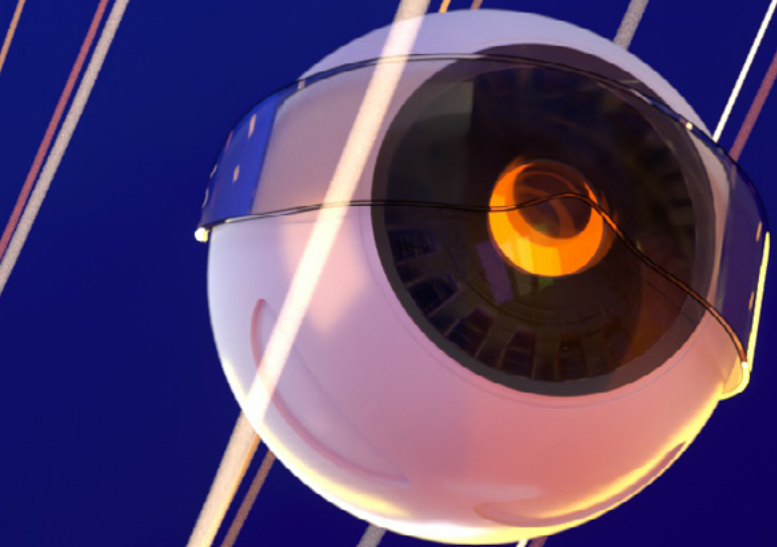
Investment Recipes

by AtonRā Partners



SPECIAL ISSUE

COVID-19: Medicine Fights Back

1 APRIL 2020

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On the Menu

Editorial

As the COVID-19 health crisis continues to make headlines, we decided to focus this issue of our Investment Recipes on the medical answers that are being prepared.

As stated in our previous reports, we believe that once the market realizes that measures implemented in countries such as Italy work in containing the contagion, volatility should calm down, and allow the markets to start looking forward more positively. In this respect, we expect the attention to gradually shift towards the fiscal and monetary policies being enacted.

The healthcare system is focusing all its efforts to find a cure and help mitigate the effects of the COVID-19 pandemic. As a result of this crisis, its role for our society at large is going to gain importance. Investment is likely to pour into the sector and contribute to making it better prepared to face the future crisis.

At the same time, looking forward implies understanding how a return to some « normality » is likely to happen. We believe that testing is going to be crucial, as people would need to be sure they don't get the virus coming out of confinement. It is difficult to predict if a split between healthy and non-healthy people is going to occur in the same form as currently in China, but in our view, testing will be unavoidable.

Similarly, masks will likely be part of our daily life (as it is already the case in many parts of Asia) for the next few months, and they could be made mandatory everywhere, from public spaces to trains, airports, etc. The quicker masks and tests are available for everyone, and the faster we are likely to get out from this standstill.

We believe that rightly anticipation of the return to a more "normal" life is of sheer importance and think that everyone now understands that social distancing was just the first step.

The AtonRâ Team

COVID-19: MEDICINE FIGHTS BACK

How It Works

A known family of viruses

COVID-19 is a strain of virus part of the larger Coronaviruses family, which causes infections of the respiratory system, and is transmitted through respiratory droplets reaching the mucoses (mouth, nose, eyes) of the « target ».

- Middle-East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) belong to the same family of viruses and have already caused major epidemic outbreaks over the last two decades.

Affecting the lungs

The COVID-19 virus triggers an immune (thus inflammatory) reaction in the lungs, at the alveoli level. Inflammatory fluid accumulates and fills space that is needed for air to provide oxygen to the blood, shutting the lungs and leading to pneumonia.

- Incubation period is still uncertain, but experts estimate a maximum of ca. 14 days.
- About 80% of people recover without needing any special treatment.
- Age and comorbidity (i.e., already existing health problems, such as high blood pressure, asthma, or diabetes) seem to relate to the severity of symptoms.

Multiple attack angles

All over the world, drug manufacturers and researchers rush to develop a medical solution to the COVID-19 outbreak. Companies are currently exploring four approaches to fight against COVID-19: passive immunization, antivirals, anti-inflammatory drugs and active immunization (vaccines).

- There are currently more than 100 treatments/ vaccines in development (from preclinical to Phase 3 stages).
- These cumulative efforts are likely to help rapidly bring the outbreak under control.

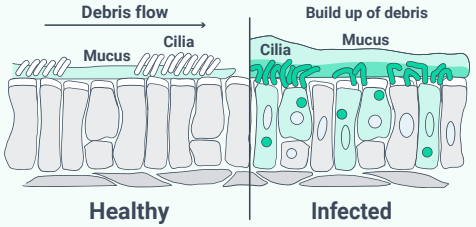
Four Approaches To Treat Covid-19

Passive immunization
- Monoclonal antibodies
- Immunoglobulins

Active immunization
- Classical vaccination
- RNA vaccines
- others

1.Infection

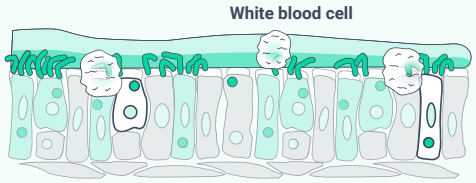
2. Viral replication



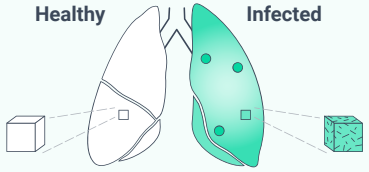
Antivirals
- RNA-polymerase inhibitors
- RNA interference
- Protease inhibitors

3. Immune hyper-reactivity

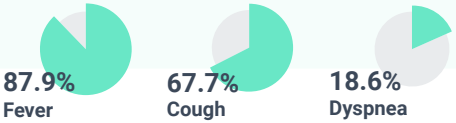
Anti-inflamatory drugs
- Anti-IL-6R antibodies



4. Lung tissue damage



Most Current Symptoms:



SOURCE:
Bellevue Investment

Antivirals

How it works

An antiviral works by chemically disrupting a specific point in the replication cycle of a virus. It thus slows down the infection by limiting the multiplication of viral particles, and effectively "helping" the immune response if taken soon enough.

- Antivirals rarely achieve stopping a viral infection, but are an effective method of virus control, and help gain time pending the development of a vaccine.
- Antivirals are often coupled to drugs stimulating the immune system's response.

Impact

Given similarities between viruses' mechanisms, antivirals already developed for other diseases are being tested. We expect multiple options to be available and fast-tracked approved in the next few months.

- Most already proved their efficacy in other diseases (Ebola, H1N1, influenza).
- Chloroquine (already approved on malaria and arthritis, and off-patent) has so far shown promising results in a small study and is experimentally already being used.

Key technologies and players

There are four types of antivirals: RNA polymerase inhibitors, RNA interference, protease inhibitors, and lysosomal enzyme inhibitors. They act at different stages of the replication cycle of the virus.

- Gilead is leading the race on RNA polymerase inhibitors.
- Chloroquine and Hydroxychloroquine are part of the Lysosomal enzyme inhibitors.
- Zhejiang Hisun / Fujifilm are the closest to a possible approval with Favilavir, a drug initially used for influenza, and that has been experimentally used in China.

An Overview: Antivirals 1/2

Company	Gilead	Ascletis Pharma	Zhejiang Hisun Pharmaceutical	Aim Immunotech
Name	Remdesivir	Ganovo (Danoprevir) And Ritonavir Combination Therapy	Favilavir (Marketed With The Label Avigan)	Rintatolimod (Tradename: Ampligen)
Category	Rna Polymerase Inhibitors	Rna Polymerase Inhibitors	Rna Polymerase Inhibitors	Rna Polymerase Inhibitors
Stage	Phase 3. Five clinical trials are undergoing all around the world - two of them can provide results in early April. More than 1,000 patients are being recruited to investigate whether multiple doses of Remdesivir can successfully reverse the infection. The main objectives are to reduce fever and to help patients leave the hospital within two weeks. The drug, which has already failed in an Ebola study, is administered intravenously.	Phase 1. Last month, 11 patients, with COVID-19 that had pneumonia, have been enrolled. All 11, who received a cocktail of Danoprevir and Ritonavir, were eventually discharged. First patient enrolled in the study on February 17.	It has been the first antiviral to be tested on humans in China for coronavirus treatment. The drug has reportedly shown efficacy in treating the disease with minimal side effects in a clinical trial involving 70 patients. The trial is conducted in Shenzhen, Guangdong province. There is no indication on when Favilavir could be definitively approved in China or elsewhere for the treatment of coronaviruses. However, the drug is already being used in China and Japan off label. The Italian Pharmaceuticals Agency AIFA has also authorized testing against COVID-19.	Discovery.
Mechanism of action	Antiviral Remdesivir (RNA polymerase inhibitor) promising. Could become a «Tamiflu against Corona».	A combination of antivirals, one approved for HIV and one approved for hepatitis C, that might treat coronavirus infection. Ganovo is an oral inhibitor of Hepatitis C virus (HCV) protease. Ritonavir is a protease inhibitor manufactured by AbbVie.	Favilavir's drug mechanism of action is as an antiviral. It attacks RNA viruses by inhibiting RdRp (RNA polymerase).	The drug is based on double-stranded RNA molecules able to bind to TLR-3 receptors. When Rintatolimod binds to TLR-3 receptors, the virus cannot do so, inactivating the innate immune system, rendering it unable to signal the rest of the body's defenses.
Opportunities	Looking at its mechanism of action, it seems that the drug could be effective for several types of coronaviruses, if the genetic sequences of the polymerases are similar enough.	–	–	100% survival rate on treated mice up to now. Ampligen is used in clinical trials to evaluate its effectiveness on different types of cancer.
Challenges	It is not clear yet if an enough amount of drug (which is delivered intravenously in the bloodstream) is able to reach the lungs.	–	–	–
Drug repositioning?	Yes, the drug has been already tested for Ebola but showed no efficacy. For COVID-19, it has already showed some positive outcomes.	Yes, the combination of these antivirals has been used for HIV and Hepatitis C.	Yes, used for Influenza in China and Japan.	Yes, approved for chronic fatigue syndrome in many countries (under the name Ampligen).

An Overview: Antivirals 2/2

Company	Alnylam	Abbvie	Off-Patent. (Among Drug Makers: Rising Pharmaceuticals (Private), Sanofi, Bayer, Teva, Mylan...)
Name	Rnai Drug (No Name Yet)	Lopinavir / Ritonavir	Chloroquine And Hydroxychloroquine (A Related Drug That Is Thought To Have Less Severe Side Effects)
Category	Rna Interference	Protease Inhibitors	Lysosomal Enzymes Inhibitors
Stage	Preclinical stage.	A Chinese study published on March 18 involving 199 patients with Covid-19 found no benefit from using the lopinavir/ritonavir combination. Completion in July 2020.	Preclinical (entering soon in clinical trials). Doctors are already prescribing the drug off-label. Some Universities recommend the use of these drugs for very sick patients. FDA has given emergency authorization for distributing donations by Novartis and Bayer.
Mechanism of action	Gene silencing of conserved parts of the SARS-CoV-2 genome, i.e. silencing of gene activity with small interfering RNA molecules (siRNA).	Alternative use of anti-HIV drugs (Lopinavir/Ritonavir = Kaletra) against COVID-19. Lopinavir inhibits viral enzyme's (proteases). Ritonavir inhibits in addition Lopinavir's degradation in the liver (CYP3A4).	The drug raises the Ph of host-cells lysosomes, which prevents the virus' attempt to acidify the lysosomes (necessary for it to enter the host-cells).
Opportunities	Alnylam synthesized more than 350 siRNAs targeting all available genomes of SARS-CoV-2 and SARS-CoV. Some of the siRNA hit the regions of viral RNA: they may be hugely efficacious against Covid.	–	The drug is very cheap (off-patent).
Challenges	–	–	The drug seems to be related to important side effects which include heart and nerve damage and suicidal thoughts.
Drug repositioning?	No.	Yes, anti-HIV drugs.	Yes, approved for malaria and arthritis.

Anti-Inflammatory Drugs

How it works

An infection of the upper and lower respiratory tract causes a respiratory syndrome, inducing the release of pro-inflammatory cytokines. Anti-inflammatory drugs control cytokines release and avoid an immune hyper reaction.

- Cytokines release is a necessary step to fight off the viral infection. But their excessive production may lead to autoimmune damages, potentially lethal.

Impact

These drugs could be useful to treat severely ill patients for the underlying consequence of COVID-19, pneumonia. Anti-inflammatory drugs could receive an emergency approval by the FDA and other drugs agencies in the world in the coming months.

- Most advanced trials are in Phase 2/3, and more top-line data are expected in the next few weeks.
- China has already approved Roche's Actemra in China for the treatment of severe complications related to COVID-19.

Key technologies and players

IL-6 is a pro-inflammatory cytokine that may play a role in driving the overactive inflammatory response in the lungs of patients who are severely or critically ill with COVID-19 infection.

- The role of IL-6 is supported by preliminary data from a single-arm study in China using another IL-6 receptor antibody.
- The two leaders on this field (Sanofi/Regeneron and Roche/Chugai) are in Phase 2/3.

Company	Sanofi/ Regeneron	Roche / Chugai
Name	Kevzara	Actemra (Tocilizumab)
Category	**Anti-Il 6R Antibodies**	**Anti-Il 6R Antibodies**
Stage	Phase 2/3.	Phase 3 is set to begin (already has Chinese approval).
Mechanism of action	Anti-inflammatory drug Kevzara/Sarilumab against immune hyperreaction. It is an anti-IL-6 receptor. More info here.	It is an anti-IL-6 receptor.
Opportunities	It plays an important role in driving the overactive inflammatory response in the lungs of patients severely or critically ill with COVID-19.	–
Challenges	–	–
Drug repositioning?	Yes, initially approved for Rheumatoid Arthritis.	Yes, initially approved for Rheumatoid Arthritis.

Passive Immunization

How it works

Passive immunization provides exogenous, pre-formed antibodies that can prevent or treat infectious diseases. A person receives antibodies or lymphocytes that have been produced by another individual's immune system.

- Production is usually constrained by the need of donor blood (healed patients).
- This approach was already used in several infections such as Ebola, or H1N1.

Impact

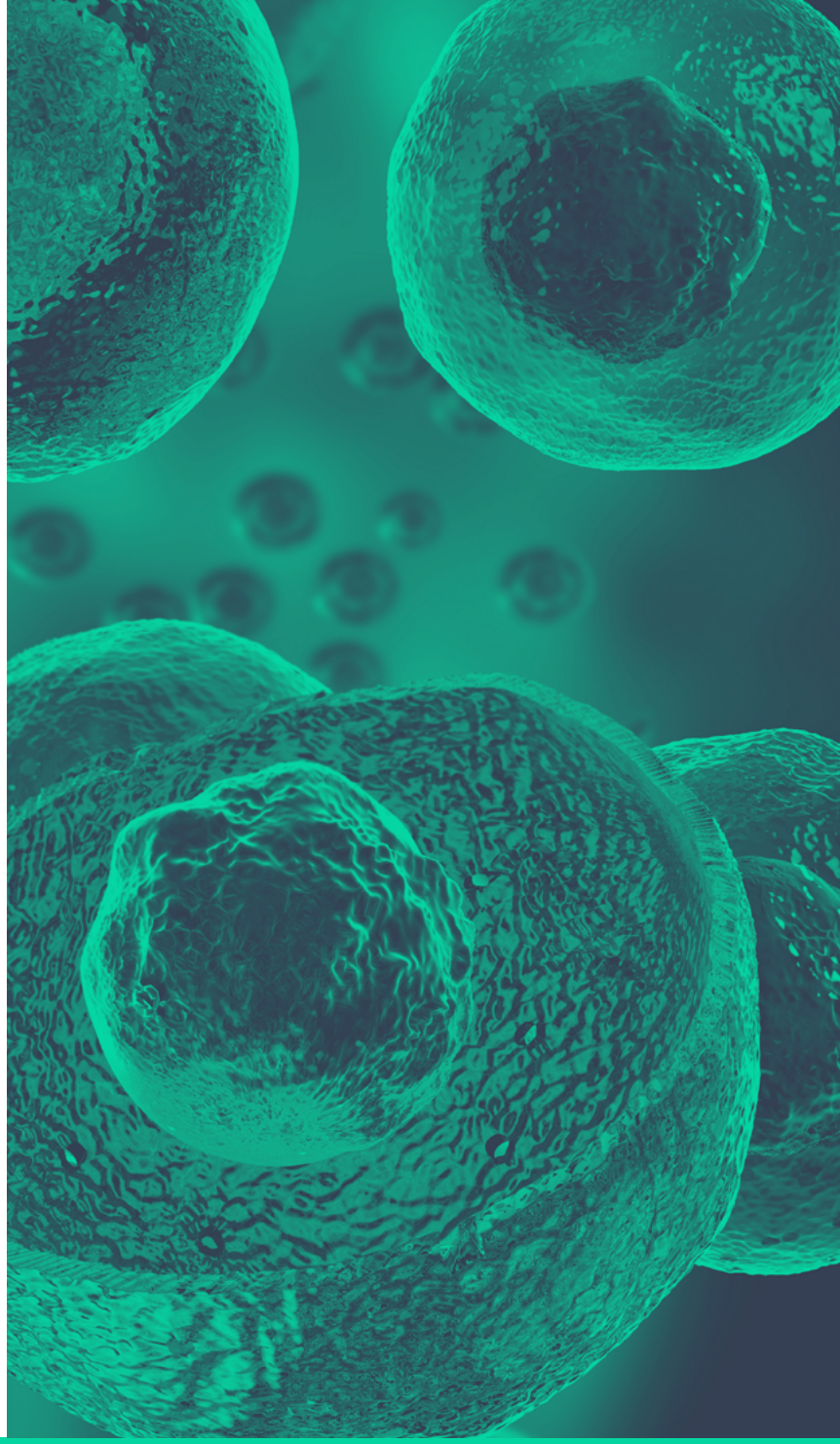
Passive immunization approach has the potential to enhance our immune system to fight against the virus. Compared to a classical vaccine that stimulates the body to produce its own antibodies, passive immunization would be quicker to deploy and effective also on already infected patients.

- A novel approach, but most treatments for COVID-19 are still in preclinical trials.

Key technologies and players

Regeneron is the technological leader, having developed a proprietary platform that is able to produce antibodies using mice, thus avoiding the need for donor blood that constrains most other players.

- Regeneron has already demonstrated the effectiveness of its antibody platform during the Ebola epidemic in Congo. A comparative study of its treatment was stopped ahead of schedule as the results were extremely positive.
- The technology also allows for a quick ramp-up of capacities for large-scale production.



An Overview: Passive immunization

Company	Regeneron	Vir Biotech / Wuxi (Together With Biogen, Vir, Eli Lilly And Abcellera)	Takeda
Name	Regn3048-3051	–	Tak-888
Category	–	–	–
Stage	Preclinical (human studies by early summer).	Preclinical. The company hasn't specified when it expects to have products ready for human testing.	Preclinical. It could skip Phase I and Phase III. Immunoglobulin therapy has a long history of clinical use and, according to the company, the therapy could be available to patients in 12 to 18 months.
Mechanism of action	Monoclonal antibodies are proteins produced by the immune system that can neutralize pathogens. The antibodies target a protein, the spike protein, located on the surface of the virus. The company has immunized its own antibody-generating animal models with a harmless substitute of the new coronavirus, thereby generating potential treatments for the infection. Regeneron will then select the two most potent antibodies to create a "cock-tail" to target the spike protein.	Antibody treatments for coronavirus infection. From a blood sample from a coronavirus survivor, AbCellera (VVancouver-based biotech) identified more than 500 antibodies that might protect against the virus. Wuxi (CDMO) will enhance Vir Biotech manufac-turing capacity.	The principle of the treatment is based on the concentration of Covid-19-specific antibodies present in the plasma collected from cured patients. By transferring these antibodies to a new patient, TAK-888 may strengthen the immune system and help it to better respond to infection. A mechanism of action that has already been proven in other respiratory infections.
Opportunities	Regeneron has its own antibody-generation animal models and doesn't need the plasma of cured patients. The company has the capacity to generate at large scale the amount of antibodies needed.	–	–
Challenges	–	–	Takeda will need to determine the volume of plasma to be collected to prepare a treatment dose and find many donors to ensure efficient production of the treatment. After each collection the plasma must undergo a quarantine period of 60 days before it can be used and therefore the drug could take at least a year to be developed.
Drug repositioning?	No. The passive immunization is a treatment approach already used for several infections such as Ebola, or H1N1. However, each time the cocktail of antibodies is specific to the COVID-19.	No.	No. This type of treatment had been tested in the treatment of H1N1. The antibodies however are specific to the COVID-19.

Active Immunization (Vaccines)

How it works

A vaccine works by training the immune system to recognize and combat pathogens, using weakened (or killed) versions. The body reacts to the vaccine by making anti-bodies, thus ensuring immunization.

- Only specific molecules called antigens (present on all viruses and bacteria) must be introduced into the body to trigger an immune response without risking illness.

Impact

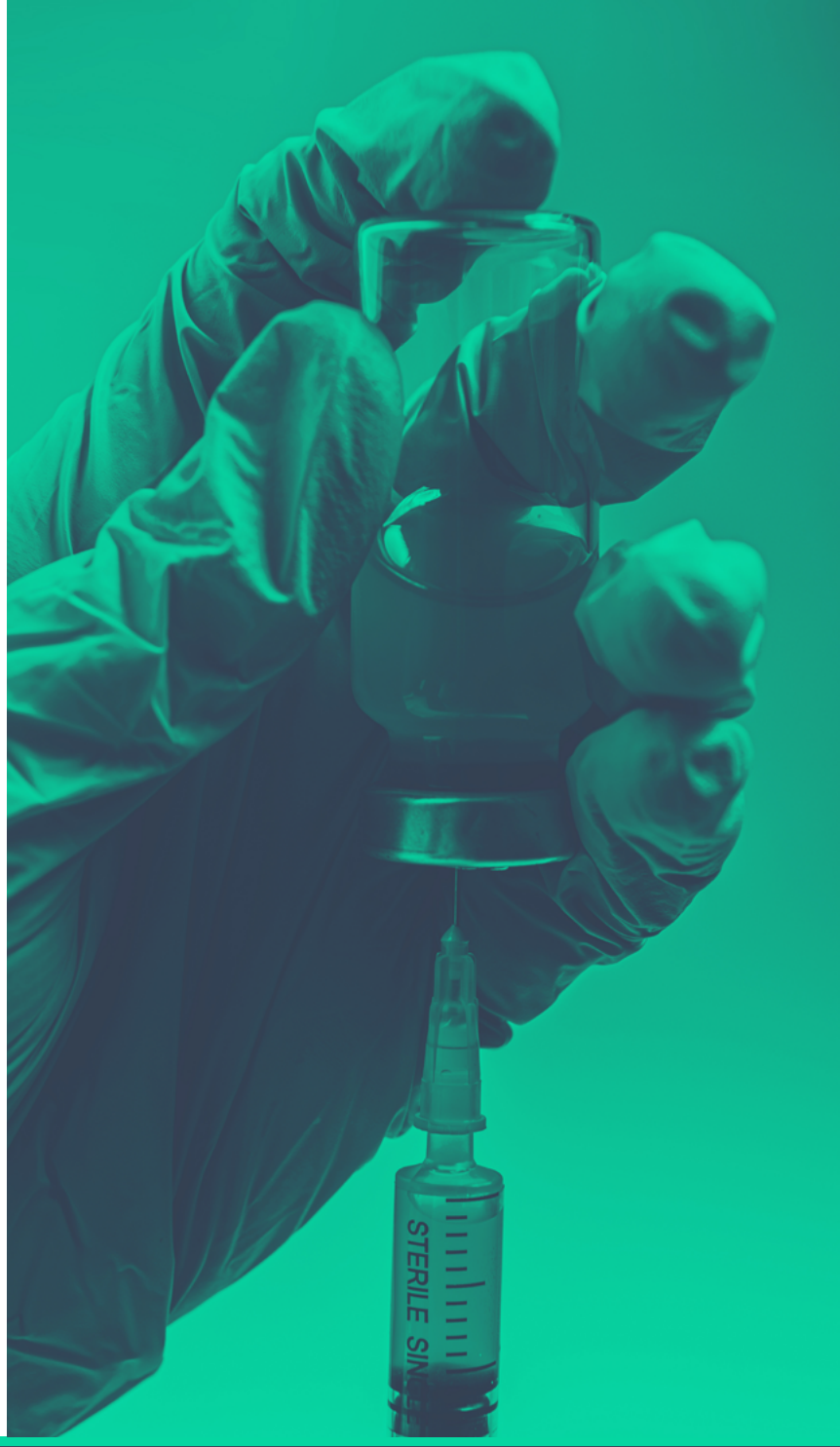
Over the medium term, in order to prevent future COVID-19 outbreaks a vaccine is the only solution. But the real breakthrough would be the development of a universal coronavirus vaccine, which works for every member of the virus family, even when the virus mutates.

- Despite this seeming far-fetched, according to Icosovax (a synthetic biology start-up) it should be feasible and the company is moving its vaccine towards clinical trials.

Key technologies and players

Beyond classical vaccine technologies, novel approaches such as mRNA- and DNA-based are being developed. The main benefits compared to conventional vaccines are lower cost and faster production, allowing a rapid response to epidemics, and they may also have fewer side effects.

- Moderna is leading the race of the vaccine development and is already in Phase 1, using a mRNA- based approach.
- If a mRNA vaccine gets approved for COVID-19, this would be a first for this innovative technology, opening the way for it to be applied to every other type of infection (and even disease).



An Overview: Active Immunization (Vaccines) 1/2

Company	Sanofi	GSK	J&J	Cansino Biologics	Translate Bio/ Sanofi
Name	Protein Subunit Vaccine (Matrix)	As03 Adjuvant System	TBD	Ad5-Ncov	TBD
Category	Classical Vaccines	Classical Vaccines	Classical Vaccines	Classical Vaccines	Rna-Based Vaccines
Stage	Preclinical (Phase 1 clinical trial between March 2021 and August 2021).	Preclinical.	Preclinical – Phase 1 clinical trial by the end of 2020 (September).	Phase 1 to begin. In China, healthy adults 18 to 60 years of age in Wuhan will be tested.	Research
Mechanism of action	Sanofi Pasteur is a leading vaccine maker. The company uses its recombinant DNA platform to produce antigens (found on the surface of COVID19).	GSK is a leading vaccine maker (human papillomavirus (HPV), seasonal flu, etc.). This compound is an adjuvant - it will be used jointly with other compounds to strenghten their action.	The vaccine would introduce patients to a deactivated version of the virus, triggering an immune response without causing infection.	CanSino's approach is to take a piece of genetic code from the coronavirus and wrap it with a harmless virus, exposing healthy volunteers to a new infection and stimulating the production of antibodies.	The company uses strands of mRNA to spur the production of protective antibodies.
Opportunities	–	–	–	–	–
Challenges	–	–	–	–	–
Drug repositioning?	No.	It is an adjuvant. GSK used AS03 in the Pandemrix vaccine it developed to protect people against a pandemic H1N1 strain that circulated in 2009 and 2010.	No. The vaccine program will leverage Janssen's AdVac® and PER.C6® technologies that provide the ability to rapidly upscale production of the optimal vaccine candidate. These are the same technologies that were used in the development and manufacturing of Janssen's investigational Ebola vaccine, which is currently deployed in the Democratic Republic of Congo and Rwanda. They were also used for the Company's Zika.	No. Ad5-nCoV is developed with Cansino's adenovirus-based viral vector vaccine technology platform, which utilizes adenoviruses as viral vectors to deliver vaccine antigens to the human cell. Previously, the technology platform was key in enabling Cansino to translate its Ebola virus disease vaccine, Ad5-EBOV, from a concept to an approved product in merely three years.	No.

An Overview: Active Immunization (Vaccines) 2/2

Company	Moderna	Biontech/ Pfizer	Curevac (Private)	Inovio	Distributed Bio (Private)
Name	mRNA-1273	Bnt162	Sars-Cov 2 Mrna Vaccine	Ino-4800	Centivax
Category	Rna-Based Vaccines	Rna-Based Vaccines	Rna-Based Vaccines	Other Vaccines Techniques	Other Vaccines Techniques
Stage	Phase 1. The project builds on four years of work, including six positive Phase 1 clinical readout. Moderna has a technological platform with more than 20 products in development, a fully integrated manufacturing and development site. It benefits from the support of the NIH, which places it in a favourable position to respond to public health threats. If mRNA-1273 proves safe in Phase 1, Moderna will enrol a larger population of other patients to determine whether the vaccine is effective.	Preclinical. Clinical trials expected in late April in the US and Germany.	Preclinical. CureVac expects to have a vaccine ready for animal testing by April, with the intention of initiating a clinical study this summer. Phase 1 in June or July.	Preclinical.	Preclinical.
Mechanism of action	Moderna's product is a synthetic strand of messenger RNA, or mRNA, designed to induce cells to produce antibodies against the virus.	The company uses strands of mRNA to spur the production of protective antibodies.	The company uses strands of mRNA to spur the production of protective antibodies.	It uses DNA sequences from the virus to target specific parts of the pathogen, which they believe the body will mount the strongest response to. They then use the patient's cells to become a vaccine factory, increasing the body's natural immune response mechanisms. Inovio expects its vaccine to be tested in humans in early summer.	A computational approach that finds the unique molecular features on the surface of a range of different pathogens, then uses antibodies against the parts of those pathogens that do not mutate over time. A universal vaccine designed for almost any virus at a fast pace.
Opportunities	Speed in clinical trials.	Partnership with Pfizer will facilitate manufacturing and distribution hurdles.	–	–	As their influenza program works towards being applied to the $165M animal market and $3.2B human market, they also expand studies into other critical unmet needs, such as flaviviruses and HIV.
Challenges	Safety tests of mRNA vaccines have turned up adverse side effects, and it's not clear how potent they'll be. mRNA vaccines remain unproven, but they have proven to have faster development timeline. Moderna may not have the manufacturing capability to ramp up vaccine production in large scale.	–	–	–	–
Drug repositioning?	No.	No.	No.	No.	No.

Diagnostic Testing

How it works

Diagnostic testing is based on three possible approaches: detect viral RNA, detect antibodies, detect the presence of pulmonary pathology.

- Currently the most used tests are those detecting the viral RNA: tests could have high specificity, but will only detect an « active infection ».
- Detecting antibodies involves exposing a blood sample to proteins that mimic the coronavirus' spiky casing; if antibodies in the blood attack the protein, the sample changes color. The risk is missing early-stage infections.
- CT scans help identify and characterize pneumonia. However, the technique is not able to differentiate among different types of pneumonia.

Impact

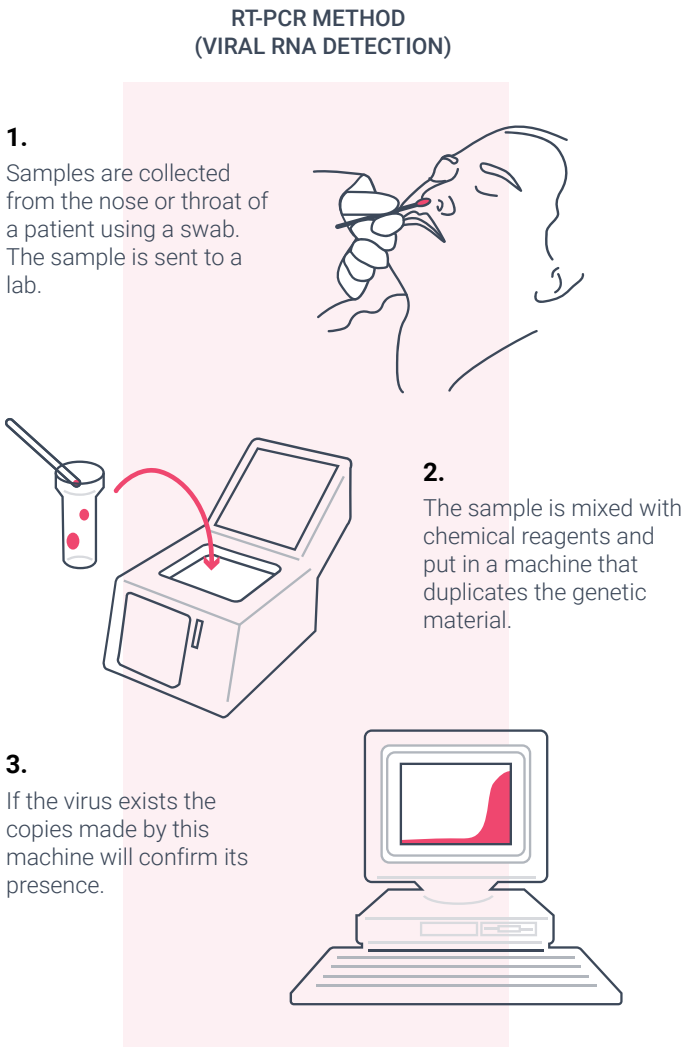
Diagnostic testing is one of the critical factors in the fight against the spread of COVID-19: patients and suspected people are identified and isolated more quickly. Early diagnosis allows adequate public safety measures to be put in place and to decongest hospitals.

- In countries where tests have been conducted at massive scale (notably in South Korea), a flatter spread curve has been observed.

Key technologies and players

The main technological race is in the detection of viral RNA, where RT-PCR tests are the current « golden standard », but Next Generation Sequencing (NGS) and CRISPR-Cas are quickly becoming valid alternatives.

- RT-PCR suffers from a number of shortcomings, notably in terms of time to result and false negatives rate, impacted by elements exogenous to the test itself.
- NGS allows to detect presence of an infectious agent even without knowing which one it is, and read its full genome sequence, which allows also to track mutations.
- CRISPR-Cas machinery provides an accurate response in 10-15 minutes, but the technology is still in its testing phase, and is not yet widely available.



An Overview: Diagnostic Testing

Test detects:	Presence of the viral RNA	Presence of the viral RNA	Presence of the viral RNA	Antibodies produced	Presence of pulmanory pathology
Subtype	**RT-PCR**	**Next-Generation Sequencing**	**CRISPR-Cas**	**Serology**	**CT Scan**
Mechanism	The classic way to detect the presence of the virus into our bodies is using tests based on Real-Time Polymerase Chain Reaction (RT-PCR) machines. A doctor collects samples from the patient by swabbing his nose or throat. The sample is sent to a laboratory and mixed with reagents in a tube. The tube is finally put into a RT-PCR machine. In the case of the corona-virus, RT-PCR machines make use of reverse transcriptase-polymerase chain reaction. As coronaviruses have genomes encoded by RNA, RNA is copied in the reverse direction to get a complimentary copy of the virus genome in the form of DNA.	The technology allows to detect viruses before previous knowledge of the infectious agent, and read the complete genome of the Covid-19 for research and diagnostic purposes (compare strains, differentiate them from other coronaviruses and perform surveillance activities right at the time of diagnosis).	CRISPR-Cas machinery is able to rec-ognize specific genetic sequences and cut them off. The test could diagnose the coronavirus in 10 to 15 minutes.	The Covid-19 infection causes the immune response and the produc-tion of antibodies. These antibodies include the Immunoglobulins M (Ig M) and the Immunoglobulins G (Ig G). A big goal is to develop a test able to detect antibodies that someone has produced to fight the virus, which could enable to detect asymptomatic patients and those who have already recovered. In addition, serology can be used to study antibodies' production of recovered patients and how long the immunity of the virus lasts, which is essential to develop a good vaccine.	CT scan imaging helps identify and characterize pneumonia. However, the technique is not able to differentiate among different types of pneumonia.
Company	See detailed overview in next table	Illumina (together with IDbyDNA), BGI (together with Areas Genetics)	Mammoth Bioscicence, Sherlock Bioscience with Cepheid (Danaher), Caspr Biotech	Scanwell Health; Innovita Biological Technology Co. Ltd.; Lemonaid Health, CTK Biotech, Guangzhou Wondfo Biotech, Jiangsu Medomics Medical Technologies, Snibe Diagnostic, Sona Nanotech, Zheijiang Orient Gene Bio-tech, Biomerica, Sugentech, Xiamen AmonMed Biotechnology, Pharmact	Philips, Fujifilms Holdings, GE Health-care, Siemens Healthcare, Shimadzu Corporation, Hologic

Focus On RT-PCR diagnostics: Market Overview 1/2

RT-PCR Manufacturers	Quest Diagnostics and LabCorp.	Abbott	Roche	Thermo Fisher	Cepheid (Danaher subsidiary)	Mesa Biotech	Beckton Dickinson
Name	Tests are actually administered by diagnostic laboratories, including large companies like LabCorp and Quest Diagnostics.	m2000 RealTime system / ID Now System	Cobas 6800/8800	Applied Biosystems 7500 Fast Dx Real-time PCR instrument	GeneXpert Xpress COV-ID-19 test systems	Accula System	BD Max systems
Stage	Habilitated to offer Covid-19 diagnostic services.	EUA granted.	EUA granted. CE Mark.	EUA granted.	EUA granted.	EUA granted. CE Mark.	Submitted to the FDA. CE Mark.
Time to run the test	3 to 4 days turnaround time.	The systems have the ability to run high volumes of up to 470 tests in 24 hours / The system detects the disease in 5 minutes.	The device provides up to 96 results in about three hours.	Provides results within 4 hours.	About 45 minutes to deliver results as the test can be based near an emergency room or operating room.	Point-of-care coronavirus test: available anywhere outside of the laboratory in about 30 minutes.	Its test is complete in two to three hours (and 120 tests in 8 hours per machine).
Current capacity	These big U.S. laboratories have significantly increased the nation's coronavirus testing capacity in recent weeks (20'000/25'000 tests a day) and are increasing capacity further.	Abbott will immediately ship 150,000 tests to existing U.S customers / The most widely available molecular point of care testing platform.	In total, there are currently 827 of the systems distributed worldwide, over a hundred of which are in the U.S.	More than 1.5 million tests available to ship at 2,000 labs.	The company said there are nearly 5,000 of the automated systems currently deployed throughout the U.S., with more than 23,000 around the world. The test doesn't require cotton swabs, which are running in short supply in some places. Doctors can use saline to aspirate fluid from the nose with a catheter instead. In addition, the test is the first point-of-care coronavirus test.	–	There are 500 of those systems in the U.S. and another 500 in Europe.
Expected capacity	The companies will soon be able to process more than 100'000/300'000 tests weekly.	The goal is providing up to 1 million tests per week / Combined with the tests run on m2000 system, the goal is to produce 5 million tests per month.	Roche said it could manufacture millions of tests a month (400,000 per week).	Thermo Fisher said it will be able to produce 5 million tests a week by April.	Cepheid will produce millions of tests over the next few months.	–	–

Focus On RT-PCR diagnostics: Market Overview 2/2

RT-PCR Manufacturers	Biomerieux	Novacyt	Hologic	EveryWell	Eurofins Scientific	Qiagen	Other
Name	Diagnostics	Genesig real-time PCR COVID-2019 assay	Panther Fusion SARS-CoV-2 assay	COVID-19 test	BioFire COVID-19 test	"QiAstat Dx detection kit (acquisition by Thermo Fisher)"	BGI Group, Kogenebiotech GenMark Diagnostics, Quidel Corp., Diasorin, Q2 Solutions, Heat Biologics, Dixon Corporation, Co-Diagnostics , Sophia Genetics, Bio.Rad
Stage	EUA granted.	EUA granted CE Mark.	EUA granted.	EUA granted.	EUA granted.	Submitted to the FDA.	–
Time to run the test	It will deliver results in 45 minutes.	Capable of providing results in 24-48 hours.	The test is designed for use in a system that can process up to 1,000 tests in 24 hours.	"At-home Covid-19 test. (FDA update cautioning against at-home tests; in response, the test is now restricted to health care professionals and hospitals or health care companies.)"	It will deliver results in 45 minutes.	It will deliver results in 1 hour.	–
Current capacity	–	–	–	–	10'000 tests per day	–	–
Expected capacity	–	–	Expects to ship tens of thousands of tests this month.	–	15'000 tests per day	10 millon tests total	–

Respiratory Machines

How it works

Ventilators are machines that support breathing. These machines are mainly used in hospitals, and are of different types: noninvasive ventilation (NIV), invasive ventilation (IV), bilevel devices (BLDs).

- NIVs deliver air to the patients through a mask or a mouthpiece.
- IVs deliver air through a tube inserted in the trachea by either intubation or tracheotomy.
- BLDs (non-invasive) deliver two distinct air pressures for inhaling and exhaling.

Impact

Ventilators get oxygen into the lungs, remove carbon dioxide from the body, and basically support patients with respiratory insufficiency and failure. They are essential for critical cases, where the COVID-19 infection has caused damage to the lungs' tissues and pneumonia is worsening.

- Hospitals have a limited number of machines and if they get overwhelmed during massive outbreaks, it becomes impossible to provide adequate care to all patients.

Key technologies and players

Technology is fairly standardised, and the race is to both produce the ventilators in volumes, and « multiply » the number of patients that can be served by an existing machine.

- Major medical devices producers have these machines in their catalogs.
- Automotive manufacturer are being pushed to provide manufacturing capacity by converting existing plants.
- Prisma Health announced a breakthrough system allowing the use of a single ventilator machine on four patients at the same time.

Catalysts

- **Improving COVID-19 data from Italy.** Passing the peak and showing that confinement measures work will reboost hope and confidence.
- **New treatment.** Any drug that shows reliable positive results from advanced trials will help reduce fears in the population.
- **China.** Continued control of the epidemic and resuming « normal » life will provide a useful benchmark to start anticipating how the future will shape.

Risks

- **Italy setback.** A renewed deterioration in case numbers it Italy would undercut all current hopes that measures are working.
- **Delay in flattening the curve after peak.** Confinement measures lasting too long risks being worse than the ill they are attempting to cure.
- **China.** The materialization of the feared second outbreak would be a blow to all hopes of bringing the situation under control.

Bottom Line

- The medical world is on the front line fighting the COVID-19 pandemic, at all levels.
- Technological breakthrough and innovation often come in times of need and emergency, and we believe this will not be the exception. As energies are focused on fighting the coronavirus outbreak, novel methodologies are being deployed and tested in real-time. They are likely to remain once this battle is over.
- We remain convinced that the alliance of technology and medicine remains the key driver going forward. It is a structural trend that is being reinforced by the COVID-19 crisis and that we continue to leverage through our investment themes in Biotechnology, Bionics, and Artificial Intelligence & Robotics.

Companies mentioned in this article:

Abbott (ABT US); Abbvie (ABBV US); Abcellera (not listed); AIM Immunotech Inc (AIM US); Alnylam Pharmaceuticals (ALNY US); Altimmune (ALT US); Ascletis Pharma (1672 HK); Bayer (BAY GR); Becton Dickinson (BDX US); BGI Genomics (300676 CN); Biogen (BIIB US); Biomerica Inc (BMRA US); Biomerieux (BIOX FR); Biontech (BNTX US); Cansino Biologics (6185 HK); Chugai (4519 JP); Co-Diagnostics (CODX US); CTK Biotech (not listed); Curevac (not listed); Danaher (DHR US); Diasorin (DIAS IT); Distributed Bio (not listed); Dixon Corporation (not listed); Eli Lilly and Company (LLY US); EUROIMMUN (subsidiary of PerkinElemer Inc, PKI US); EveryWell (not listed); Eurofins Scientific (EUFI FR); Fujifilm (4901 JP); General Electric (GE US); GenMerk Diagnostics (not listed); Gilead Sciences Inc (GILD US); GlaxoSmithKline (GSK LN); Guangzhou Wondfo Biotech (300482 CN); Heat Biologics (HTBX US); Hologic (HOLX US); Illumina (ILMN US); Innovita Biological Technology (not listed); Inovio (INO US); Jiangsu Medomics Medical Technologies (not listed) ;Johnson & Johnson (JNJ US); Kogene Biotech (not listed); LabCorp (LH US); Lemonaid Health (not listed); Mammoth Biosciences (not listed); Medicago (not listed); Mesa Biotech (not listed); Moderna Therapeutics (MRNA US); No Borders (not listed); Novacyt (ALNOV FR); Pfizer (PFI US); PharmACT Holding AG (not listed); Philips (PHG NV); Quest Diagnostics (DGX US); Qiagen NV (QGEN US); Quidel Corp (QDEL US); Q2 Solutions (not listed); Regeneron (REGN US); Rising Pharmaceuticals (not listed); Roche (ROCG SW); Sanofi (SAN FP); Scanwell Health (not listed); Sherlock Biosciences (not listed); Shimadzu Corporation (7701 JP); Siemens (SIE GR); Snibe Diagnostic (not listed); Sona Nanotech (SONA CA); Sophia Holdings Co (6942 JP); Sugentech Inc (253840 KR); Takeda Pharmaceuticals (4502 JP); Thermo Fisher Scientific (TMO US); Tonix (TNXP US); Translate Bio (TBIO US); Vaxart Inc (VXRT US); Veredus Laboratories (not listed); VIR Biotechnology (VIR US); Wuxi Biologics Cayman (2269 HK); Xiamen AmonMed Biotechnology (not listed); Zhejiang Hisun Pharmaceutical (6002676 CN), Zheijiang Orient Gene Biotech (688298 CN)

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