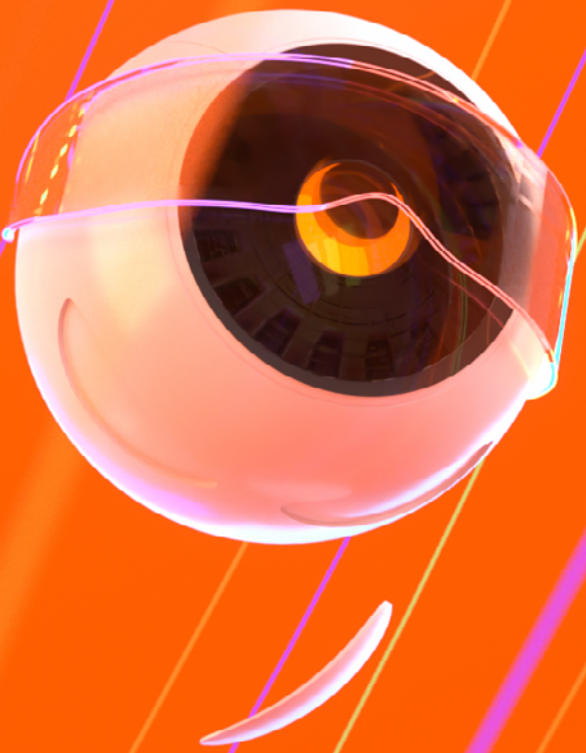
Investment Recipes

by AtonRā Partners



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On the Menu

HUMAN-LIKE MACHINE VISION

Sensors Inspired By Neurosciences

New opportunities for machine vision

Event-based vision systems, built on the foundation of neuromorphic engineering, are making the leap from lab to market.

- Event-cameras are mimicking the way human vision works and demonstrate orders-of-magnitude performance gains vs. conventional sensors (100x faster).
- Autonomous cars drive an explosive demand for sensors, and the market for such sensors is expected to grow to $11bn over the next 15 years.

A new breed of camera sensors

Neuromorphic sensing takes advantage of biological sensory functions to enable the design of machine vision systems aiming at sensing information.

- Leveraging this approach, Sony presented the first Artificial Intelligence (AI) Integrated Image Sensor in May 2020.
- Pre-processing of visual information allows for a faster, cheaper deep-learning pipeline and lower power usage, enabling edge computing.

Leveraging biology and silicon opens new markets

Associating the natural performance of biology-inspired systems and the benefits of the silicon capabilities and economies of scale enables new market opportunities.

- Big names like Tesla, Ambarella and Mobileye / Intel are developing autonomous driving vehicles using neuromorphic sensor-based cameras.
- Cost-sensitive markets which cannot afford LiDAR (see our previous article) like robotics and augmented/virtual reality (AR/VR) are likely to leverage this emerging technology.

SOURCE:
Yole: "Neuromorphic Sensing and Computing 2019" – September 2019

Brain-Inspired Electronic Structures

Drawing inspiration from the human brain

Neuromorphic technologies describe cybernetic systems (silicon and software) that mimic the brain structures, organization and functions with the goal of leveraging its amazing sensing and computing capability.

- Neuromorphic sensing and computing market is expected to grow at a CAGR of 100% in the next 15 years, from a very low base to $26bn in 2034.

The silicon brain

Fundamental research in neuroscience to unveil brain mechanisms is attracting a lot of attention and funding. Understanding the dynamic processes in and around the brain accelerates the emergence of neuromorphic technologies.

- The Human Brain Project is the largest scientific project ever funded by the European Union (€1bn grant awarded in 2013).
- The US BRAIN Initiative has obtained over 700 awards totaling ~$1.3bn.

A massive leap forward in performance

Neuromorphic engineering is bringing a new level of power and performance in machine vision systems, by mimicking the way human neurosensory system separates events from the background.

- Prophesee's bio-inspired image sensors produce up to 1'000 times fewer data than usual sensors whilst achieving a frame rate up to 10'000 fps.
- Intel's Loihi is as much as 1'000 times faster and 10'000 times more efficient at certain tasks than conventional processors.

SOURCE:
Yole "Neuromorphic Sensing and Computing 2019" – September 2019

The Human Visual System

Vision, the human dominant sense

The eye is the sensory organ detecting visual information from the environment and relaying it to the visual cortex, giving us the sense of sight.

- 80% of all sensory data processed by the human brain is acquired by the visual system. Processing starts in the retina itself.
- The visual information perceived by the eye is the light reflected by objects in the environment converted into electrical spikes.

The retina architecture

Photoreceptor cells found in the retina are specialized in converting perceived light into electrical information, transmitted to the brain for processing.

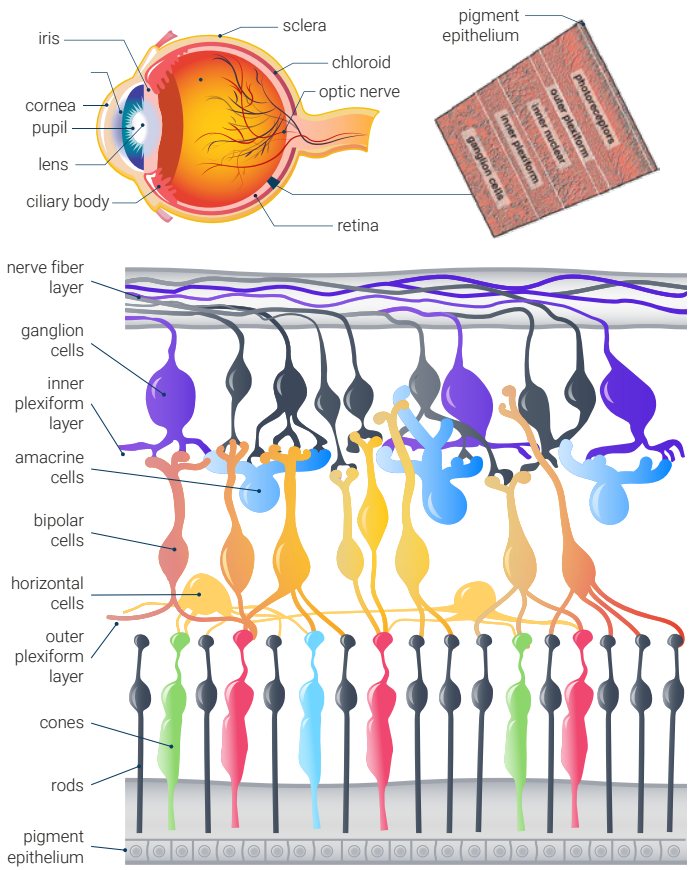
- Human retina contains about 130 million photoreceptors (rods and cones) that can be related to pixels in conventional image sensors.
- Emerging neuromorphic sensors mimic the organization of the photoreceptors composing human retina.

How do we process visual information?

The visual system doesn't work like a standard camera which synchronously acquire the full information from the environment. Photoreceptors in our eyes are firing (activated) only to changes in the scene.

- This mechanism allows to eliminate useless information and therefore reduces dramatically the energy consumed.
- It also favors visual motion sensing, which is crucial for detecting a potential mate, prey, or predator, hence is articulated with cognitive processes.

THE HUMAN EYE AND RETINA STRUCTURE



SOURCE:
Research Gate

The Silicon Retina

Conventional cameras - inspired by nature

Cameras' structure have long been inspired by the human eye: external lenses fronting sensors with multiple pixels sensing light. Motion has been captured by photographing and playing back stroboscopic sequences of images (or frames).

- Human eye can achieve real-time information capture up to 500mn pixels.
- Best photo systems reach this range, yet video only reaches 8K (33mn pixels).

Event-based cameras - inspired by neuroscience

A step forward has recently been achieved in neuromorphic sensing thanks to a better understanding of dynamic vision. The human eye is designed to provide the brain only useful information from the environment.

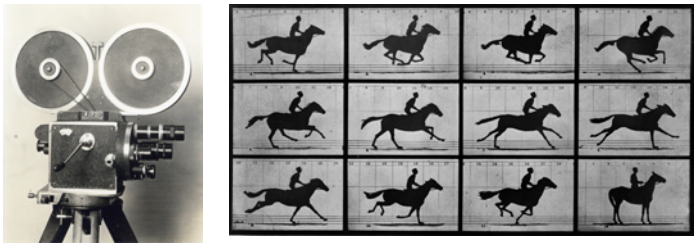
- Event-based cameras, like the human eye, only capture changes or events in scenes and ignore non-useful information.
- Event-based cameras achieve much better temporal resolution than conventional cameras while consuming less energy.

Less but more informative data

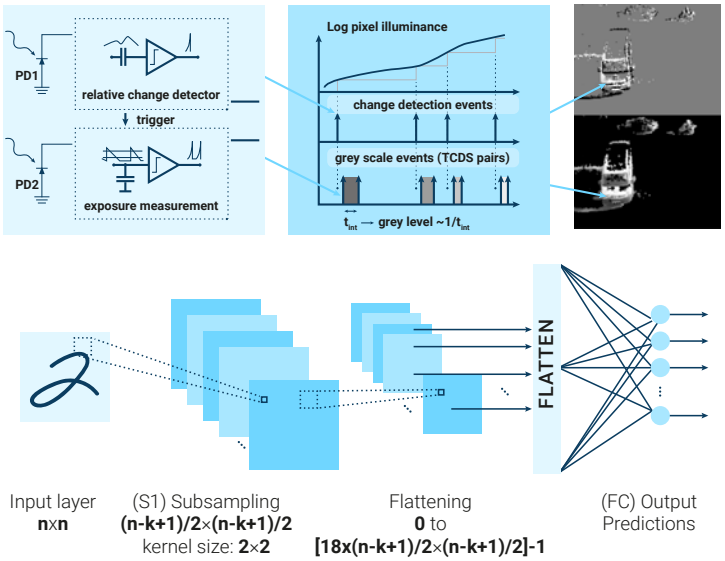
Neuromorphic vision sensors allow to surpass the limit imposed by conventional commercial cameras on deep-learning applications.

- Asynchronous data capture enables up to 10'000 fps vs. 30 to 60 fps for conventional sensors, thus faster training and inferring.
- As only events are recorded, edges are filtered by construction and the amount of data to compute is much lower (up to 1'000x less data) allowing for high-speed AI processing already at the edge device level.

CONVENTIONAL IMAGE SENSOR CAPTURE FRAMES – GENERATING A LOT OF DATA

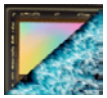


NEUROMORPHIC SENSORS CAPTURE INFORMATION



SOURCE:
Wikimedia – Digital Commons,
"An asynchronous time-based image sensor",
2008 IEEE International Symposium on Circuits and Systems and "An Event-Driven Classifier for Spiking Neural Networks Fed with Synthetic or Dynamic Vision Sensor Data", Frontiers in Neuroscience

Event-Based Vision – An Approach To Rule Them All?

	RADAR	LIDAR	ULTRASOUND	FRAME-CAMERA	EVENT-CAMERA
					
Light independent	✓	✓	✓	✗	✓
Computational cost	=	−	=	✗	✓
Detection speed	✓	−	✗	−	✓
Optical information	=	✗	=	✓	✓
Passive	✗	✗	✗	✓	✓

SOURCE:
Adapted from "A new neuromorphic strategy for the future of vision for machines" – X. Lagorce . ICRA 2017 (International Conference on Robotics and Automation), Prophesee.ai

Large Industrial Market Opportunities

Advanced driver-assistance systems (ADAS)

ADAS' goal is to increase safety and minimize human errors. Electrical and self-driving vehicles require more sensors and computing power, which account for consumption of up to 50% of the battery's capacity.

- Event-based sensors have a very low power consumption and can capture movements 1'000x faster than current cameras to help obstacle avoidance.
- Renault-Nissan and Robert Bosch invested in Prophesee (partnering with Sony).

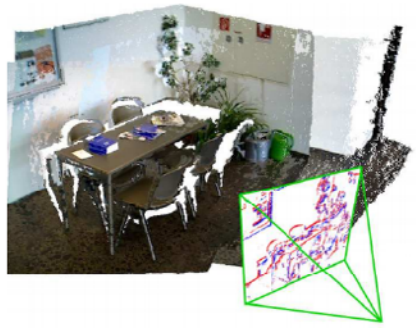
GoPro Hero 6

Event Camera by Prophesee

AR/VR

Head-mounted VR and AR devices need to both provide and receive real-time information about where things are located and how they are moving in order to create the illusion of reality (tracking both the environment and the eye's fast motion).

- Very low latency and low power consumption make event-based cameras very appealing for applications in this domain.
- Apple, Google and Facebook have been acquiring eye-tracking companies.



Smart factories

Machine vision is a key component of manufacturing automation, enabling costs reduction while increasing productivity. Robots and inspection equipment should identify defective products and sort them in real time.

- Event-driven paradigm is seen as an essential part of next-generation real-time autonomous robots – current field studies show ~2'000x power reduction.
- Global Industrial Vision Market is expected to grow at $16bn by 2025, ~10% CAGR, driven by smart factory automation, autonomy and security.

SOURCE:
Prophesee.ai,
"Event-based, 6-DOF Camera Tracking from Photometric Depth Maps", IEEE transactions on pattern analysis and machine intelligence

Catalysts

- **Autonomous vehicles.** Power-efficiency and high dynamic range (up to 140dB) of event-based cameras accelerate the transition towards autonomous vehicles (simpler sensors and AI pipelines).
- **Prophesee/Sony world's first sensors with on-board AI processing.** Image sensors will be in products by the end of the year, with original equipment manufacturers expected to adopt them in 2021.
- **Partnerships and M&A.** Computer vision leaders (Sony/Samsung) acquiring/partnering with startup developing dynamic vision systems (Insightness/IniVation) leads to mass availability and cost reduction.

Risks

- **Automotive industry inertia.** Although ADAS is a fast-growing market, the automotive industry tends to favor a 'belt and braces' approach as safety and reliability are of paramount importance.
- **Lower prices for competing technologies.** LiDAR, RADAR and SONAR are already widely accepted in complementing conventional imaging systems, and have been on a cost reduction trend for some time.
- **High-dynamic range sensors.** Specialized image sensor companies (ON Semiconductor, STMicroelectronics) improve global-shutter sensors for machine vision – extending the market reach of current solutions.

Bottom Line

- Event-based vision systems are now reaching the market. We believe this opens new opportunities for the machine vision industry, robotics and autonomous vehicles. Event-cameras are already competitive vs. LiDAR and RADAR solutions and can leverage the semiconductor sensors economy of scale to enable machine vision growth in cost-sensitive markets.
- Automotive (autonomous vehicles) is seen as the most promising opportunity for neuromorphic cameras. Such architecture could enable high-value differentiated products for image sensor leaders and reinforce the leading position of image-based ADAS companies, to which our portfolios are already exposed.

Companies mentioned in this article:

Ambarella (AMBA.US), Baidu (BIDU.US), CelePixel (not listed), IniVation (not listed), Intel (INTC.US), Prophesee (not listed), Sony (6758.JP), Samsung Electronics (005930.KS), Tesla (TSLA.US)

PC IS DEAD, LONG LIVE THE CLOUD

Cloud Computing Is Everywhere

Datacenters demand driven by cloud computing services

In a recent article we outlined the potential for chip players at warehouse-scale datacenters, and the increasing need for computing performance and power efficiency. Cloud computing services are the driving force as they are major users of these datacenters.

- By 2022, 90% of companies will be using cloud services.
- 32% of IT budgets will be dedicated to the cloud in 2021.

A “big tech” battleground

Through cloud computing, firms outsource data management to focus on what they do best, their core business. Tech giants quickly understood the disruptive power of remotely hosted infrastructure and the potential of an improved developer experience.

- Amazon Web Service with a cloud computing offering was launched in 2006, Microsoft Azure in 2010.

The era of cloud computing is only beginning

Cloud computing is only starting. Organizations are going to increase their exposure to cloud providers, which are the only one able to address the demand for more storage, more computing power, and faster software integration.

- Future developments in cloud computing are linked to ubiquitous AI, 5G and higher integration with edge computing, multi-cloud approaches, etc.

SOURCE:
Gartner, IDG Cloud Computing Survey 2020

A Fast-Growing Market (1/2)

Untapped potential is huge

Cloud computing is not only about servers and storage. It covers all computing services including analytics and intelligence and allows faster innovation, flexible resources and economies of scale. In a quickly digitizing world, the covered market is still relatively small, and potential remains huge.

- The total cloud market is expected to reach approx. $500bn by 2025, growing at a CAGR of 18%.

Classification of cloud services

Cloud computing is mostly offered in a service-oriented architecture, where users can check the services they want to outsource. For vendors, Everything-as-a-Service models result in recurring revenues and higher customer retention.

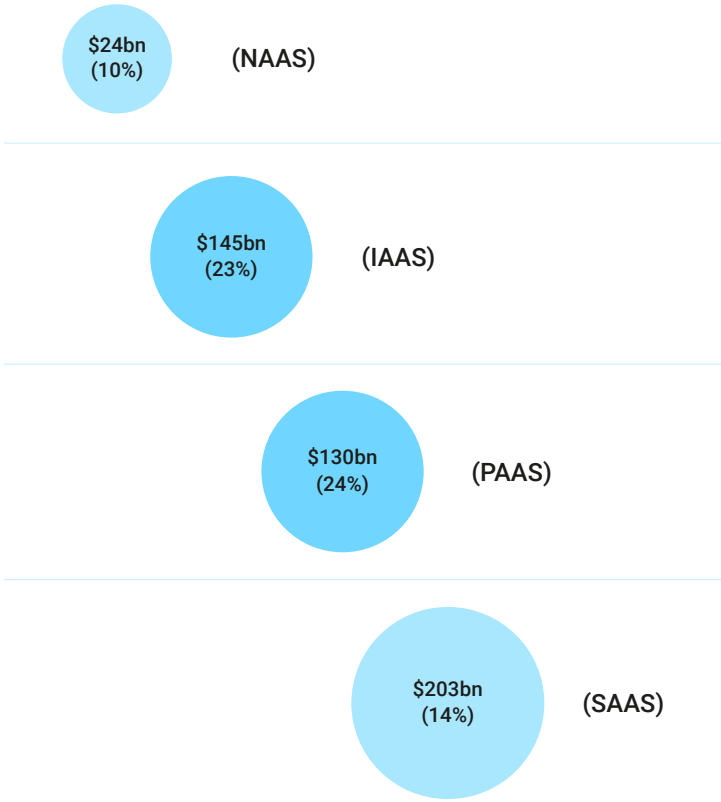
- Over time the offer bundles have expanded, going from Network-as-a-Service (NaaS), to Software-as-a-Service (SaaS).

COVID-19 has boosted cloud computing

Cloud computing enables people to work from any location. Following the COVID-19 outbreak, organizations were forced to shift to remote working for the safety of employees. But this transition is only starting, as many companies and organizations remain under-exposed to cloud solutions.

- According to Gartner, 37% of companies plan to shift some of their employees to remote working permanently.
- As per Global Workplace Analytics, 25-30% of the US workforce will work from home several days a week by the end of 2021 (vs <5% before).

FORECASTED 2025 MARKET SIZE (5-YEAR CAGR IN %)



SOURCE:
Global Workplace Analytics, Gartner, AtonRâ Partners

A Fast-Growing Market (2/2)

Network-as-a-Service (NaaS)	Infrastructure- as-a-service (IaaS)	Platform-as-a-Service (PaaS)	Software-as-a-Service (SaaS)
Optimization of resource allocations by considering network and computing resources as a unified whole	For users who don't want to acquire and maintain equipment in their own facility	Tools for development, testing, deployment, hosting and application maintenance	Applications running on a cloud infrastructure
Firewalls, security	Firewalls, security	Firewalls, security	Firewalls, security
Networking	Networking	Networking	Networking
	Virtualization	Virtualization	Virtualization
	Storage	Storage	Storage
	Data center & servers	Data center & servers	Data center & servers
		Operating systems	Operating systems
		Middleware	Middleware
		Development tools	Development tools
			Hosted applications
			Data

SOURCE:
Global Workplace Analytics, Gartner, AtonRâ Partners

A Large Pie For A Few Players

A cloud oligopoly due to high barriers to entry

Big Tech companies are the undisputed leaders in the cloud industry. They have the required financial resources to expand and maintain the infrastructure. Moreover, they have managed datacenters for their own use for years, building up the required know-how and experience for selling such services.

- The combined market share of Amazon, Microsoft and Google for public IaaS and PaaS is north of 60% (and rising).

Competitors are trying to increase their presence

The potential market is large enough for additional players to develop behind the three market leaders. Given the size difference, various tactics are deployed to gain market shares: niche offering, pricing, interoperability, etc.

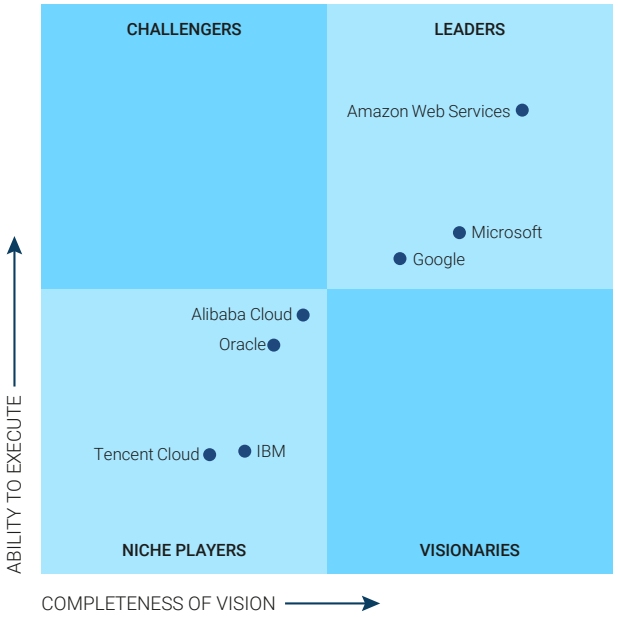
- IBM acquired Red Hat for $34bn in 2019 to transform its business model, targeting primarily its historical clients (e.g. in finance).
- DigitalOcean was founded in 2011, focusing on the developer experience.

Watch out for China

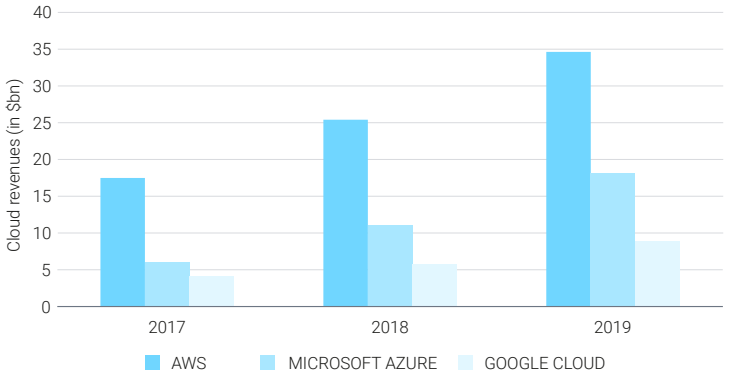
Cloud computing is developing quickly in the APAC region, especially in China where large investments and accommodative policies have supported local companies. A geographical divide remains as western organizations remain reluctant to store data on Chinese (and broadly, Asian) clouds and viceversa.

- Alibaba Cloud generated $1.7bn in the last quarter (+53% YoY, 8% of total revenues), and should become profitable this financial year.
- Alibaba plans to invest CNY200bn ($30bn) to scale up its cloud infrastructure over the next three years.

GARTNER'S MAGIC QUADRANT FOR CLOUD INFRASTRUCTURE AND PLATFORM SERVICES



CLOUD REVENUE EVOLUTION OF MARKET LEADERS



SOURCE:
Gartner, Deloitte, companies' financial reports, AtonRâ Partners

Artificial Intelligence And Cloud Computing

AI is better on the cloud

Cloud-based AI incorporates services that provide tools and APIs without the need for the users to have custom machine-learning models and in-house computing power. Moreover, third-party clouds have the advantage of transforming a capital expenditure into an operating expense, while requiring lower expertise to get started.

- In 2018, 49% of companies that have deployed AI used cloud-based services.

Tailor-made solutions

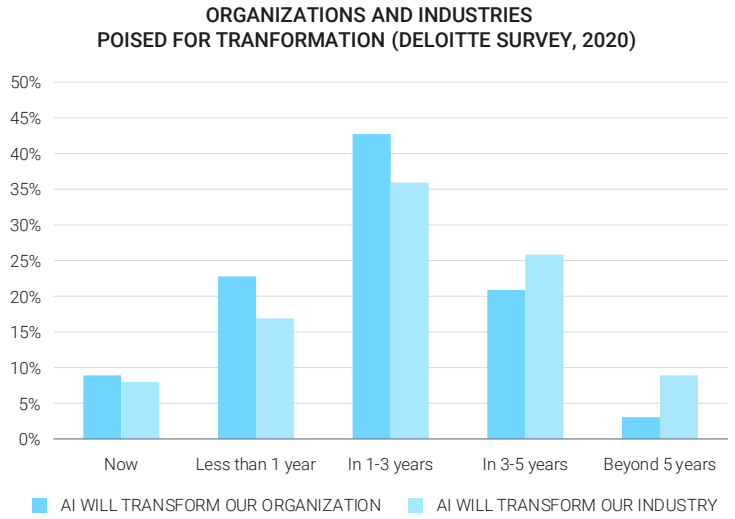
Cloud providers are enhancing their AI services by proposing easy-to-implement packages, as matching users' needs facilitates the mass deployment of AI and ultimately increases the dependency to a their own platform.

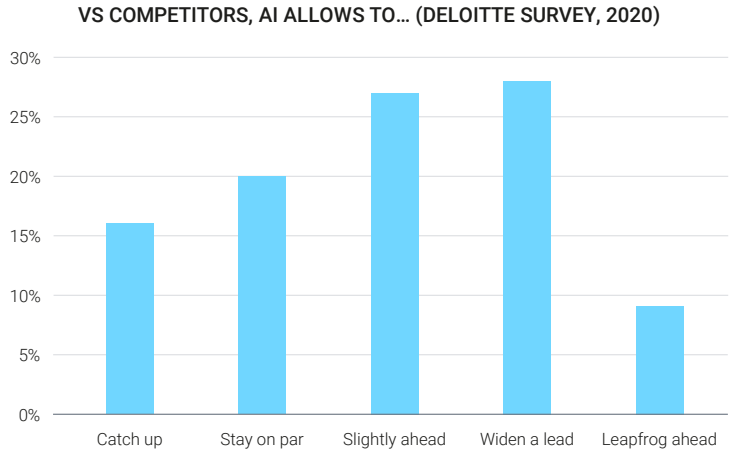
- Example of Google's AI bundles are Cloud Talent Solutions, helping faster hire of talents, and LendingDoc, AI tailored for the mortgage industry.

All industries will be impacted

Companies are finally understanding the competitive advantage they can get from AI. Despite the complexity of organizations hindering the progress of real-life applications of AI (compared to mere technological advances), artificial intelligence has started reshaping all industries, along societal changes.

- In the financial industry, AI transforms internal operations and improves business efficiency.
- In education the use of AI is spreading to the full teaching process.





SOURCE:
Deloitte, AtonRâ Partners

Next Trends In Cloud Computing

Internet of Things (IoT) and new data sets

Connected devices will generate an unprecedented quantity of data. The advent of deep-learning algorithms (see our previous article) into cloud computing will facilitate the processing of IoT data, resulting in better predictions and more complex automations.

- Within PaaS, IoT is experiencing the highest growth in usage (+21% YoY), ahead of container-as-a-service and machine-learning/AI (+17%).

Flexibility through hybrid cloud and multi-cloud

Public clouds offer the opportunity to scale resources. But certain industries, e.g. law firms or banks, need to keep sensitive data on local servers. Most firms rely on hybrid cloud strategies, using both private and public clouds. Multi-could approaches, where customer cherry-pick the best solution from each vendor, complement this solution.

- As per Flexera, large organizations are using 2.2 public and 2.2 private clouds on average, while experimenting an additional 1.2 public and 1.7 private clouds.

Increase in storage capacity

COVID-19 has highlighted the necessity to have sound disaster recovery plans. The shift from on-premises backup storage to public cloud will accelerate, improving resiliency and data protection.

- Storage developers of flash memory or hard drives are likely to benefit from higher demand driven by public clouds in 2021.

SOURCE:
Flexera, QA Limited, Forrester

Catalysts

- **5G.** High-bandwidth speeds and low latency are essential to offer a good experience to cloud users. 5G will accelerate the development of mobile cloud computing, through distributed edge networking.
- **Cognitive Computing APIs.** Developments in algorithms that combine pattern recognition, language processing, and data mining will facilitate the addition of AI technology into existing cloud-based applications, without the need to code from scratch.
- **COVID-19.** As a second wave has been hitting several countries, organizations will accelerate their migration to public clouds.

Risks

- **Antitrust regulations.** Amazon faces U.S. antitrust scrutiny on its cloud-computing business. The same holds true for Google in Italy. Regulatory pressure could reduce investments and slow down future developments.
- **Data privacy.** Cloud service providers may store personal data within their database and process them on behalf of the clients. More regulations on privacy could imply additional costs for the clients who will have to deep dive into storage location, underlying architecture, and data ownership.
- **Price wars.** New competitors to the three market leaders could try to gain market shares by aggressively reducing prices.

Bottom Line

- Lockdown measures are accelerating the use of remote working and the transition to cloud computing. As more organizations migrate to cloud solutions, providers develop solutions requiring less expertise and facilitating the large-scale deployment of AI.
- In addition to the market leaders covered in this Investment Recipe, the ecosystem of companies benefitting from the growth of cloud computing is huge. We have geared our portfolios to have exposure to the whole ecosystem at different levels of the value chain.

Companies mentioned in this article:

Alibaba (BABA US), Alphabet (GOOG US), Amazon (AMZN US), IBM (IBM US), JD.com (JD (US), Microsoft (MSFT US), DigitalOcean (not listed), Tencent (700 HK)

A GROUNDBREAKING TECHNOLOGY FOR CANCER THERAPY

A New Weapon In The War Against Cancer

Cancer treatment still lags behind

Surgery, radiation and pharmacological therapies have been used for decades as the primary weapons to fight cancer. Despite the progress made in each of these three areas, cancer is still a leading cause of death worldwide.

- Every year ~10mn people die from cancer, of which nearly 600k in the U.S. alone.
- Most of the time patients are treated with a combination of multiple approaches.

Turning to physics to treat cancer

Tumor Treating Field (TTF) therapy is based on the discovery that turning an electric field to a specific frequency would inhibit cell division in certain types of cells. This disrupts the mechanisms that allows tumors to develop.

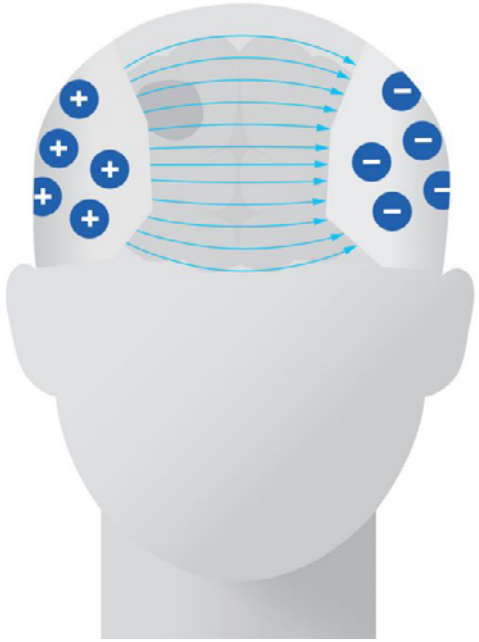
- The man behind this discovery, Professor Palti eventually founded Novocure to develop a portable electric field generator, called Optune, used to treat a wide range of solid tumors.

A unique player

Novocure holds the monopoly of this rapidly emerging technology. New partnerships and excellent results are validating the approach. Optune, has the potential to improve survival rates of a wide range of solid tumors, alone and in combination with current standard-of-care treatments.

- Already approved for glioblastoma (GBM), the most common stage 4 brain cancer in adults, and mesothelioma (MPM), an aggressive and rare form of lung cancer.
- The approach is being studied for Non-Small Cell Lung Carcinoma (NSCLC), ovarian, liver and gastric cancers, as well as brain metastases.

novocure®



SOURCE:
https://www.novocure.com/

The Cruel Killer Still Haunts The World

Understanding cancer

Tumors occur when abnormal cells (cells with a mutated DNA) start to proliferate out of control. Cancer arises when the tumor also spreads to other tissues through blood and lymph systems, generating metastases. While some types of cancer and benign tumors have high cure rates, others are incurable, often because by the time the first signs and symptoms show up, the condition is already too advanced.

- The treatment plan for cancer depends on the type, size and stage, as well as the age and the health condition of the patient.

Joining forces together

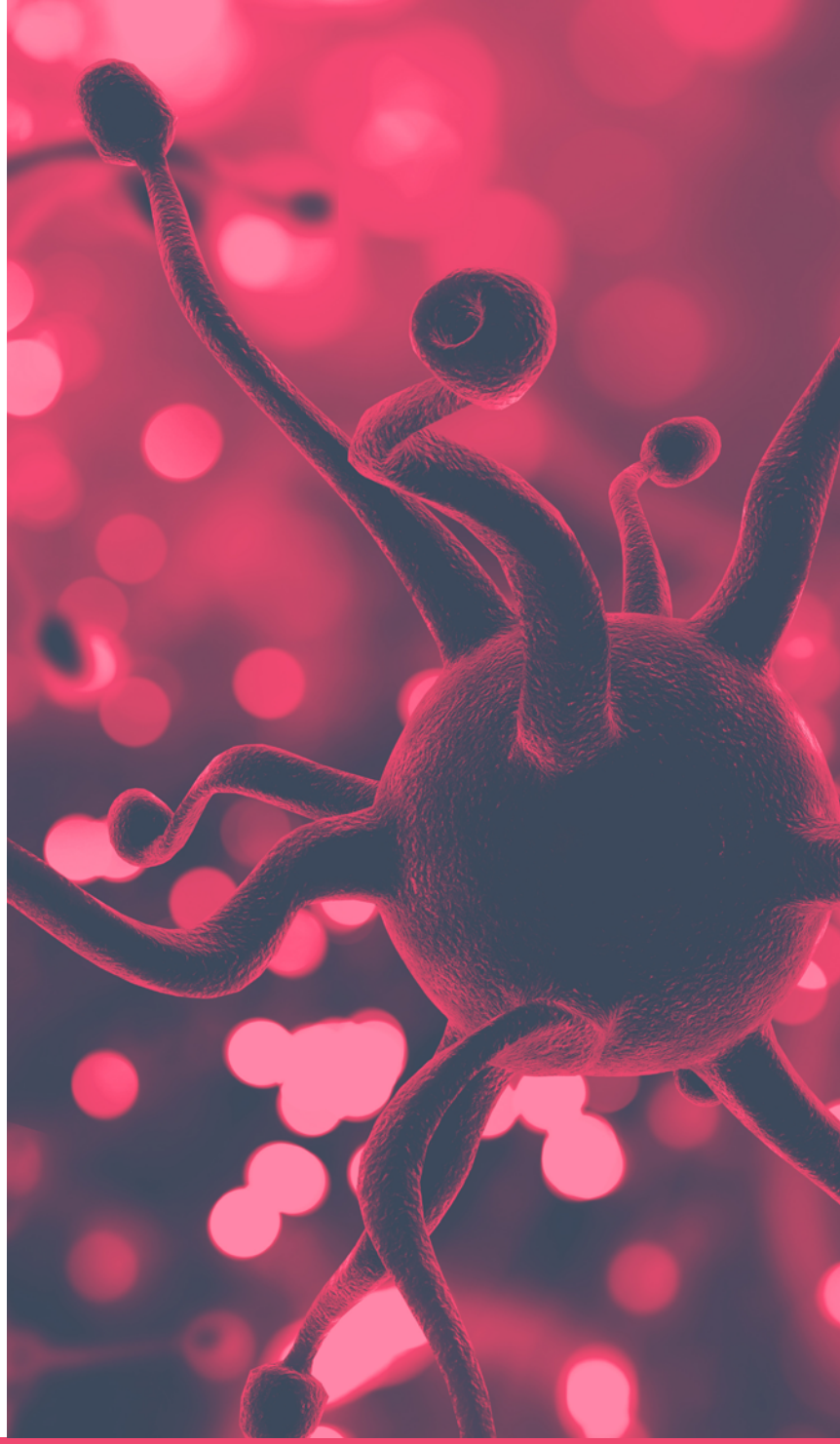
The goal for cancer treatments is to cure (if possible), prolong survival or improve the quality of life during and after treatment. Cancer is a very complex disease, and several pathways and mechanisms contribute to its development. By using different approaches that target different mechanisms, a synergistic action may be achieved.

- Combination therapies tend to increase the therapeutic benefit, prevent drug resistance and reduce the duration of the treatment.

Brutal sides effects are the flip side of the coin

Conventional cancer treatments usually cause important side effects and supportive therapies are often used to manage and reduce them. Today's research efforts aim at finding new, more effective therapies with minimal adverse effects.

- Examples of side effects include: nausea, organ damage, pain, fatigue, neuropathy, hair loss and cognitive impairment.



Types Of Cancer Treatment

	Surgery	Radiation Therapy	Chemotherapy (pharmacological treatment)	Immunotherapy (pharmacological treatment)	Hormones therapy (pharmacological treatment)	Stem cell transplant	Targeted therapy (pharmacological treatment)	Gene therapy
Description	A procedure in which a surgeon removes cancer from the body. The technique may also reduce the size of a tumor prior to the application of other therapies.	Uses high-energy beams or particles to kill cancer cells and shrink tumors.	Uses drugs that attack cells that grow quickly.	Helps the immune system fight cancer.	Blocks or reduces the levels of the body's natural hormones in order to slow or stop the growth of breast and prostate cancers (that require hormones to grow).	Procedure to restore blood-forming stem cells in cancer patients who have had theirs destroyed by very high doses of chemotherapy or radiation therapy.	Targets proteins that control how cancer cells grow, divide, and spread.	Modifies the genetic information of the cancerous cell to cause cell death or slow the growth of the cancer.
Effect	Localized	Localized	Systemic	Systemic	Systemic	Localized	Systemic	Localized
Examples	• Cryosurgery • Lasers • Hyperthermia • Photodynamic therapy • Heat or chemical ablation	• External beam radiation therapy • Internal radiation therapy (Brachytherapy)	• Small molecules • Biologics	• Immune checkpoint inhibitors • T-cell transfer therapy • Monoclonal antibodies • Treatment Vaccines • Immune system modulators	• Small molecules • Biologics	• Autologous stem cells • Allogeneic stem cells • Syngeneic stem cells	• Small-molecules • Monoclonal antibodies	• CRISPR/Cas9 • Gene addition • ZFNs • TALENs

Disrupting The Treatment Paradigm

Applying an electric field to stop cellular division

During cellular division, some proteins, called tubulins and septins, align to form respectively the mitotic spindle and the contractile ring, allowing the cell to divide. These proteins are highly polar, so when a low-intensity alternating electric field (which exerts force on charges and polarized molecules) is applied, it causes them to misalign, avoiding the formation of the mitotic spindle and the contractile ring.

- The electric field has shown to inhibit cell proliferation and DNA damage repair, induce autophagy and immunogenic death, as well as reduce cell migration.

Non-invasive, portable and localized with minimal side-effects

The electric field is applied at a frequency that alternates between 100k to 300k times per second according to the target cancer tissue. The device is composed by a battery or wall-powered electric field generator and single-use transducer arrays placed on the skin's surface that surrounds the tumor.

- Most common side effects of using TTF therapy alone include skin irritation and headache. The device causes no systemic toxicity.

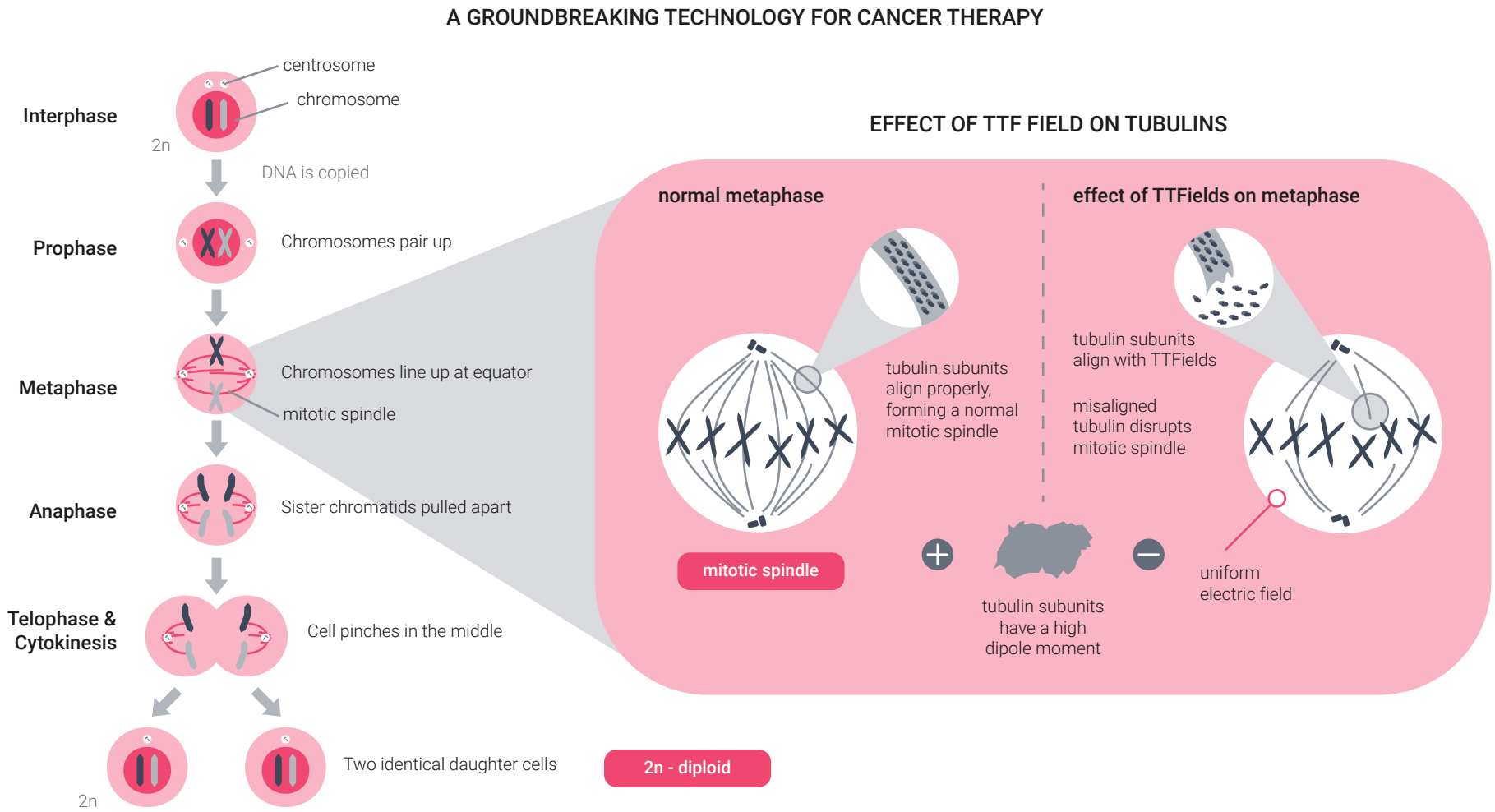
Adoption is growing at a fast pace

The FDA has been regularly approving Optune for new uses, and since 2019 it is covered by Medicare for certain uses, as its price is in line with other current treatments. Sales are growing at a very fast pace as the system is also approved in the E.U., Japan, and licensed in China.

- FDA approved Optune first in 2011 for recurring GBM, then in 2015 for newly diagnosed GBM, and in 2019 for MPM.
- Revenue 5Y CAGR is around 87%.

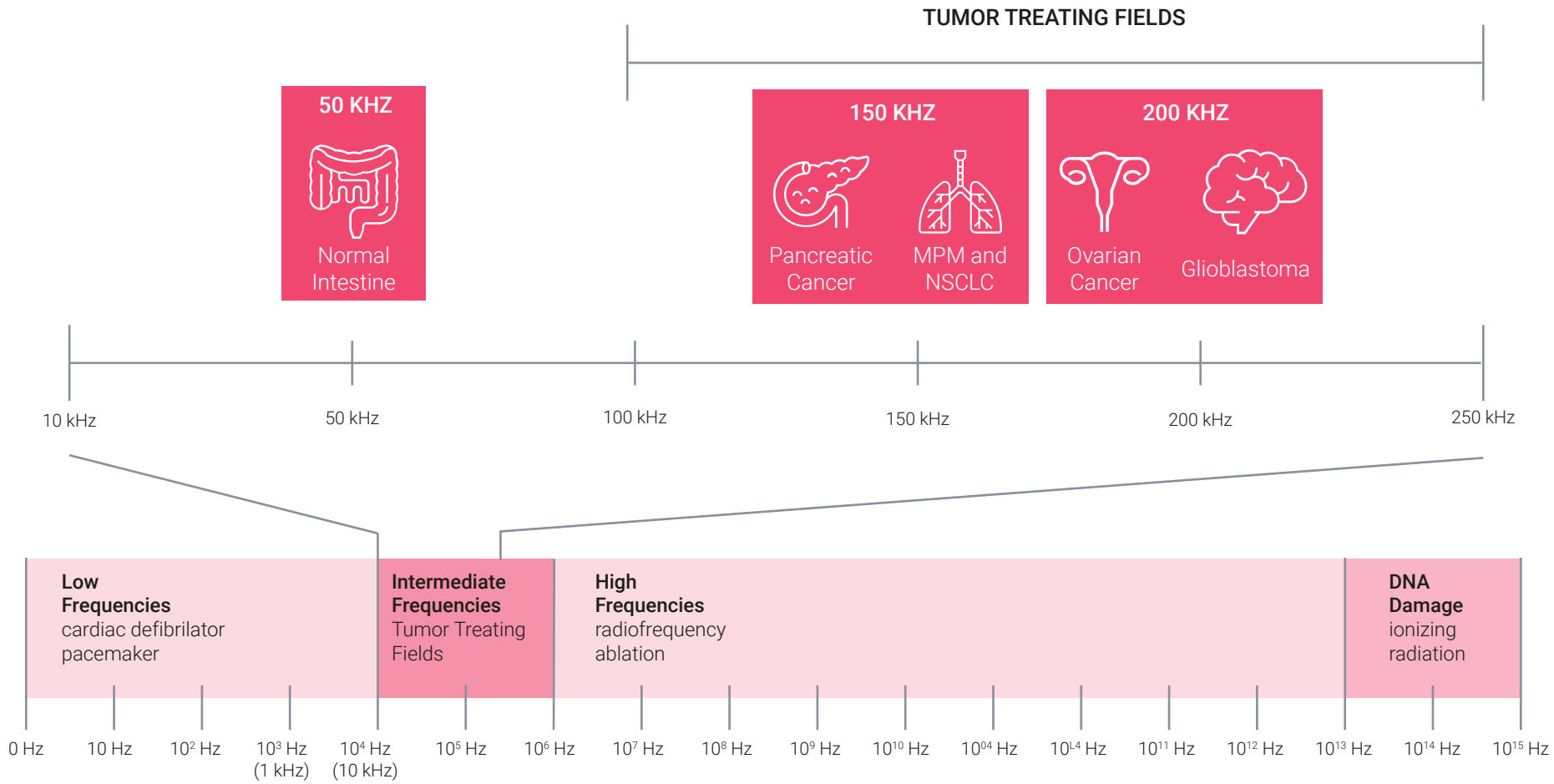
SOURCE:
https://www.novocure.com/

TTF Therapy Mechanism



SOURCE:
Novocure updated August 2019

Frequency of TTF Therapy



SOURCE:
Novocure updated October 2019

Novocure Trailblazing

Novocure holds a monopoly on the TTF Therapy

Novocure's TTF Therapy has no direct competitor and neither competes against any other type of cancer treatments such as surgery, radiation, and drug therapy. Instead, the approach is demonstrating to have a synergistic action, increasing the effectiveness of the cancer therapy when in combination with other techniques.

- Using Optune, alone and in combination with current standard-of-care treatments, led to improved survival rates in GBM and mesothelioma.
- Optune extends the overall survival rate by 5 months when combined with temozolomide, the standard treatment for GBM. Results increase when extending the time of use and the energy level.

Many catalysts on the horizon

Novocure's product is under investigation for six other indications, which could remarkably expand its potential addressable market. Important catalysts are on the horizon with many critical data interim readouts expected in 2021 and beyond.

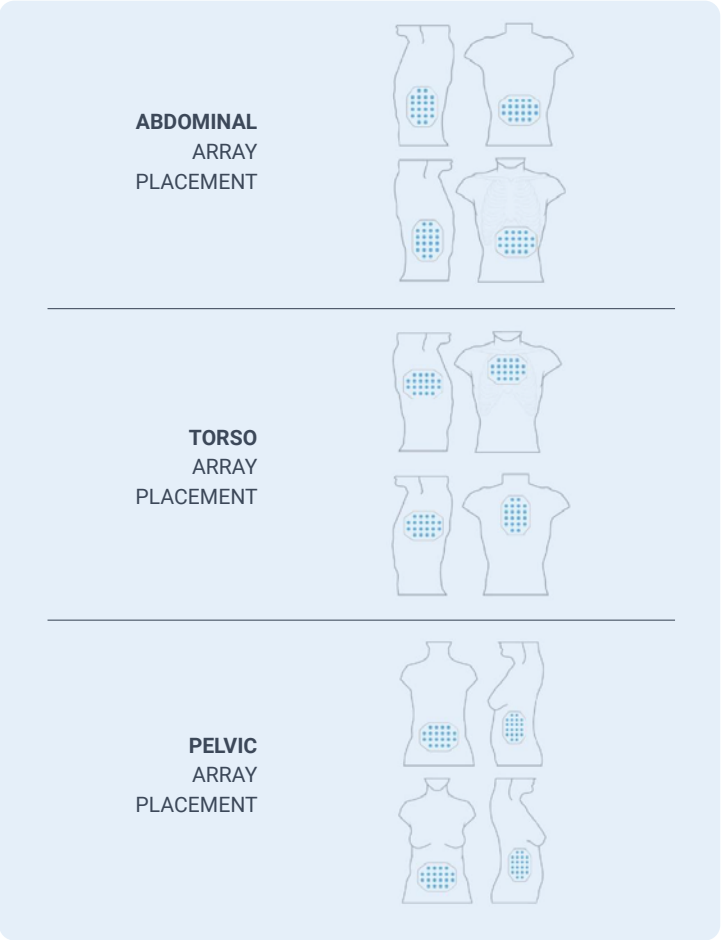
- Novocure is currently conducting pivotal phase III studies for brain metastases, Non-Small Cell Lung Carcinoma (NSCLC), and ovarian cancer, and phase II studies for liver and gastric cancers.
- Final data of phase II pilot trials in liver and gastric cancers are expected in 2021.

New partnerships are validating Novocure's approach

Novocure has recently signed a deal with Merck to test TTF in combination with Keytruda (Merck's blockbuster anti-PD1 immune checkpoint inhibitor) as a first line therapy in advanced NSCLC, potentially opening a large market.

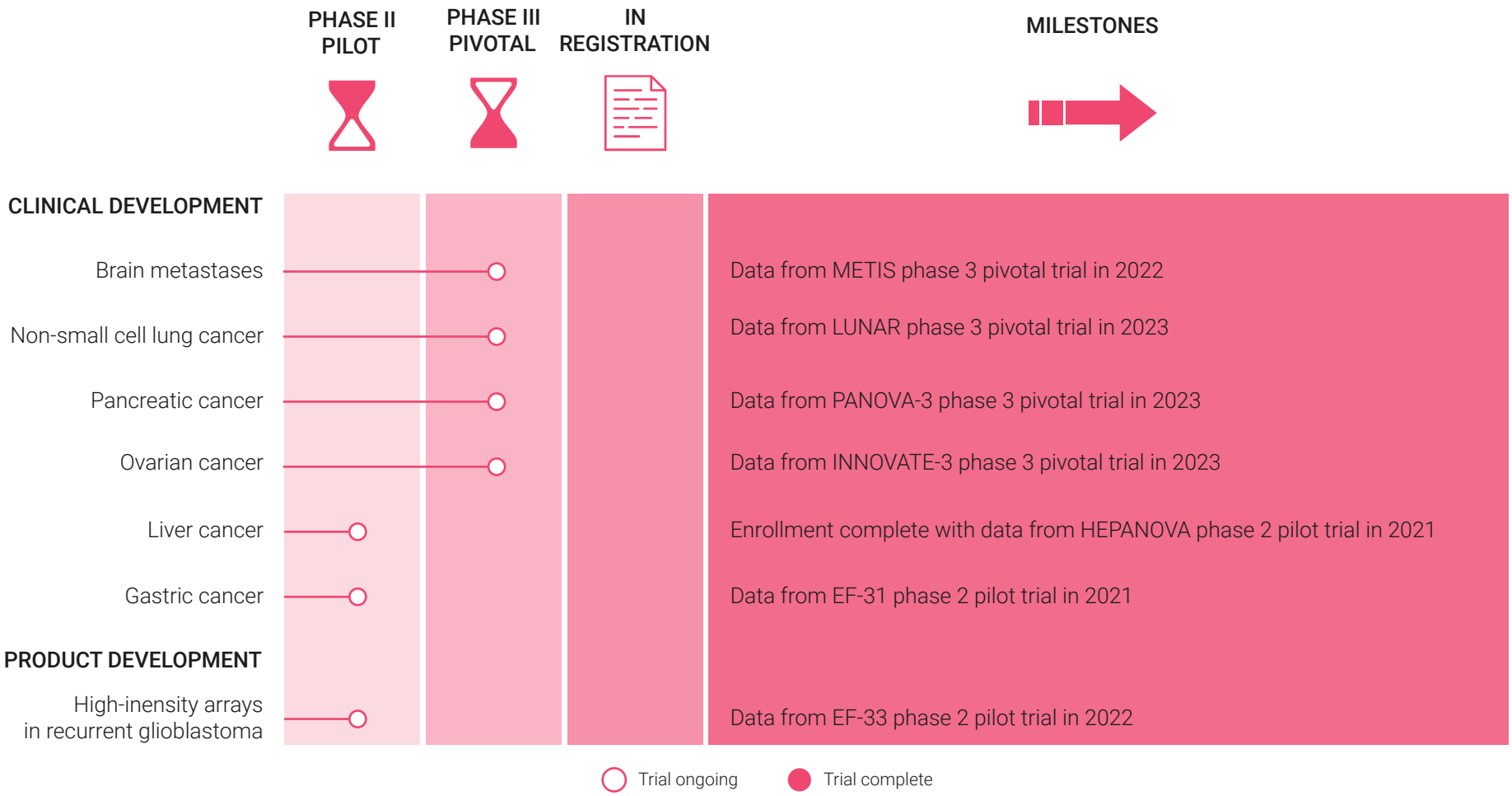
- The partnership is built upon the clinical studies showing a significant increase in efficacy when the two treatments are used in combination.
- A 66-patient Phase 2 trial will evaluate the tumor size reduction and survival rate.

TRANSDUCER ARRAY PLACEMENT OUTSIDE OF THE HEAD



SOURCE:
Novocure updated August 2019

Novocure Pipeline



SOURCE:
Novocure updated August 2019

Catalysts

- **Geographical expansion.** In August, Optune received a Chinese innovative medical device designation that speeds up the regulatory process, and could launch Optune for GBM in China already this year.
- **Approval in new indications.** The approach can be extended to new indications. Four indications (liver, pancreatic, ovarian and brain metastatic cancer) are in late stage of development.
- **Partnership & reimbursement expansion.** As the company continues to build evidence of the Optune's efficacy, we expect to see new partnerships with biopharma players and coverage from insurance companies.

Risks

- **High price & reimbursement uncertainties.** Given the high price of the device (~$21k/month vs ~$10-12k for conventional treatment), the company needs to build solid clinical data to ensure coverage by insurance companies.
- **Reliance on a single application.** Novocure business is at risk if unable expand its addressable market through the regulatory approval of new indications or successfully commercialize its current and future products.
- **Competition and new disruptive treatments.** Despite the substantial intellectual property behind its technology (over 140 issued patents, and 40 more pending), the oncology space is highly competitive and several MedTech, biotech and pharma companies are currently spending significant resources to find new groundbreaking treatments.

Bottom Line

- Technology is offering new weapons to fight cancer and medical devices are emerging that promise to disrupt the oncology space. TTF therapy addresses indications with highly unmet needs. The approach continues to be validated by clinical data and new partnerships, driving acceptance and payer coverage in the right direction.
- Standing at the convergence of biology and technology, our Bionics portfolio is exposed to very exciting opportunities for the future treatment of cancer, ranging from prevention, to diagnosis and treatment (including TTF therapy).

Companies mentioned in this article:

Merck (MRK US), Novocure (NVCR US), Zai Lab (ZLAD US),

COVID-19 VACCINE – THE FINISH LINE IN SIGHT?

Roadmap To First Vaccine Approval

Prophylaxis operates on multiple weapons

Multiple methods exist to prevent the spread of a disease and preserve the health of individuals. For COVID-19, vaccines appear to be the most important modality to exit the public health crisis.

- Vaccines are protective by nature, and with large scale adoption could promote herd immunity.
- Their relatively modest production cost (vs. neutralizing antibodies therapy on prophylactic settings) makes distribution to large populations feasible.

Turbulent ride for vaccine makers

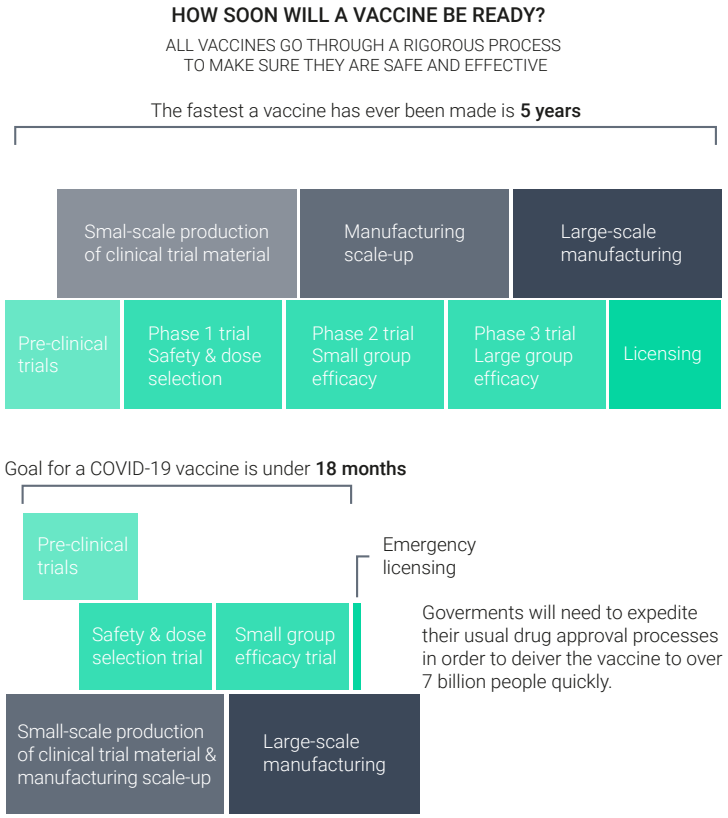
Development timeline for the first-generation vaccine has been unprecedented, however this fast pace does not come without a cost.

- Two of the four main vaccines candidates in ph.3 encountered safety signals possibly related to the vaccine (AstraZeneca and Johnson & Johnson).
- mRNA has proven to be the safest technology so far, however, this being a novel technology, there are no longer-term safety data.

First vaccine efficacy results are expected soon

The development timeline is unprecedented (from first virus sequencing to potential approvals in less than 12 months) and despite a large body of biological evidence on the virus activity and the vaccine's ability to generate a humoral and cellular response, there is still no certainty that this immune response mounts to protection from the virus.

- First evidence of actual preventive efficacy is expected before the end of the year from the front runners in the race and will have a huge impact.



SOURCE:
NEJM (2020),
What you need to know about the COVID-19 vaccine

Back To Vaccine Innovation

Prevention is key

Preventing a disease before it occurs allows for savings on health care costs, and vaccines are the best tool.

- Based on a study of children born between 1994 and 2013, the CDC estimated that vaccines prevented 732'000 deaths and saved $1.3tn in total societal costs.
- In the U.S., vaccines are rightly considered strategic and the country heavily subsidizes vaccine manufacturers. Europe is lagging behind, but COVID-19 is likely to help it play catch-up.

Vaccines are life-saving but not that attractive

For several years, the vaccine field had experienced impressive growth rates with many vaccines in development (HPV, flu…). However, recently there has been a marked slowdown in this field as pharma companies focused on more profitable therapeutic areas such as rare diseases.

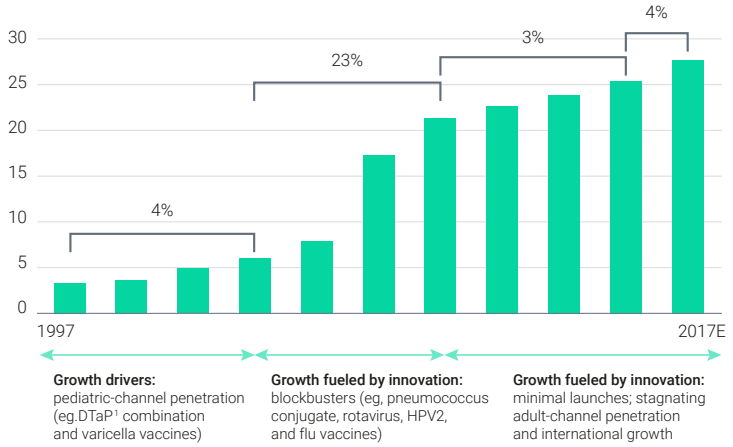
- Over the last five years growth has been <5%.
- Vaccines development requires large clinical trials involving tens of thousands of volunteers, so only few small biotech companies have been able to successfully complete the development of new types of vaccines.

The COVID-19 outbreak will refuel the vaccine innovation machine

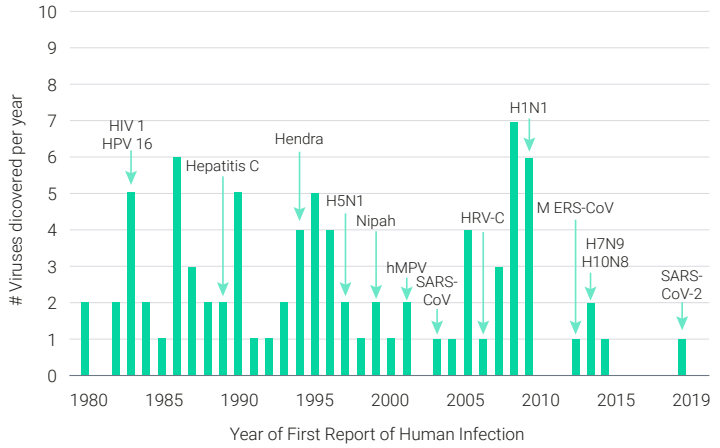
With the COVID outbreak, biotech developing new types of vaccines, such as mRNA-based, are regaining the interest of investors and large pharmaceutical companies.

- The next generation of vaccines could target modalities with high unmet need (e.g. CMV, or HIV). Influenza vaccines still have a low effectiveness (40% to 60%).
- More than 80 virus have been discovered since 1980 but only 4% have a vaccine available in the U.S.

GLOBAL VACCINE SALES, BIENNIAL, 1998-2017E, $ BILLION



NOVEL VIRUSES DISCOVERED (1980 - 2019)



SOURCE:
CDC – Centers for Disease Control and Prevention- Whitney, Cynthia G, Zhou, Fangjun, Singleton, James, Schuchat, Anne. Benefits from Immunization During the Vaccines for Children Program Era –United States, 1994-2013. CDC, 2014 April

Drastic Times Call For Lenient Measures

The FDA is looking for first signs of large-scale efficacy and safety

The U.S. agency has put forth guidelines to vaccine makers on development requirements leading to potential approvals.

- Given the scale and severity of the pandemic, the agency is willing to consider an accelerated approval relying on prior data supporting the technological merits.
- Along these lines, minimum safety threshold for Emergency Use Approval (EUA) is set at a median of 2-months follow-up after the last dose.

How to measure efficacy of a COVID-19 vaccine

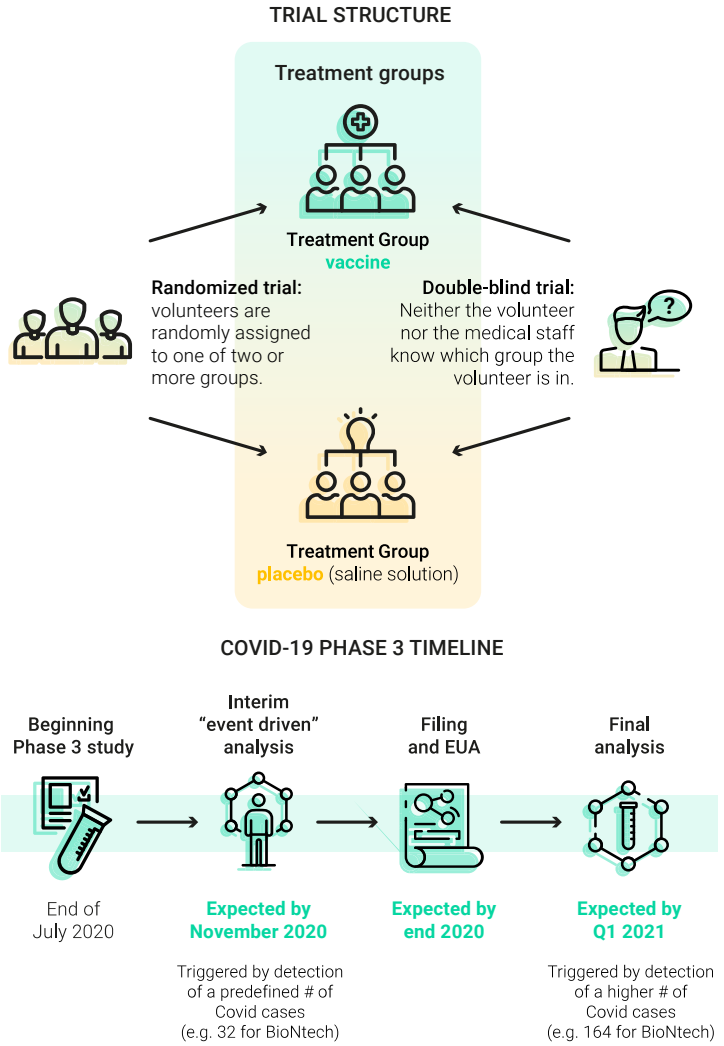
Large scale studies supporting approval need to be randomized, double-blind and placebo controlled. These studies are event-driven, meaning that the efficacy outcome will be determined by a predefined number of symptomatic COVID-19 cases through interim and final analysis.

- The efficacy is measured by the rate of disease prevalence between vaccinated and unvaccinated population. Vaccine must show a minimum efficacy of 50% for all approval modalities.

Ensuring the safety

Safety database supporting EUA needs to include 3'000 volunteers, a relatively easy-to-achieve target given that all ph.3 programs are recruiting 10-15 times that number.

- Final approval (unlike EUA) will need to be supported by at least 6 months follow-up, which will be key for broader uptake with general population.



And The mRNA Frontrunners Up Are ...

At the beginning of the pandemic, we wrote on the different approaches to prevent and treat the COVID-19.

- The most advanced programs in vaccines are in Phase 3, and already published ph.1 immunogenicity data, demonstrating an induction of an immune response: Neutralizing antibodies (Nab) and T-cells response.
- Two m-RNA programs (BioNTech, Moderna) expect to file by the end of the year for an Emergency Use Approval.

Program	BNT 162b2
Technology	mRNA
Sponsor	Pfizer/BioNtech
# of trial participants	44.000 (37,800 enrolled)
Doses	2, 21 days apart
Initiated	July 27th 2020
Primary Endpoint (PE) Timing	7 days post 2nd dose
Nab vs CS* in Ph.1	x3.8
Events (1st interim and final)**	32/164
Estimated Filing	Oct-20
Price Per Dose	$19.5
2021 Manufacturing Capacity (mn)	1300

Program	mRNA-1273
Technology	mRNA
Sponsor	Moderna
# of trial participants	30.000 (28,600 enrolled)
Doses	2, 28 days apart
Initiated	July 27th 2020
PE Timing	14 days post 2nd dose
Nab vs CS in Ph.1	x2.3
Events (1st interim and final)	53/151
Estimated Filing	Nov-20
Price Per Dose	$15.25
2021 Manufacturing Capacity (mn)	500–1000

*CS - Convalescent Sera: - blood serum that is obtained from an individual who has recovered from COVID-19
** This means that BioNtech will initially assess efficacy data after 32 cases of symptomatic COVID-19 have occurred in trial participants and ultimately when at least 164 cases of COVID-19 occur in both vaccinated and placebo participants.

BioNtech: First In Line

Timeline

Several trial features make BioNtech likely to be the first to cross the finish line.

- Dosing schedule between prime and boost is 3-weeks apart, compared to 4 weeks in most 2-doses programs.
- Minimum follow-up for an event (symptomatic disease) is 7 days, vs. 14 days in other studies implying their confidence in faster onset.
- Per the ph.3 statistical plan, only 36 events are required to trigger an interim efficacy analysis, vs. >50 in other studies.

Efficacy

BioNtech presented robust ph.1 immunogenicity dataset, demonstrating both Neutralizing antibodies and T-cell responses.

- To be validated on the first interim, the vaccine will need to show +76% efficacy in the primary endpoint. The company will then file for EAU.
- BioNtech's trial has a higher probability for succeeding at earlier time points, resulting from a more aggressive statistical plan, compared to parallel programs.
- Higher than anticipated infection rate across study sites could be beneficial both in terms of efficacy as well as timeline.

Safety

Data did not yet reveal any major safety concerns on the vaccine.

- Ph. 1 data revealed systematic adverse events (AE) including fever, fatigue and chills, however these AE's were mostly mild to moderate.
- Blinded safety interim data from the ph.3, mostly reaffirmed previous findings.
- As primary endpoint event in the study is subjective (a participant reporting symptoms), a higher rate of adverse events could actually support efficacy, as onset of AE's is effectively unblinding the study.

*Source: Company Filings and JP Morgan Estimates

Estimated Timeline*		
	BNT 162	
Vaccine Efficacy	1st Interim	2nd Interim
70%	19-Oct	08-Nov
80%	21-Oct	11-Nov
90%	23-Oct	14-Nov

Probability of Success at Interim Readouts		
	BNT 162	
Vaccine Efficacy	1st Interim	2nd Interim
70%	32%	68%
80%	68%	96%
90%	98%	100%

Moderna: Just Behind

Timeline

Early success for BioNtech could be a double-edged sword for Moderna, on one hand validating the mRNA technology platform, but on the other, setting a high efficacy bar.

- We estimate Moderna's first interims and final data to be approximately 1-2 months behind BioNtech, despite both studies launching about the same date.
- 2-months delay in approval could be challenging commercially going up against Pfizer, especially if the vaccine profile is not very differentiated.
- A first release of Moderna's efficacy data may come around December.

Efficacy

Moderna presented an impressive ph.1 immunogenicity dataset and was the first to validate the mRNA approach in inducing a strong immune response.

- The more conservative statistical plan means an early success for Moderna has a lower probability in this phase, but higher in later phases.
- Early efficacy data showed only modest T cell response, which in our view could be an issue with secondary endpoints relating to disease' severity.
- Moderna's early data sets were especially impressive in older adults (>55 years), a potentially important differentiator given COVID-19 pathogenesis.

Safety

Moderna's vaccine was relatively well tolerated according to data so far.

- Ph. 1 data revealed systematic adverse events including fever, fatigue and chills, though those were in line with parallel programs.
- Tolerability profile was especially favorable with older adults at the 100µg ph.3 dose.
- With a relatively long follow-up since ph.1 readout and almost complete enrollment to ph.3, none of the safety concerns seen with other vaccines have surfaced to date, despite this being the biggest risk for the mRNA platform in the longer term.

Estimated Timeline*		
	MRNA-1273	
Vaccine Efficacy	1st Interim	2nd Interim
70%	13-Dec	23-Feb
80%	20-Dec	07-Mar
90%	28-Dec	22-Mar

Probability of Success at Interim Readouts		
	MRNA-1273	
Vaccine Efficacy	1st Interim	2nd Interim
70%	13%	92%
80%	53%	100%
90%	97%	100%

*Source: Company Filings and JP Morgan Estimates

Catalysts

- **Emergency Use Approval.** We expect first efficacy data from the front runners to be published in the coming weeks, and, assuming a positive readout, EUA could come as soon as late November.
- **Robust efficacy data.** We are becoming increasingly confident that we will see robust efficacy from the leading vaccines, based on their strong antibody response after 2 doses.
- **Validation of the vaccination strategy.** It will mark a turning point in the fight against the virus and will drive biotech stocks (if not the broader market).

Risks

- **Biological risk.** There's an inherent biological risk as eventually this will be the first efficacy look both in terms of platform as well as antigen.
- **Time to complete data.** It may take some time to gather substantial evidence on how the primary endpoint (prevention of symptomatic disease) correlates with preventing actual infection, or reducing the probability of re-infection, which will be key for eventual uptake.
- **Commodity-like pricing.** Similar efficacy will make vaccines suffer from commodity-like pricing, promoting margin erosions on future government orders.

Bottom Line

- As one of the most historically-crucial scientific races approaches its clinical-stage finish line, we believe the outcome could have a resounding impact on race participants, but even more importantly, on global financial markets. A failure, especially from the least controversial players such as Moderna and BioNtech could send stocks on a bearish spiral, while a success, as is often the case, would be more detail-sensitive. With the totality of biological and clinical data we have to date, we believe readouts could exceed regulatory hurdles, and be clinically meaningful.
- We believe the probability of success is high, given the impressive efficacy at an earlier timepoint. Consequently, ahead of the upcoming clinical data readouts, we have increased our portfolios' exposure to the mRNA space.

Companies mentioned in this article:

AstraZeneca (AZN LN), BioNtech (BNTX US), Moderna (MRNA US), Pfizer (PFE US)

U.S. ELECTIONS – SPECIAL FOCUS ON CLIMATE

Climate Change: A Campaign Priority

Four years of Trumpism didn't hurt that much

Despite Trump's withdrawal from the 2015 Paris Climate Agreement, things did not go as bad as initially expected, with renewable energy production soaring to record-levels and coal-fired power plants closing at the fastest pace ever.

- Solar and wind power generation grew 40% over the 2016-2019 period.
- Over the same period, coal-based power generation fell 22%.

Biden's plan could accelerate the transition

Joe Biden already announced an aggressive $2tn energy & climate plan, aiming to accelerate investments in renewables, energy storage, electric vehicles (EVs), charging infrastructure, energy efficiency, etc.

- Biden aims for the U.S. to achieve zero-carbon power production by 2030 and net-zero emissions by 2050.
- He would also rejoin the Paris Agreement and reverse Trump's decision.

Structural changes will happen regardless of election's outcome

No matter who wins the U.S. elections, we believe that some structural trends are here to stay, and the ongoing energy transition will only accelerate from now on. Energy independence and resiliency are key targets that benefit from bipartisan support. Despite Trump's climate-skepticism, he remains favorable to infrastructure development & modernization.

- With nearly 3,5mn Americans working in clean energy, the segment keeps on gaining economic & social importance.
- Infrastructure modernization could indirectly benefit clean technologies, notably if investments go to power transmission, water distribution, railroads, etc.

SOURCE:
Joe Biden – Clean energy

Trump: The “Cleanest President”

Killed the coal industry

Despite Trump’s attempts to revive the industry, coal-fired power generation kept on falling at a faster pace than during Obama’s last term, to end up reaching a 43-year low in 2019. Coal has become an uneconomical option in most regions and there were no coal-supportive policies to slow down the decline.

- U.S. utilities are replacing coal with natural gas and renewables, a trend that has accelerated during the COVID pandemic.
- In 2019, Murry Energy (US’ largest private coal miner) became the eights US coal producer of the year to file for bankruptcy.

Renewables grew like never before

U.S. Solar and wind market have flourished benefiting from declining technology costs and supportive states. Even if Trump’s administration in 2018 did impose tariffs on imported solar cells & modules (section 201) the industry reached new records.

- From 2016 to 2020, solar and wind represented close to 60% of U.S.’ new electric generating capacity additions.
- Cumulative solar & wind deployment during Trump presidency is to exceed 83GW (the previous 4-year record was 56GW during Obama’s second term)

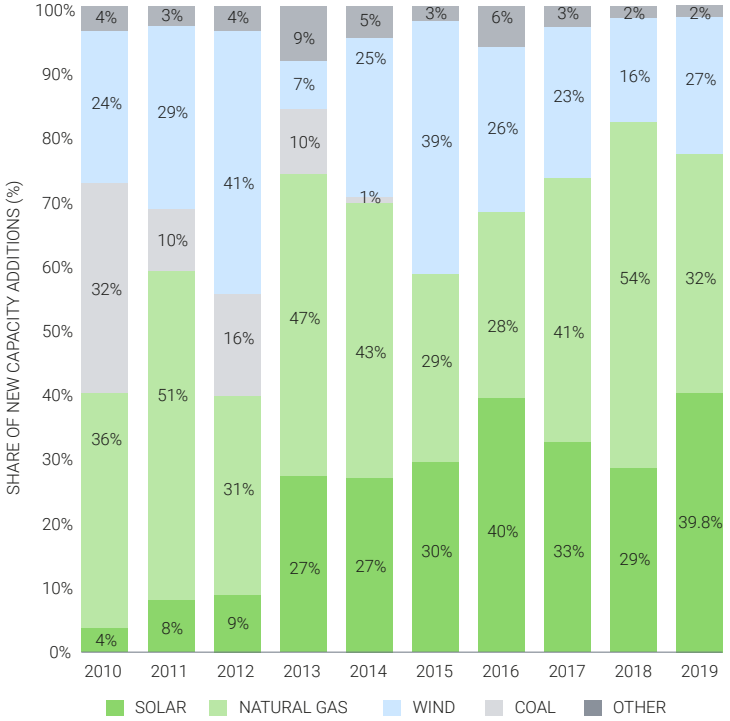
Battery storage hit records

Trump’s administration did coincide with the best four years in the battery industry’s history. This success must be attributed to aggressive policies implemented by a few states (e.g., California, Hawaii, New York, Massachusetts) as well as more competitive market dynamics.

- From 2017 to 2020, annual battery installations have more than quintupled.
- The Escondido project, completed in 2017, is U.S.’ largest battery storage system with 30MW capacity capable of powering 20’000 homes for four hours.

SOURCE:
NREL Solar Industry Update, Q1/Q2 2020

NEW U.S. ELECTRICITY GENERATION CAPACITY ADDITIONS



Biden's Ambitious Climate Plan

Decarbonize the electricity

Biden's most ambitious climate goal is arguably the 100% carbon-free electricity by 2035. If executed, such plan would entail one of the most aggressive renewable infrastructure build-up with notably a 7x expansion of utility solar & onshore wind generation capacity.

- Annual solar module demand would exceed 100GW (vs. 30GW this year).
- Required investments for renewable energy & storage would be over $2.2tn.

Boost electric vehicles sales

Biden plans on stimulating the EV industry by tightening fuel-efficiency requirements to automakers, provide new tax incentives to EV purchase and expand charging infrastructure.

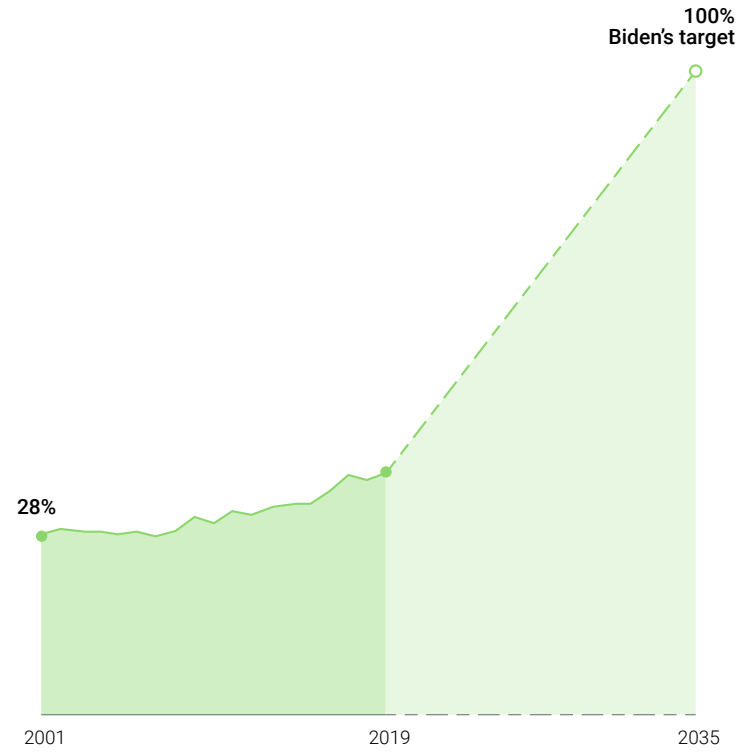
- Biden is to increase the EV tax credit, currently granted only to the first 200k car sold.
- The proposal calls for 500'000 EV charging stations by 2030.

Congress control remains key

Even with Biden's victory, there is no guarantee that he will be able to fully implement his energy & climate plan. Most fundings remain subject to Senate approval and a Republican-controlled chamber could hamper the process.

- Tax credits, national renewable energy standard, or EV purchase incentives are all proposals that will need legislative authorization to be implemented.

US CARBON-FREE ELECTRICITY GENERATION



SOURCE:
What's at Stake for Clean Energy in the US Election?
The Biden Plan to Build a Modern, Sustainable Infrastructure and an Equitable Clean Energy Future

Some Sectors To Grow Anyway

Infrastructure benefits bipartisan support

Both candidates agree on the need to speed up infrastructure development. While oil, gas and coal infrastructure remain the subject of discord, a common ground exists when it comes to electric grid, railway, water, buildings etc.

- In June this year, Trump was considering a new $1tn stimulus package dedicated to infrastructures spending (e.g., roads, bridges, clean water, etc.)
- Biden's plan does also mention "rebuilding America's crumbling infrastructure", i.e. roads, bridges, water systems, electricity grids, etc.

Covid-19 initiated a structural shift

As we wrote in a previous note, the COVID19 pandemic has somehow accelerated the energy transition and highlighted the importance of energy independence and resiliency. Oil supply/demand imbalances have badly hit the oil industry which many now expect to peak in the next couple of years.

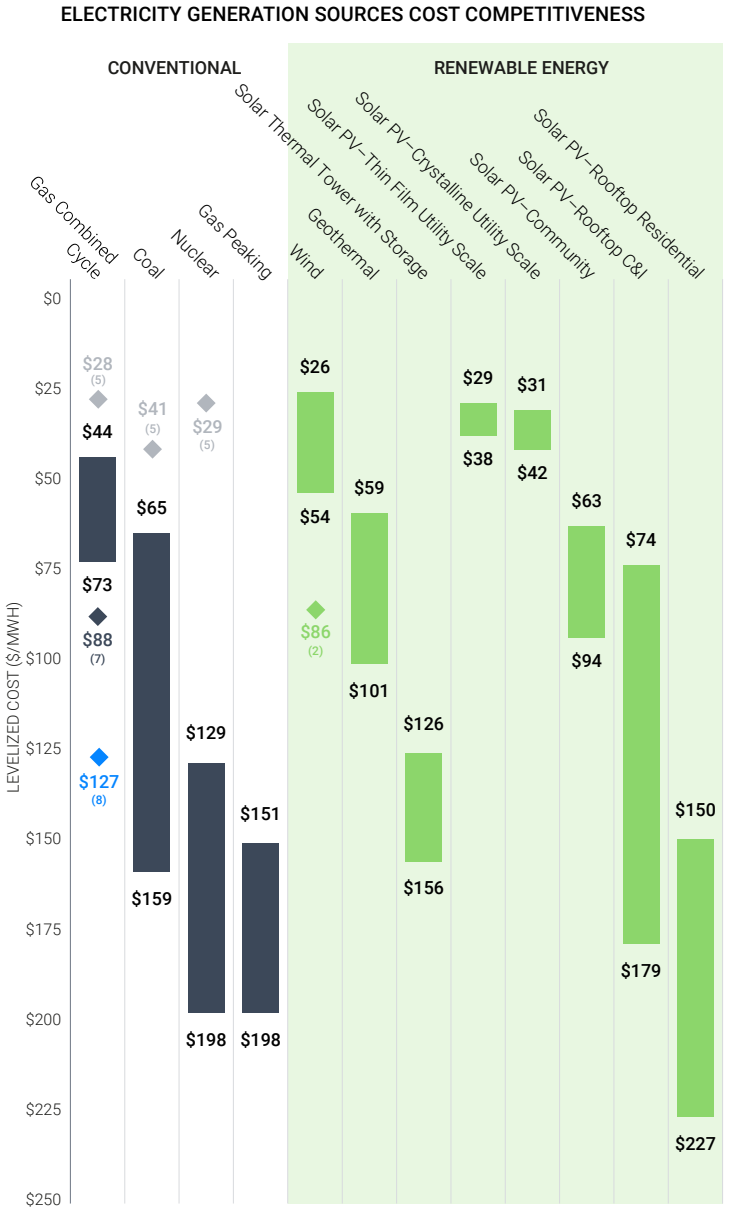
- Germany recently included EV chargers as part of a €2.5bn stimulus plan.
- China is to invest $2.1bn for EV infrastructure.
- The EU set a goal of 1mn public chargers by 2030 (from 200k today).

Renewables' cost competitiveness to drive future growth

Renewables (solar and wind) have become not only cost-competitive with conventional generation technologies on a new-built basis, but also tend to become competitive with marginal cost of operation of existing conventional plants.

- Texas (historically known for its oil) is already the national leader in wind energy and the 3rd state when it comes to solar power deployment.
- Wind turbine technicians & solar photovoltaic installers are expected to be the 1st and 3rd fastest growing jobs for the next decade.

SOURCE:
US Oil Rig Count, Fastest Growing Occupations, Household Solar Demand Surges Through the Roof in 2020
Levelized Cost of Energy and Levelized Cost of Storage 2019



Catalysts

- **Biden's double win.** If Biden wins both the elections and the congress majority, he will be able to fully implement his $2tn energy & climate plan.
- **New support mechanism.** Whether through tax credit extension (ITC & PTC) or carbon pricing, the reform and/or extension of federal support mechanisms could provide extra boost to the sector.
- **Made-in-USA comeback.** Cleantech companies building new manufacturing facilities in the U.S. (e.g., Tesla in Texas) could foster general acceptance above political divisions.

Risks

- **High hopes with low results.** Biden failing to deliver as per his plan (in case of victory) would negatively impact the sector.
- **COVID-19 resurgence.** New lockdowns measures could slowdown economic activity in the short term.
- **Split results.** Regardless of who wins, a president with no congress majority would add uncertainty, often negatively perceived by the market.

Bottom Line

- Biden's victory, along with congress control would undoubtedly provide an additional stimulus to the clean technologies and allow the U.S. the energy transition to happen faster than anticipated. However, we believe that there's no bad outcome for clean energy and some key sectors will continue to thrive no matter who wins.
- Our Sustainable Future portfolio is exposed to sectors that are undergoing deep-rooted transformations and have long term implications for our future society and current elections won't reverse the ongoing transition.

Companies mentioned in this article:
First Solar (FSLR US), Tesla (TSLA US)

CHARTS FOR THOUGHTS

A Leading Indicator Skewed By COVID?

Business applications and economic cycles

An interesting leading indicator for credit-driven economic cycles is the net number of new businesses. The charts clearly show how new business applications tend to lead GDP variations.

- During economic expansion, optimism and easy access to credit lead to the creation of new businesses which in turn fuel the expansion.
- When bank starts to tighten access to credit, which is usually met by lower growth expectations, the YoY change in new business applications goes negative, which may indicate a near recession.

A correlation breakdown

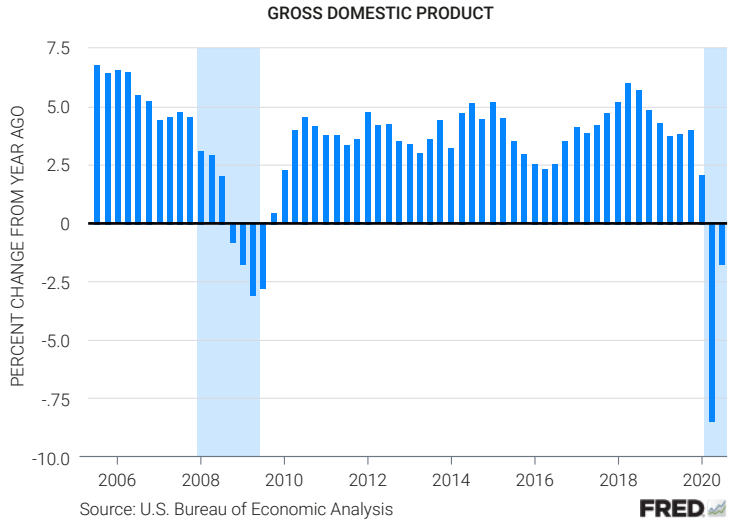
The latest read of this data is intriguing. While we faced a major recession, the rate of change in High-Propensity Business Application jumped massively, apparently breaking what seemed a fairly robust relation.

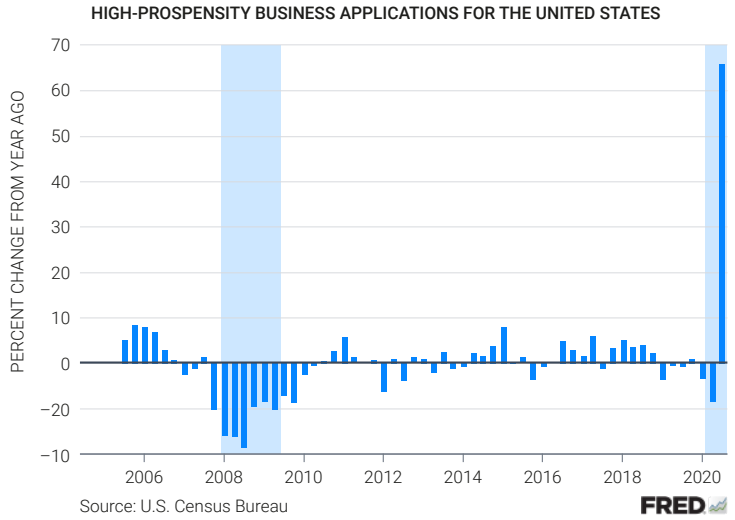
- In the chart, we only look at Business Applications that are considered to have a high propensity of turning into businesses with payroll.

What drives business creation at times of crisis?

It can be argued that COVID-related layoffs and lockdown have given many the opportunity to start a new business. But was it the only option they had, or does creating a new business suggest an optimism with regards to the future?

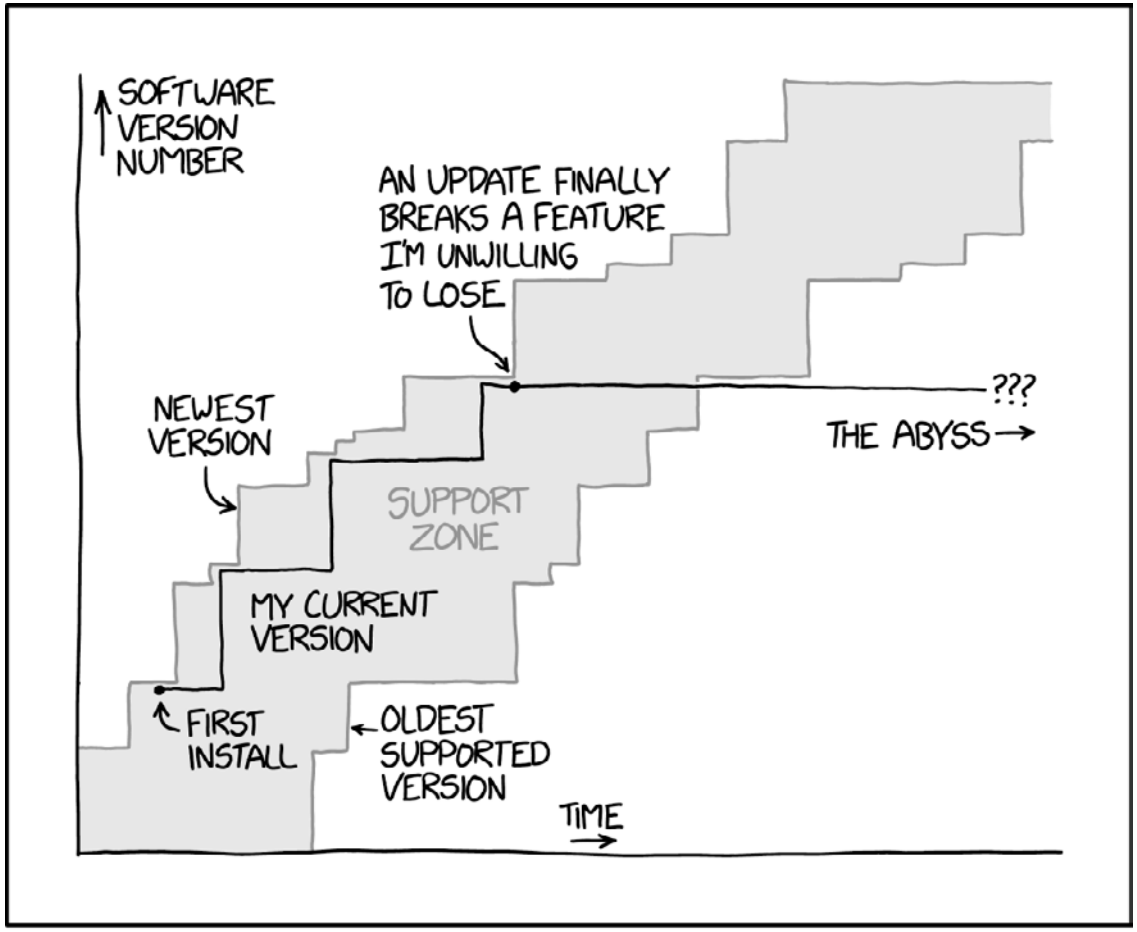
- After all, COVID may have, as an unintended consequence, sown the seeds for a new generation of entrepreneurs.





SOURCE:
FRED Economic Data

CASUAL FRIDAY



SOURCE:
https://xkcd.com/2224/

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