaccine would be delivered intranasally in a single dose.
Status: According to a company press release, animal testing is beginning, and clinical testing is slated for August 2020 or later.

Research in additional vaccine candidates

Companies: Clover Biopharmaceuticals and GlaxoSmithKline
Vaccine candidate: COVID-19 S-Trimer
Details: GSK has entered into a collaboration agreement with Chinese company Clover Pharmaceuticals to use its adjuvant technology for Clover's COVID-19 candidate S-Trimer.
Status: In a press release, GSK says it S-Trimer is being "rapidly developed," and pre-clinical studies are being planned.

Company: Heat Biologics
Vaccine candidate: gp96-based vaccine
Details: The biotech company Heat Biologics announced it is pairing with the University of Miami to use the gp96 heat shock protein backbone to develop at least one COVID-19 vaccine.
Institution: University of Miami Miller School of Medicine

Status: Added to WHO's draft landscape of COVID-19 vaccines

Companies: CSL and The University of Queensland
Vaccine candidate: Molecular clamp vaccine for COVID-19
Details: Researchers at the University of Queensland have achieved a proof-of-concept vaccine candidate for COVID-19.
Institution: The University of Queensland
Status: In a press release, the university said they will begin further development prior to pre-clinical testing.

Company: Sanofi
Vaccine candidate: No name announced
Details: Sanofi announced in February that is was developing a COVID-19 vaccine candidate under its egg-free, recombinant DNA platform using work from a previous SARS vaccine and in partnership with the Biomedical Advanced Research and Development Authority (BARDA).
Status: Preclinical.

Company: ExpreS^{2}ion Biotechnologies
Vaccine candidate: No name announced
Details: Denmark-based ExpreS^{2}ion won a European Union (EU) Horizon 2020 grant to fund a COVID-19 vaccine candidate.
Status: The company said they plan to perform a Phase 1/2a clinical trial and aim to begin clinical testing within 12 months.

Company: University of Saskatchewan Vaccine and Infectious Disease Organization-International Vaccine Centre
Vaccine candidate: No name announced
Details: The University of Saskatchewan's Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac) is developing a vaccine for COVID-19, recently received $1 million to accelerate COVID-19 vaccine candidate testing.
Status: Preclinical.

Company: EpiVax
Vaccine candidate: Ii-Key peptide vaccine
Details: EpiVax is developing two Ii-Key peptide vaccine candidates against COVID-19.
Status: EpiVax's CEO said a vaccine could be ready within 5-6 months if the company receives the right level of funding.

Company: Codagenix
Vaccine candidate: Live attenuated COVID-19 vaccine
Details: Codagenix announced in February that it had used the nCoV genome to map out several vaccine candidate genomes for COVID-19.
Status: The company said the next step is to grow and test the vaccine viruses *in*

vivo before initiating clinical trials, but gave no timeline for when testing would begin.

Company: Zydus Cadila
Vaccine candidate: DNA and/or live attenuated recombinant COVID-19 vaccine candidate
Details: India's Zydus Cadila announced in February they are researching two vaccine candidates for COVID-19. The first would use a DNA vaccine targeting the viral entry membrane protein of the virus, while the second uses a live attenuated recombinant measles virus targeted to COVID-19.
Status: No details have been released at this time.

Company: Sinovac
Vaccine candidate: Formalin-inactivated and alum-adjuvanted candidate vaccine for COVID-19
Details: Sinovac is purportedly working on a formalin-inactivated and alum-adjuvanted candidate vaccine for COVID-19, according to the WHO draft landscape of COVID-19 vaccines.
Status: No details have been released at this time.

Company: Geovax and Bravovax
Vaccine candidate:
Details: In January, Chinese biotech companies Geovax and Bravovax announced they would collaborate to create a modified vaccinia ankara virus like particles (MVA-VLP) vaccine candidate for COVID-19.
Status: Geovax said it's currently in the process of narrowing their vaccine candidates down from three to one, and from there will move to testing in humans.

Organization: The University of Oxford
Vaccine candidate: ChAdOx1
Details: The Oxford Vaccine Group at the University of Oxford have identified a new vaccine candidate for COVID-19, a chimpanzee adenovirus vaccine vector called ChAdOx1. The team has previously developed a MERS vaccine.
Status: Development of ChAdOx1 is currently underway, but the Oxford Vaccine Group did not provide a timeline for a clinical trial in humans.

Company: Greffex
Vaccine candidate: Adenovirus-based vector vaccine for COVID-19
Details: Genetic engineering company Greffex is developing an adenovirus-based vector vaccine for COVID-19.
Status: The company recently announced its vaccine candidate has entered the animal testing stage.

Company: Walter Reed Army Institute of Research and United States Army Medical Research Institute of Infectious Diseases
Vaccine candidate: No name announced
Details: Walter Reed, together with the U.S. Army Medical Research Institute of

Infectious Diseases, is working on a COVID-19 vaccine. Researchers at Walter Reed had previously developed a MERS vaccine, and is using that work to help them create a vaccine candidate for COVID-19.
Status: Walter Reed has developed several vaccine candidates, and have begun testing in animals, but have not yet indicated when they would begin clinical testing in humans.

Organization: MIGAL Galilee Research Institute
Vaccine candidate: Modified avian coronavirus vaccine
Details: The institute said it plans to create a new COVID-19 vaccine candidate by adapting its research in developing a vaccine for the genetically-similar avian coronavirus Infectious Bronchitis Virus (IBV).
Status: On 27 February, the institute said it planned to create the vaccine within the next 8-10 weeks, will seek safety approval within 90 days, and is in discussion with partners for human trials.

Company: AJVaccines
Vaccine candidate: No name announced
Details: In March, Danish-based vaccine manufacturer AJVaccines said they would use modern antigen technology to develop a COVID-19 vaccine candidate that would have a "high protection with a low reactogenicity and favorable safety profile."
Status: The company has not given a timeline for further development or testing.

Organization: Baylor College of Medicine
Vaccine candidate: Re-purposed SARS vaccine for COVID-19; S1 or RBD protein vaccine candidate
Details: Researchers at the Baylor College of Medicine say they have a shelved vaccine from the 2003 SARS outbreak that could be repurposed for use in the COVID-19 pandemic. They are also developing an S1 or RBD protein vaccine as a targeted vaccine candidate for COVID-19.
Status: The university has not released details on developing or testing at this time.

Organization: Institut Pasteur
Vaccine candidate: No name announced
Details: Institut Pasteur is partnering with the Coalition for Epidemic Preparedness Innovations (CEPI) to develop a COVID-19 vaccine candidate.
Status: No other details have been released at this time.

Company: Tonix Pharmaceuticals and Southern Research
Vaccine candidate: Horsepox vaccine with percutaneous administration
Details: Biopharmaceuticals company Tonix is partnering with Southern Research to develop a COVID-19 vaccine candidate based on the company's horsepox vaccine, TNX-1800, is working
Status: Tonix hasn't offered a timeline for further development or testing.

Organizations: Fudan University, Shanghai JiaoTong University, and RNACure

Biopharma
Vaccine candidate: mRNA vaccine candidate for COVID-19
Details: Fudan University has entered into a partnership with Shanghai JiaoTang University, and RNACure to develop a COVID-19 mRNA vaccine candidate. They are using two methods to develop an mRNA-based vaccine: using mRNA to express the receptor-binding domain of the spike protein of COVID-19 to induce neutralizing-antibodies, and developing mRNAs that can instruct the host to produce virus-like particles similar to SARS-CoV-2.
Status: No details on further development or testing are available at this time.

Company: Arcturus Therapeutics and Duke-NUS Medical School
Vaccine candidate: No name announced
Details: Arcturus and Duke are partnering to develop a COVID-19 vaccine candidate that uses Arcturus' self-replicating RNA and nanoparticle non-viral delivery system.
Status: The companies have not released further details about development or testing.

Organization: University of Pittsburgh's Center for Vaccine Research
Vaccine candidate: No name announced
Details: Researchers at the University of Pittsburgh have received a $4.9 million grant from CEPI to develop a COVID-19 vaccine candidate.
Status: No other details are available at this time.

Organization: Peter Doherty Institute for Infection and Immunity
Vaccine candidate: No name announced
Details: The Doherty Institute has received $3.2 million from the Jack Ma foundation to accelerate the creation of a COVID-19 vaccine with an active and passive platform.
Status: No other details have been released at this time.

Organization: Tulane University
Vaccine candidate: The Tulane National Primate Research Center has launched a COVID-19 research program to help develop a vaccine candidate.
Status: The organization has not established a timeline for testing, but has indicated it will use a primate model for animal testing.

Therapeutics

Small Molecules:

AbbVie

- Collaborating with select health authorities and institutions globally to determine antiviral activity, efficacy and safety of lopinavir/ritonavir against COVID-19. AbbVie is supporting clinical studies and basic research with lopinavir/ritonavir, working closely with European health authorities and the FDA, CDC, NIH and BARDA. Also joined IMI to support research and discovery of targeted medicines

Gilead (with BrightGene Biomedical Tech)

- Working with government, NGOs and regulatory authorities to develop a strategy for its investigational compound, remdesivir, to patients with COVID-19 for emergency treatment in the absence of any approved treatment options, and to support clinical trials to determine whether it can safely and effectively be used to treat COVID-19. Together with health authorities in China, Gilead has initiated two clinical trials in patients who have been infected with COVID-19 to determine the safety and efficacy of remdesivir as a potential treatment for the coronavirus. Both trials are now enrolling participants with results expected May 2020.. In anticipation of potential future needs, Gilead has accelerated manufacturing timelines to increase its available supply of remdesivir as rapidly as possible.

J&J

- Initiated a review of known pathways in coronavirus pathophysiology to determine whether previously tested medicines can be used to help patients survive a COVID-19 infection and reduce the severity of disease in non-lethal cases. Expanded partnership with BARDA to seek treatment solutions, includes testing of anti-viral compounds to build on J&J's multipronged response to the outbreak. Joined a Horizon 2020 consortium for Horizon 2020 led by Johan Neyts (REGA institute) with focus on identifying of therapeutics. Janssen participating in a consulting capacity. Engaged in IMI consortium development efforts for anti-viral screening.

Pfizer

- Developing potential antiviral therapies. Committed to sharing clinical development and regulatory expertise

Large Molecules / Biologics:

AbCellera Biologics (with Eli Lilly)

- Developing a therapy against the SARS-CoV-2 virus by getting hold of a blood sample from one of the first U.S. patients to recover from the pathogen. Screened 5 million immune cells and identified 500+ fully human antibody sequences. With the project now advancing to an assessment of the antibodies' effectiveness against SARS-CoV-2. AbCellera has enlisted Lilly to help keep the program moving forward quickly. The partners aim to have an antibody in the clinic within four months.

AstraZeneca

- Mobilized research efforts to discovering novel coronavirus-neutralizing antibodies as a treatment to prevent COVID-19 disease. Tailoring its Pandemic Prevention Platform (P3) program, funded in part by the U.S. government, to address the 2019-nCoV outbreak and identifying monoclonal antibodies to progress into clinical trial evaluation.

Regeneron

- Collaborating to develop new coronavirus drugs- namely preclinical monoclonal antibody treatment. The company will utilize its VelociSuite® technologies comprising of the VelocImmune® platform that uses a genetically-engineered mouse with a humanized immune system. The platform can be used to quickly identify, validate, and development antibody candidates. Schedule for phase 1 testing in August 2020.

Regeneron (with Sanofi)

- Rheumatoid arthritis drug Kevzara will be used in an international study of patients infected with the new coronavirus and suffering from acute respiratory distress syndrome, Regeneron Pharmaceuticals and Sanofi announced Monday.
- The trial will kick off in disease hotspot New York City, expanding to a total of 16 U.S. sites and enrolling 400 patients. The companies aim to study whether Kevzara can reduce fever and the need for supplemental oxygen in patients severely affected by COVID-19, the illness caused by the virus

PharmaMar

- In vitro study results of Aplidin (plitidepsin) on the human coronavirus HCoV-229E (similar multiplication and propagation mechanism to COVID-19) have been positive with a potency of the nanomolar order. These studies were conducted at the National Biotechnology Centre of the Spanish National Research Council and confirm that the therapeutic target of Aplidin, which is EF1A, is key to the multiplication and spread of the virus. Evaluating options for studies on patients infected with COVID-19.

Sirnaomics

- Engaged research teams in the US and China to develop RNA interference (RNAi)-based prophylactics and therapeutics. Previously, the company used small interfering RNA (siRNA) drugs to treat SARS coronavirus, H5N1 influenza and other respiratory viral infections.

Sorrento Therapeutics (with Celularity)

- Collaboration to expand the therapeutic use of Celularity's CYNK-001, an allogeneic, off-the-shelf, placental-derived Natural Killer (NK) cell therapy, to the treatment and prevention of coronavirus infections.NK cells are the foundation of the natural innate immune response. NK cells derived from the placenta are well tolerated, intrinsically safe and versatile, allowing potential uses across a range of organs and tissues. NK cell therapy is currently being investigated as a treatment for various liquid and solid tumors, but also has the demonstrated potential to be effective against virally infected cells.

Southwest Research Institute (SwRI)

- Using virtual screening to identify coronavirus treatments. SwRI's virtual screening tool recently evaluated two million drug compounds in a few days, hoping to identify high-probability drugs that may have efficacy against the coronavirus with minimal adverse side effects.

Takeda

- Developing an anti-SARS-CoV-2 polyclonal hyperimmune globulin (H-IG) to treat high-risk individuals with COVID-19, which is being referred to as TAK-888. Hyperimmune globulins are plasma derived-therapies that have previously been shown to be effective in the treatment of severe acute viral respiratory infections. In discussions with multiple national health and regulatory agencies and health care partners in the US, Asia and Europe to expeditiously move the research into TAK-888 forward.

Vir Biotechnology (with Alnylam Pharmaceuticals)

- Announced an expansion of their existing collaboration to include the development and commercialization of RNAi therapeutics targeting SARS-CoV-2, the virus that causes the disease COVID-19. Under the agreement, the companies will utilize Alnylam's recent advances in lung delivery of novel conjugates of siRNA – the molecules that mediate RNAi – together with Vir's infectious disease expertise and established capabilities, to bring forward one or more siRNAs to treat SARS-CoV-2 and potentially other coronaviruses as well.

Vir Biotechnology (with WuXi Biologics)

- Collaboration for global development of antibodies to treat COVID-19. A number of monoclonal antibodies that bind to SARS-CoV-2 have been identified that were isolated from individuals who had survived a SARS (Severe Acute Respiratory Syndrome) infection. The company is conducting research to determine if its antibodies, or additional antibodies that it may be able to identify, can be effective as treatment and/or prophylaxis against SARS-CoV-2.

Ongoing and upcoming Clinical Trials with repurposed approved compounds:

Antimalarials and antibiotics (Hydroxychloroquine, Chloroquine & Azithromycin):

Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open-label Non-randomized Clinical Trial
Single-arm protocol; 36 pts treated w/ hydroxychloroquine 200 mg tid x10days; 6 pts received azithromycin (500 mg x1dose, then 250 mg daily x4days) to prevent bacterial superinfxn: ECG was monitored daily due to higher QT prolongation risk w/ this combo
Treated pts had significant reduction in viral carriage at day 6 and much lower carriage duration vs controls; addition of azithromycin resulted in significantly more efficient virus elimination
Access free full-text IJAA article
Post-exposure Prophylaxis for SARS-Coronavirus-2: A Pragmatic Randomized Clinical Trial
RCT of healthcare workers or household contacts exposed to COVID-19 case w/in 3 days
Randomized to hydroxychloroquine 800 mg once, then 600 mg in 6-8 hrs, then 600 mg daily x6days, or placebo
University of Minnesota
ClinicalTrials.gov

Upcoming Trial: **Chloroquine** Prevention of Coronavirus Disease (COVID-19) in the Healthcare Setting (COPCOV)
Multi-center, double-blind study of healthcare workers not already infected w/ COVID-19
Randomized to chloroquine (loading dose, 10 mg base/kg, followed by 150 mg daily) or placebo x3mo, or until COVID-19 dx
Not yet recruiting. (ClinicalTrials.gov)

Antivirals (Remdesivir, Lopinavir, Ritonavir & Faripiravir):

US trials of antiviral drug remdesivir
Some COVID-19 pts have received IV remdesivir for compassionate use1 outside of clinical trials2
Adaptive COVID-19 Treatment Trial. NIH multicenter RCT in hospitalized adults (ClinicalTrials.gov)
Study to Evaluate the Safety and Antiviral Activity of **Remdesivir** (GS-5734™). Gilead Sciences sponsoring 2 trials, one in pts w/ severe coronavirus dz (ClinicalTrials.gov), and one in those with moderate dz (ClinicalTrials.gov)
Footnotes

1 Key inclusion criteria for compassionate use: hospitalized, confirmed SARS-CoV-2 by PCR, invasive mechanical ventilation. Manufacturer not currently accepting new requests pending transition to expanded access program. More details (manufacturer website)

Clinical Trial Results: A Trial of **Lopinavir–Ritonavir** in Adults Hospitalized w/ Severe Covid-19 (NEJM)
Randomized, controlled, open-label trial; N=199 hospitalized adult pts w/ confirmed SARS-CoV-2, O2 sat ≤94%
No benefit in time to clinical improvement; mortality at 28 days numerically lower w/ lopinavir/ritonavir but difference not statistically significant
Access the free full-text NEJM article

Favipiravir (AKA favilavir, fapilavir; Avigan): Available in Japan for tx of influenza; first approved drug in China for tx of COVID-19
Umifenovir (Arbidol): Available in Russia & China for tx of influenza
Favipiravir Combined With Tocilizumab in the Treatment of Corona Virus Disease 2019
3-arm RCT
Adults w/ clinical dx of COVID-19, increased IL-6
[Favipiravir (1,600 mg PO bid on day 1; 600 mg PO bid on days 2-7) + tocilizumab 4-8 mg/kg (max 800 mg) x1 dose; then additional dose if fever still present w/in 24 hrs of 1st dose] or [favipiravir alone] or [tocilizumab alone]
Primary outcome: clinical cure rate (2 consecutive negative viral loads, improved lung imaging, normal body temp for >3 days
Location: China
ClinicalTrials.gov

Angiotensin II receptor antagonists:
Upcoming: Randomized Controlled Trial of **Losartan** for Patients With COVID-19 Requiring Hospitalization
Multi-center, double-blind study of COVID-19-infected inpatients
Randomized to daily losartan 25 mg PO daily or placebo x7 days (or to hospital discharge)
University of Minnesota
ClinicalTrials.gov
Losartan for Patients With COVID-19 Not Requiring Hospitalization
Multi-center, double-blind study of adults w/ presumptive COVID-19 not currently on an ACEI or ARB
Randomized to **losartan** 25 mg PO daily or placebo x10 days (or to hospital admission)
Primary outcome: hospital admission
University of Minnesota
ClinicalTrials.gov

Monoclonal Antibodies:

Tocilizumab in COVID-19 Pneumonia (TOCIVID-19)
Open-label, single-arm trial of hospitalized pts (any age) w/ pneumonia
2 doses of tocilizumab 8 mg/kg (max 800 mg/dose)
Primary outcome: 1-mo mortality
Location: Italy
National Cancer Institute, Naples
ClinicalTrials.gov
Tocilizumab vs CRRT in Mgmt of Cytokine Release Syndrome (CRS) in COVID-19 (TACOS)
Retrospective cohort study of adults w/ lab-confirmed COVID-19, IL-6 ≥3x ULN & ≥1 of: infiltrates on chest imaging; rales/crackles + O2 sat ≤93%; mechanical vent or supp O2 required; or sustained fever unresponsive to NSAID/steroid
Subjects received tocilizumab 8 mg/kg (in 100 mL NS) IV x1dose over at least 60 min
Primary outcome: normalization of fever, O2 sat thru day 14
Location: China
ClinicalTrials.gov

Favipiravir Combined With Tocilizumab in the Treatment of Corona Virus Disease 2019
3-arm RCT
Adults w/ clinical dx of COVID-19, increased IL-6
[Favipiravir (1,600 mg PO bid on day 1; 600 mg PO bid on days 2-7) + tocilizumab 4-8 mg/kg (max 800 mg) x1 dose; then additional dose if fever still present w/in 24 hrs of 1st dose] or [favipiravir alone] or [tocilizumab alone]
Primary outcome: clinical cure rate (2 consecutive negative viral loads, improved lung imaging, normal body temp for >3 days)
Location: China
ClinicalTrials.gov

Upcoming: **Tocilizumab** for SARS-CoV-2 Severe Pneumonitis
Single-arm trial of adults w/ COVID-19 multifocal interstitial pneumonia who need supplemental O2 and worsening lung involvement
Tocilizumab 8 mg/kg IV x1 dose
Primary outcome: Improvement in lung fxn
Location: Italy
ClinicalTrials.gov

Upcoming: Evaluation of the Efficacy and Safety of **Sarilumab** in Hospitalized Patients With COVID-19
Adult pts hospitalized w/ severe COVID-19
Single dose of IV sarilumab vs placebo
Location: New York, NY
Regeneron Pharmaceuticals
ClinicalTrials.gov