Investment Recipes

by AtonRā Partners

18 NOVEMBER 2020

18 NOVEMBER 2020

AtonRâ Partners

AtonRâ Partners SA
www.atonra.ch

research@atonra.ch
+41 22 906 16 16

7, rue de la Croix d'Or
1204 Geneva | Switzerland

On the Menu

TAKING THE WHEEL: AUTONOMY DRIVES INVESTMENTS

The Autonomous Future Is Starting Now

Autonomous vehicles are hitting the roads

The definition of autonomous vehicles (AV) has evolved since its first introduction in 1977, from driving on a specially marked street to cars making decisions themselves without relying on any external aid. There are 5 levels of autonomy ranging from level 1 "cruise control" up to level 5 "steering wheel optional".

- AVs rely on variety of data inputs such as radar, lidar, sonar, GPS, odometry, and inertia measurements allowing identification of appropriate paths and obstacles.

A driverless future is attracting investors

Successful products like Tesla's "autopilot" and the Chinese launch of Robotaxis are attracting huge investments, thanks to new technological innovations such as lidar and many advanced sensors. AVs will be fewer but safer and more profitable.

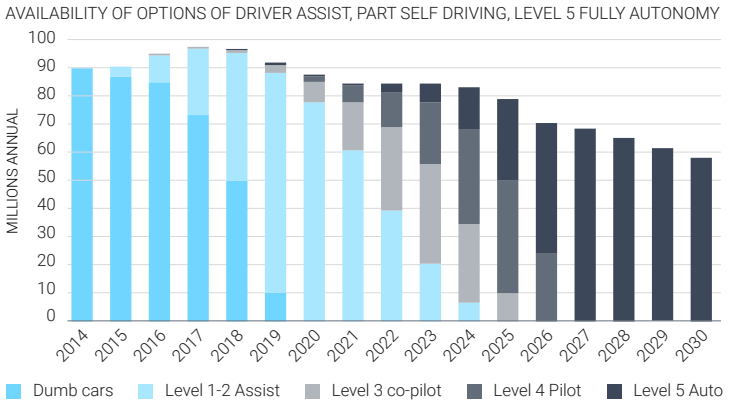
- Despite hesitation to fully trust an AI, the world is slowly transitioning to self-driving cars: currently, 90% of cars already have a computerized driving assistant.
- By 2025, 100% of vehicles are expected to be partially autonomous and 20% completely self-governing – the autonomous driver. may be replacing human drivers quicker than commonly thought.

The stars are aligned for growth

The "pure" AV market (i.e., chip/sensor manufacturers, and excluding large car manufacturers), is expected to grow to >$100bn with a 5Y CAGR of 40% boosted by positive developments in AI and improved availability of technologies.

- AI driving has matured through >20 years of experience – Mobileye started in 1999.
- AI and AVs require colossal processing power, which is now available (e.g., Nvidia).

GLOBAL VEHICLE ANNUAL SALES TO 2019
AND PREDICTED TRANSITION TO SELFDRIVING TO 2030



SOURCE:
AtonRâ Partners,
What Does the Future Hold for Self-Driving Cars?
The Osborne Effect: Why new car sales will be all electric in six years

A Long-Lasting Dream Is Finally Taking Shape

The biggest disruption to motor vehicles

Autonomous driving vastly increases vehicle utilization rates, which will lead to more road distance driven despite a decline in the global number of cars. Together with electrification, this is expected to accelerate the replacement of the existing fleet.

- Customers are more willing to buy smarter electric vehicles which have longer lifespan and may be upgraded to higher levels of autonomy via software updates.
- Self-driving disrupts the car sharing industry by creating an efficient autonomous fleet.

Safety for people and society

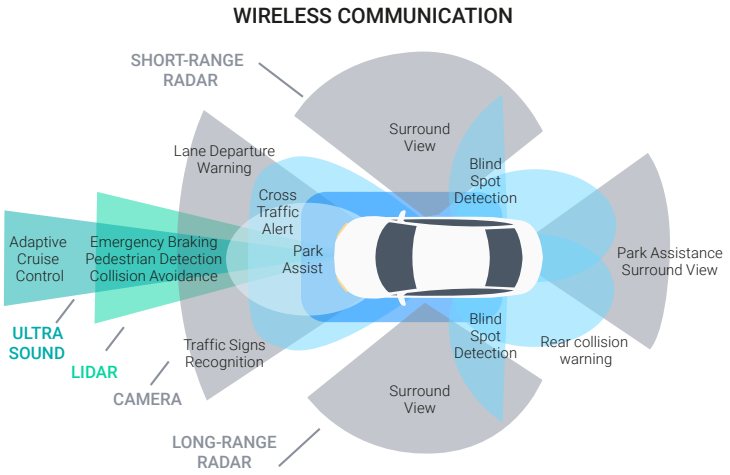
AVs are projected to bring massive social benefits such as safer roads, cleaner environment, more road throughput, efficient freight services and public transportation, amongst others. All these reasons call for government support and adoption.

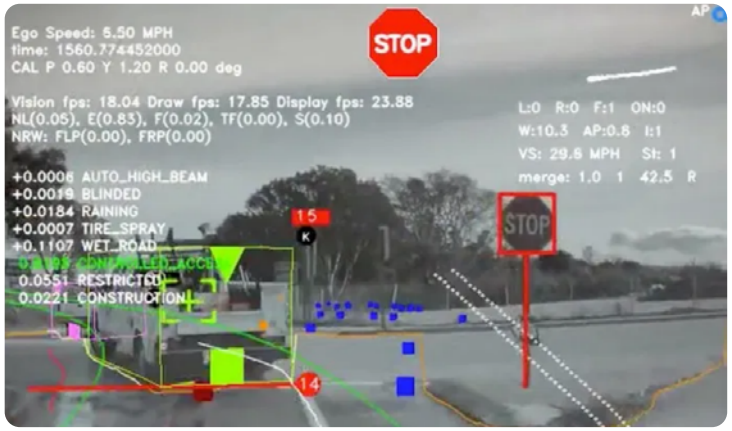
- Research shows that AVs could reduce fatal accidents by 90%, increase driving efficiency by 10% and decrease emissions by 60%.
- AVs may potentially save almost 2tn minutes annually for the entire world eliminating congestions and liberating drivers from the wheel.

Private financial benefits will drive adoption

Social benefits are complemented by billions in private savings. According to KPMG, AV owners will pay reduced insurance costs, see lower running costs and avoid problems such as parking costs and difficulty to find a parking spot.

- AVs would complement public transport by solving the 'last mile problem' (difficulty to travel the final mile between the home and the public transport drop off).
- AVs will replace taxis, Uber, etc. hence change the economics of owning a car.





Source

SOURCE:
AtonRâ Partners,
7 benefits of autonomous cars

A Driverless Future Is Attracting Investors

Towards 2030, autonomous is the new normal

For the past five years, there has been hype and enthusiasm about the introduction of self-driving cars, yet we believe that timeline to full autonomy has just been pushed out.

- Advanced-Driver Assistance Features (ADAS) are pervading the automotive industry, spending has grown 5x in the last 5 years as around 80% of the vehicles sold globally feature at least a few ADAS components.
- The global self-driving vehicle market size is expected to be ~7k units in 2020 and to expand at a CAGR of 63.1% from 2021 to 2030 to >800k units.

A highly specialized supply chain is consolidating

Assembling an autonomous car is only a final step. Multiple players are involved in software, sensors, chips, battery, and cameras production, and to improve the odds for success they are teaming up with giants like Ford and Amazon.

- The integration of multiple systems in AVs is costlier than was predicted by many specialized startups. COVID-19 has further increased the need for partnerships.
- Notable partnerships include Aptiv and Hyundai, Waymo and Jaguar, General Motors and Cruise, Argo AI with Ford, Volkswagen, Mobileye and Nio.

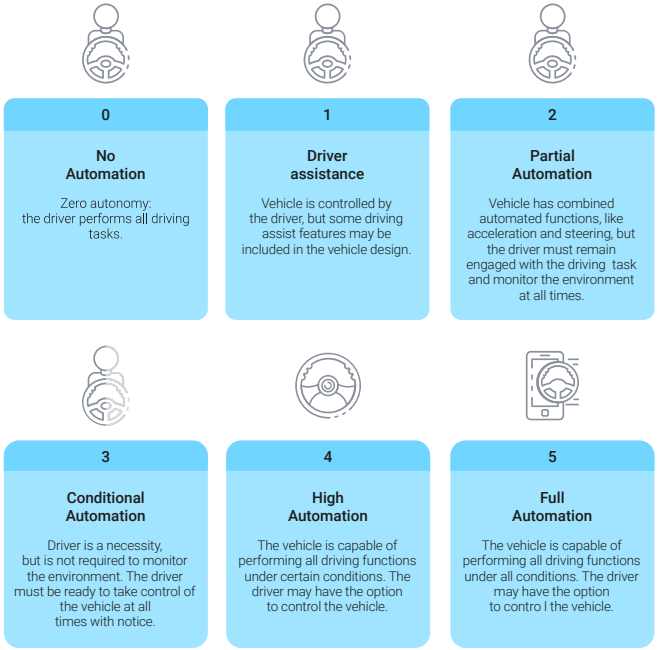
Private market is booming like never

The pandemic has slowed down investments, but the wave of partnerships has attracted investors looking for disruptive tech and quick buyout exits.

- The percentage of VC deals in AV-related startups is rising fast and many companies achieved unicorn status thanks to multiple investments from car or tech players.
- Such that the term LUnicorn has been coined for lidar companies with valuations of > $1bn, e.g. Velodyne, Quanergy, Luminar, Innoviz, and Hesai.

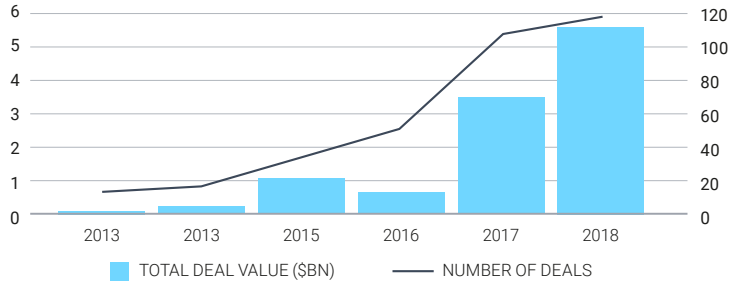
SOURCE:
Automated Vehicles for Safety
Strategy Analytics, Grand View Research

AUTOMATION LEVELS



INVESTMENT POURS INTO AUTONOMUS TECH

VC deal activity in autonomus cars



The Stars Are Aligned For Growth

Three main elements – countless opportunities

Autonomous vehicles are enabled by sensing, computing and actuation. Sensing captures the environment around the vehicle, computing makes sense of data and decides actions to be taken (or not), and actuation materializes the decision (potentially overriding the driver).

- The amount of sensors, their variety and data bandwidth requirement is pushing the envelope of silicon capabilities (for more details, read our previous article)
- As a rule of thumb, moving from one level to another requires a 10x increase in processing power – autonomous cars are indeed high-performance computers.

Core technologies are ready for prime time

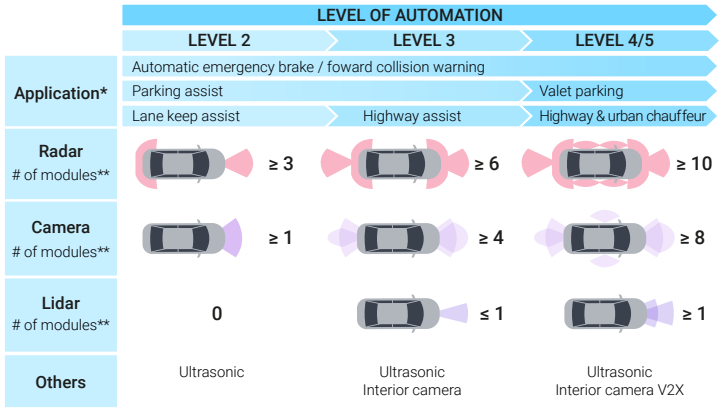
High-performance computing platforms (like Nvidia Drive, Intel Mobileye or Tesla Autopilot), leveraging fusion from multiple sensors (lidar, radar and cameras) and AI algorithms, are already outperforming human drivers.

- Tesla's autopilot feature has demonstrated being 9x safer than average driving, and Elon Musk foresees self-driving to be released to the public by end of 2020.
- NVIDIA estimates its autonomous vehicle addressable market to reach $25bn by 2025, and Intel estimates it can reach $100bn by 2030.

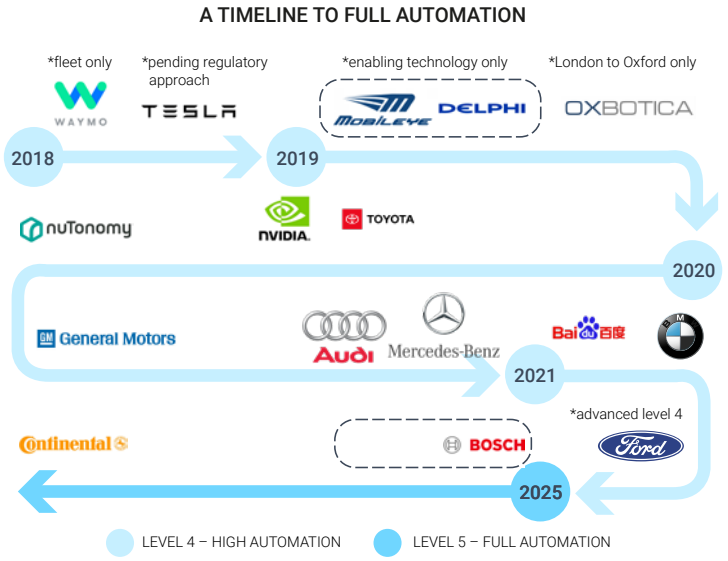
Artificial Intelligence in the driver seat

Fully autonomous driving is not required for the AI market to materialize 'explosive growth'. AI in transportation is projected to deliver $173bn in cost savings across the automotive supply chain by 2025, and self-driving technology is expected to be a $556bn market by 2026.

- Starting in 2024, the full Mercedes-Benz lineup will have autonomous capability.



* Source: VDA (german Association of the Automorive Industry); Society of Automotive Engineers
** Market assumption



SOURCE:
VDA (German Association of Automotive Industry) and NRMA (National Roads and Motorists' Association – Australia) McKinsey "Artificial intelligence as auto companies' new engine of value", Allied Market Research "Autonomous Vehicle Market Outlook – 2026"

Catalysts

- **Improved batteries and computing power.** Transitioning to autonomous driving requires massive computing power while preserving autonomy. Technology is available and competitive to deliver on promise.
- **Accurate sensors.** Starting with two cameras and a simple computer, autonomous vehicles may now recognize people, markings, signs, other cars, among thousands of other measurements. Accurate and cheap enough sensors are hitting the market, driving larger availability.
- **Favorable regulations.** Governments want to ensure both innovation and that people are at ease with AI steering the wheel. Regulation is one of the 4 pillars of AV ecosystem, among adoption, infrastructure and tech.

Risks

- **Fatal accidents.** People usually do not trust novel technology, especially the one where you entrust your life to a computer, and accidents may arise from human-driven/autonomous cohabitation.
- **Insufficient street and road markings.** Some sensors in autonomous vehicles analyse road markings and street signs. If countries do not spend budget on ensuring markings, adoption of vehicles could be limited.
- **Political instability.** Manufacturing an AV is not an easy task and requires global cooperation in terms of homogenous regulations and exchange of vital technologies. Failure to cooperate and smoothly trade may put the AV market on hold. With leading providers in E.U., U.S. and China, the value chain is global.

Bottom Line

- A market inspired by big plans and dreams for driverless future is currently in an early capex phase and is attracting millions in investments. By 2025, we are expecting 100% of sold vehicles to have partial autonomy with 20% being completely self-governing. Favorable regulations may ensure that by 2035 the entire vehicle world has a potential to reach level 4-5 autonomy.
- While some companies start testing partially autonomous vehicles, others focus on developing software and sensor hardware. We are investing across the entire value chain of self-driving cars and have considerable exposure to this industry in our AI & Robotics portfolio.

Companies mentioned in this article:

Amazon (AMZN US), Aptiv (not listed), Argo AI (not listed), Cruise (not listed), Daimler (DAI DE), Ford (F US), General Motors (GM US), Hesai (not listed), Hyundai (HYMTF US), Innoviz (not listed), Intel (INTC US), Jaguar (TTM US), Locomation (not listed), Luminar (not listed), MAN (MAN SE), MAN (not listed), Micron (MU US), Mobileye (MBBYF US), NIO (NIO US), NVidia (NVDA US), Peleton Technology (not listed), Quanergy (not listed), Scania (SCVA SS), Tata motors (TTM US), Tesla (TSLA US), Uber (UBER US), Velodyne (not listed), Volkswagen (VOW DE), Volvo (VOLV ST), Waymo (not listed)

WHAT'S NEW IN THE SLEEP APNEA TECHNOLOGY MARKET?

Neuromodulation Devices Are Tackling Sleep Apnea

A broad but underrated condition

Sleep apnea (multiple ~10-seconds stops in breathing while sleeping) is a debilitating disorder that seriously affects people's quality of life. Most people are unaware of it, even if the condition has been related to several health problems, especially cardiovascular and neurological diseases.

- According to various estimates, the condition affects 25% of middle-aged men and 10% of middle-aged women globally, or about 1bn people.

Current solution does not fit all

For the past three decades Continuous Positive Airway Pressure (CPAP) machine has been the golden standard for the treatment of obstructive sleep apnea. However, the approach faces poor patient adherence.

- A high rate of patients try a CPAP machine and end up abandoning the therapy.

Neuromodulation devices to the rescue

Recently, alternative solutions have been developed based on a minimally invasive system to treat sleep apnea using neurostimulation. The devices sense breathing patterns and electrically stimulate the nerve controlling the tongue to liberate airways.

- Inspire Medical, spun out of medical-device giant Medtronic in 2007, has the only FDA-approved implantable device for sleep apnea since 2014.

SOURCE:
A brief history of OSA

Sleep Apnea: A Very Debilitating Disease

Different types of sleep apnea

Sleep apnea is a potentially serious disorder, in which people stop breathing temporarily (about 10 seconds) multiple times during sleep. This drastically reduces sleep quality and hampers nightly "rest and recover" functions of the body.

- Obstructive Sleep Apnea (OSA) occurs when throat muscles collapse at sleep.
- Central sleep apnea occurs when the brain doesn't send proper signals to the muscles that control breathing.
- Complex sleep apnea is a combination of the two.

A very burdensome condition

Sleep apnea is often correlated to obesity, aging, anatomical characteristics, smoking, alcohol consumption, hormone abnormalities, and others. If left untreated, it can have serious and life-shortening consequences.

- Sleep apnea results in increased stress and tiredness, high blood pressure, stroke, heart failure, diabetes, depression, and more.

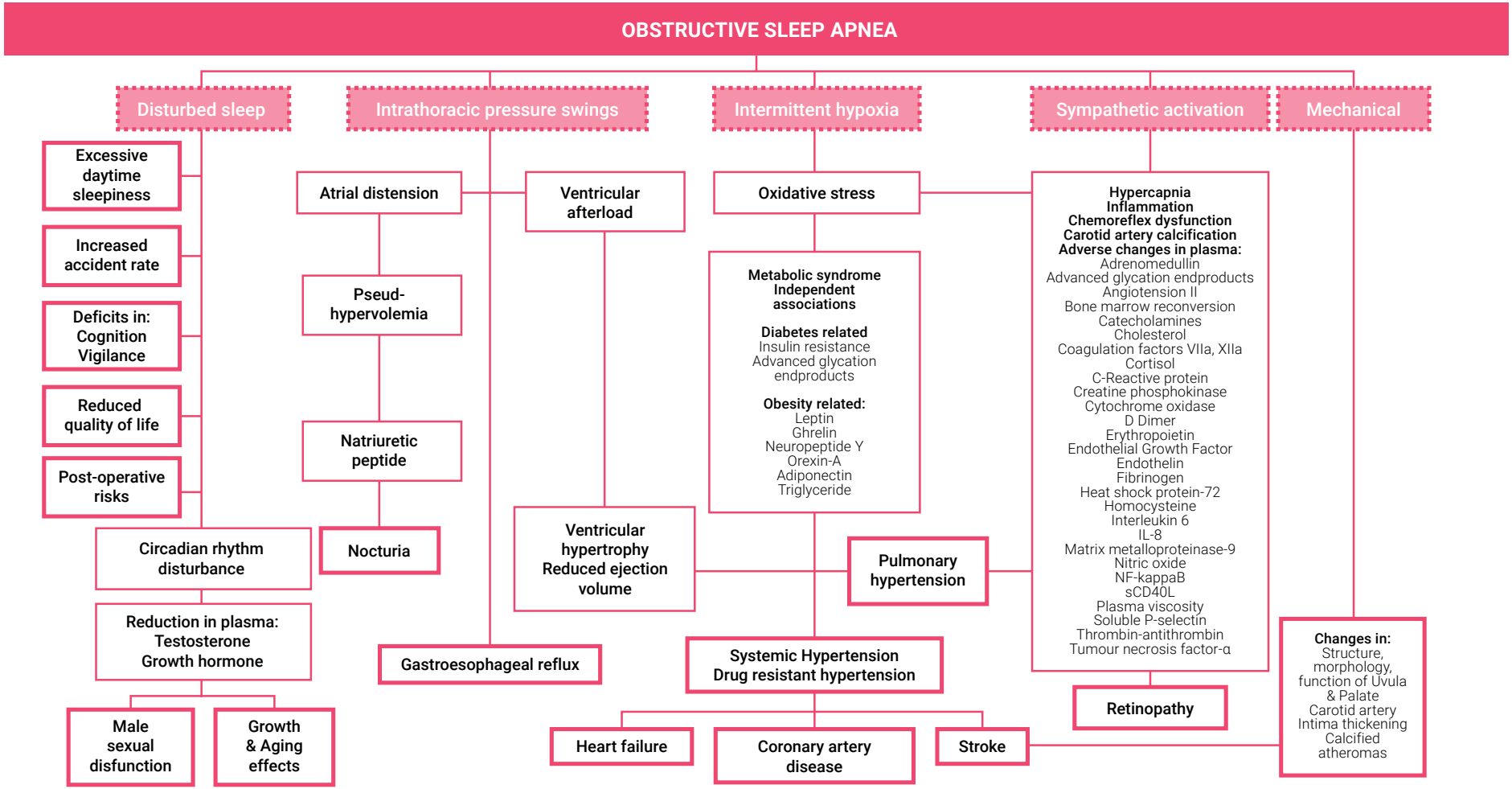
A common disease

Sleep apnea is a common condition often difficult to identify as many symptoms occur while people are asleep. Thus most cases remain undiagnosed.

- The condition affects >900mn people worldwide and 22mn people in the U.S.
- 80% of the cases of moderate and severe obstructive sleep apnea are not diagnosed.

SOURCE:
A brief history of OSA

Medical Consequences Of Obstructive Sleep Apnea



SOURCE:
A brief history of OSA

Innovation In Sleep Apnea Technology Lags Behind

The standard of care: the CPAP machine

Continuous Positive Airways Pressure (CPAP) machine is the current standard of care for sleep apnea. The technology requires patients to sleep wearing a mask hooked up to a flow generator that delivers constant and steady air pressure.

- CPAP devices are offered by device makers like ResMed and Philips.
- Annually, ~2mn people in the U.S. are prescribed a CPAP device.

Other alternatives

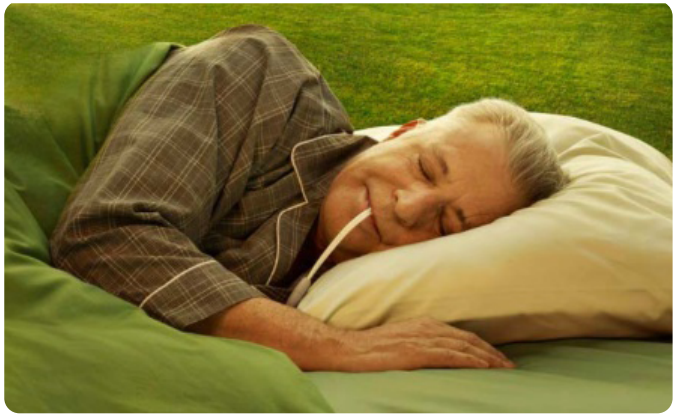
BiLevel Positive Airways Pressure (BiPAP) therapy, is often used as an alternative to CPAP for patients which also have lung issues such as Chronic Obstructive Pulmonary Diseases (COPD). Smaller devices have been recently developed.

- BiPAP uses two pressures; an inhale pressure and a lower exhale pressure.
- The Winx Sleep Therapy System, developed by Apnicure, includes a mouthpiece, tubing, and small console to apply a gentle vacuum to the soft palate and tongue.

Limits of current standard technology

Some patients find the mask uncomfortable or are otherwise unable to consistently, correctly use this device. Therefore, the rate of nonadherence is high. The technology has not improved significantly over the past 20 years.

- A literature review found the rate of nonadherence ranging between 34% and 65%.
- People wearing the CPAP machine may have trouble tolerating the air pressure or the machine's noise and may also have difficulty falling asleep.



SOURCE:
Trends in CPAP adherence over twenty years of data collection: a flattened curve
Treatments for Obstructive Sleep Apnea

The Pacemaker Of The Tongue

A less burdensome solution for OSA

Companies are developing and commercializing minimally invasive solutions that use neuromodulation to treat patients with OSA. This technology provides a no-hose, no-mask solution to significantly improve sleep apnea events.

- Inspire Medical holds the monopoly of this technology in the U.S. while Nyxoah, its main competitor, is still conducting clinical trials.

An innovative mini-invasive approach

Inspire's neuromodulation technology consists of a fully implanted sensor that tracks breathing patterns. If the device detects any blockage, it delivers targeted stimulation to the hypoglossal nerve, which controls tongue muscles and airways. The system is operated via a handheld remote device and inserted through a minimally invasive surgical procedure.

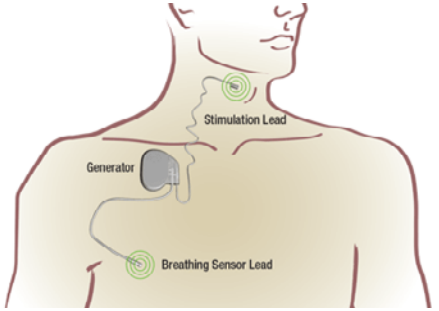
- The two-hour surgical procedure requires three small incisions in an outpatient procedure. The implanted device lasts 11 years on the original battery.

Building evidence and sustaining innovation

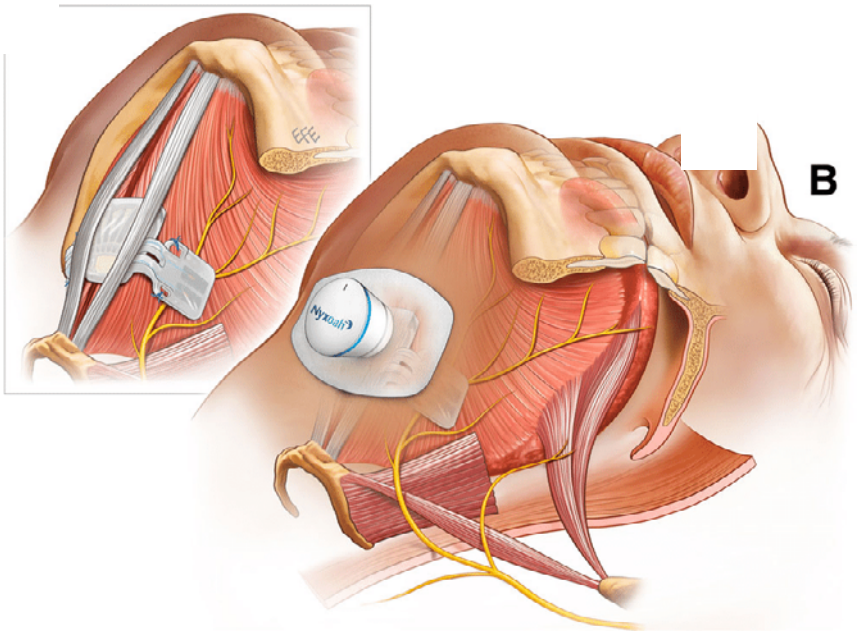
The efficacy of hypoglossal nerve stimulation has been proven over time and Inspire Medical continues to conduct clinical trials to build evidence of the effectiveness, further reducing the size and the invasiveness of the device.

- 23 studies with 2100 patients have shown the method's benefits.
- Over 90% of patients continue using the neurostimulator weekly.

INSPIRE MEDICAL'S UPPER WAY STIMULATION DEVICE



Source



Inspire Medical Systems

Growing fast

Despite its high cost, insurers have signed on to cover the device and Inspire's sales have been building. The company aims at grabbing a dominant position in the market.

- Full costs are $30–40k per patient, of which $15–20k are for the device. Medicare covers $29k per procedure.
- 3Y revenue CAGR (2016-2019) is 71%.

Rapid acceptance by insurers

Inspire has continued to expand hospital partnerships helping positive coverage decisions by insurers, now covering 182mn people and eliminating a major barrier to adoption. Coverage across the entire U.S. by Medicare is also helping.

- Aetna started covering the device in 2018, followed by UnitedHealthcare in 2019 and Cigna in 2020. Several BlueCross BlueShield plans have also stepped up to cover the device.

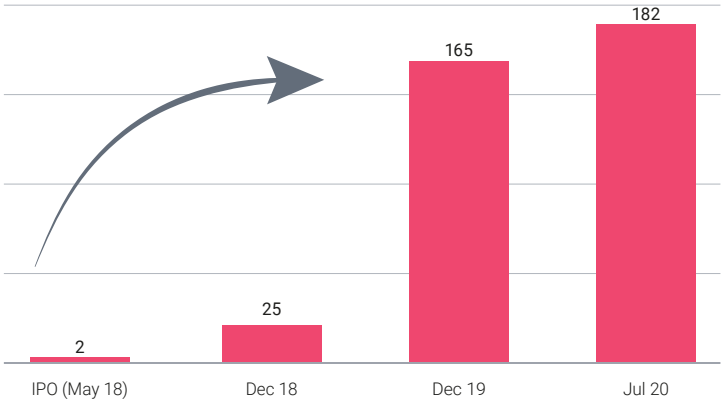
Scratching the surface of their opportunity

The device is only approved for patients with OSA that are not-compliant with CPAP and meet certain anatomy requirements. However, the addressable market remains very attractive.

- >500k patients in the U.S. qualify for Inspire's device every single year. Their opportunity in the U.S. alone is $10bn vs. $82.1mn in revenue in 2019.
- The company is also expanding outside the U.S.

Inspire
Sleep Apnea Innovation

RAPID INCREASE IN COVERED PEOPLE (MN)



SOURCE:
Novocureupdated August 2019

Catalysts

- **Market expansion.** Inspire Medical is continually working to expand the approval for the use of its device. Multiple use extensions are in the pipeline and are likely to spur increased interest in the product and the company.
- **Product is becoming affordable through insurance.** Medicare and private insurers are already onboard. Growth may significantly accelerate if insurances decide to allow patients to choose the Inspire device as their first option.
- **M&A.** Inspire Medical may represent an interesting target for companies playing in the same sector – respiratory / neurostimulation devices – e.g., Resmed, Abbott, Medtronic, Philips.

Risks

- **Competition intensifies.** LivaNova already competes with Inspire Medical in Europe but in the U.S. is still running clinical trials. Nyxoah's has received the EU CE Mark approval in 2019 and is working towards FDA approval.
- **Price.** The high price may lead insurance companies to limit access to this procedure, keeping the device as a second option after CPAP technology.
- **A single-product company.** Currently, Inspire Medical only offers one device: the neurostimulator for sleep apnea.

Bottom Line

- Sleep apnea represents a huge market opportunity to jump in. New neuromodulation technologies are disrupting this space and rapidly gaining markets share from CPAP machines. Inspire Medical Systems offers the only FDA approved implantable device for OSA since 2014, a game changer technology for people who do not tolerate the use of standard CPAP machine.
- With an increasing patient population covered and no better solution in sight, the technology has a tremendous market opportunity. Our portfolios are currently exposed to this very promising niche market.

Companies mentioned in this article:

Apnicure (not listed), Inspire Medical Systems (INSP US), Koninklijke Philips (PHIA NA), LivaNova (LIVN), Medtronic (MDT US), Nyxoah (NYXH BB), ResMed (RMD US).

FRESH BLOOD IN HEMATOLOGY

An Area Of Fast Paced Innovation

A large and important market

The hematology drug market is worth over $100bn, growing at mid double-digits. and includes hematological malignancies and diseases that alter blood functions.

- Blood cancers have seen innovations in past decades that completely altered the prognosis of these historically fatal situations.
- Other blood disorders have also seen fast paced innovation, including gene therapy and gene editing for diseases such as hemophilia, beta thalassemia and sickle cell anemia, on which we have previously written.

Room for significant improvement

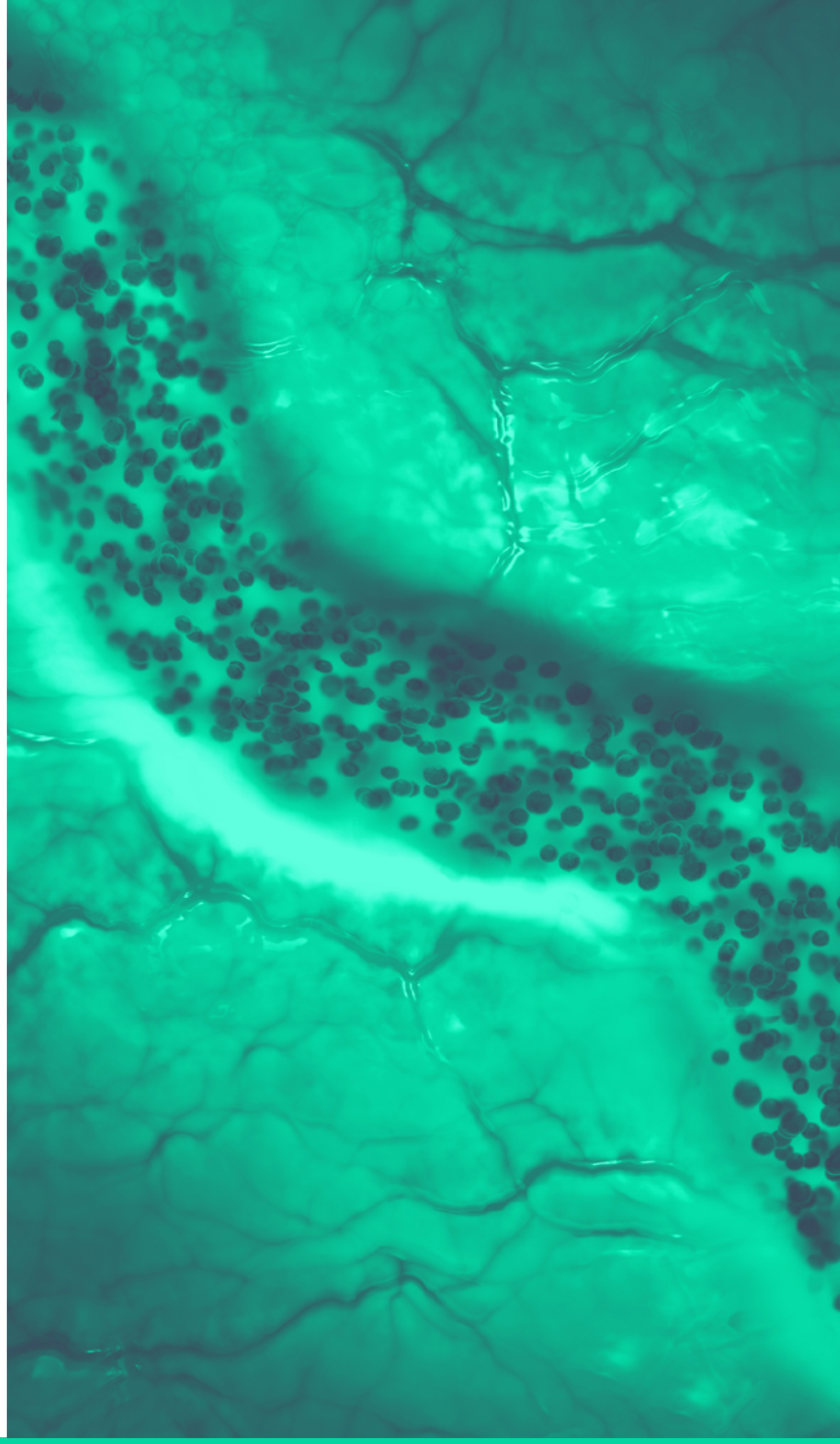
Expectations are building up about new treatments for Sickle Cell Disease (SCD) and emerging biological and cell therapy technologies for hematological malignancies, notably Non-Hodgkin Lymphoma (NHL).

- The SCD treatment landscape is rapidly evolving, as the current treatment paradigm remains suboptimal and the need for innovation is strong.
- The innovation wave in blood cancers, like for NHL, is still in full swing, despite already impressive achievements in recent years.

A key event is just around the corner

December sets stage for the most important hematology medical meeting, the American Society of Hematology (ASH) conference, where data will be presented across a range of therapeutic areas and technology platforms.

- Biopharma players use this venue (virtual this year), abundant with leading specialists and Key Opinion Leaders (KOLs), to reveal data from their clinical pipeline assets and shedding light on how novel technologies are faring.



Sickle Cell Disease – Overview

Sickle cell disease is an inherited blood disorder

The disease is autosomal (not sex related) recessive (needs 2 copies of the defected gene) and is caused by a single point mutation in the hemoglobin gene.

- Hemoglobin is a protein found in red blood cells and allows them to transport oxygen to distal (remote) tissue.
- For patients who inherit the sickle cell mutation, mutated hemoglobin polymerizes, leading to crescent sickle shaped red blood cells.

The disease causes debilitating, life-long symptoms

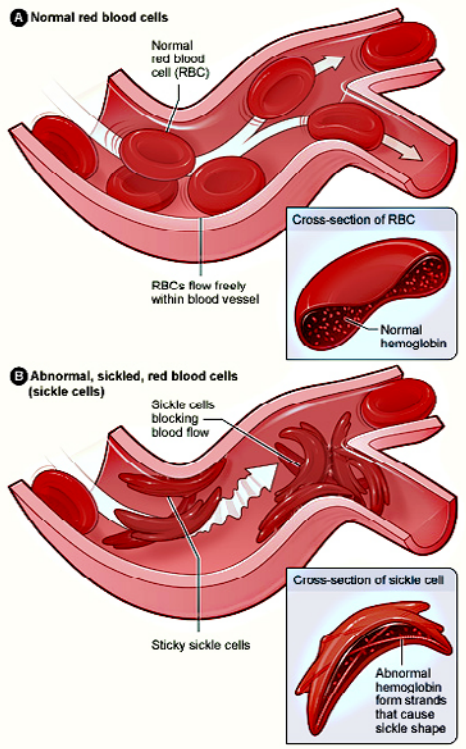
Sickle cell disease patients experience a severely reduced quality of life and shorter life expectancy, because of disease-driven complications.

- Obstruction of vascular function, leading to anemia and vaso-occolusive crises, which manifests in severe pain requiring hospitalization.
- Long-term complications include multi-organ damage such as kidney diseases, stroke and hypertension, leading to increased risk of death.

A sizeable market, but little financial incentive

Classified as a rare disease, it affects approximately 100k patients in the US, making it one of the largest in that group. It disproportionally affects minorities, predominantly African Americans.

- Annual cost for a symptomatic patient is estimated at $285k, mainly due to transfusions and hospitalizations.
- By its nature, the at-risk population (mainly minorities) had less insurance coverage, lowering the incentive to invest for biopharma companies.



SCD OVERVIEW

~ 100K	~ 55%
SCD patients in the US	Days with pain
25–30yr	↑ Risk
Reduction in average life expectancy	Stroke, Acute Chest Syndrome, Renal failure

SOURCE:
Wikipedia – Sicle cell
Forma Therapeutics

Sickle Cell Disease – Innovative treatments

Still an underserved market, despite recent developments

Possibly relating to its demographic features, patients had few treatment options, however this is changing fast and in 2019 two new drugs were brought to the market.

- Hydroxyurea, approved in the late 90's, has been the standard of care for sickle cell disease for the last decades.
- The new drugs treat either the hemoglobin polymerization or the pain episodes, but none has shown to be effective in both.

PKR activators offer new hope

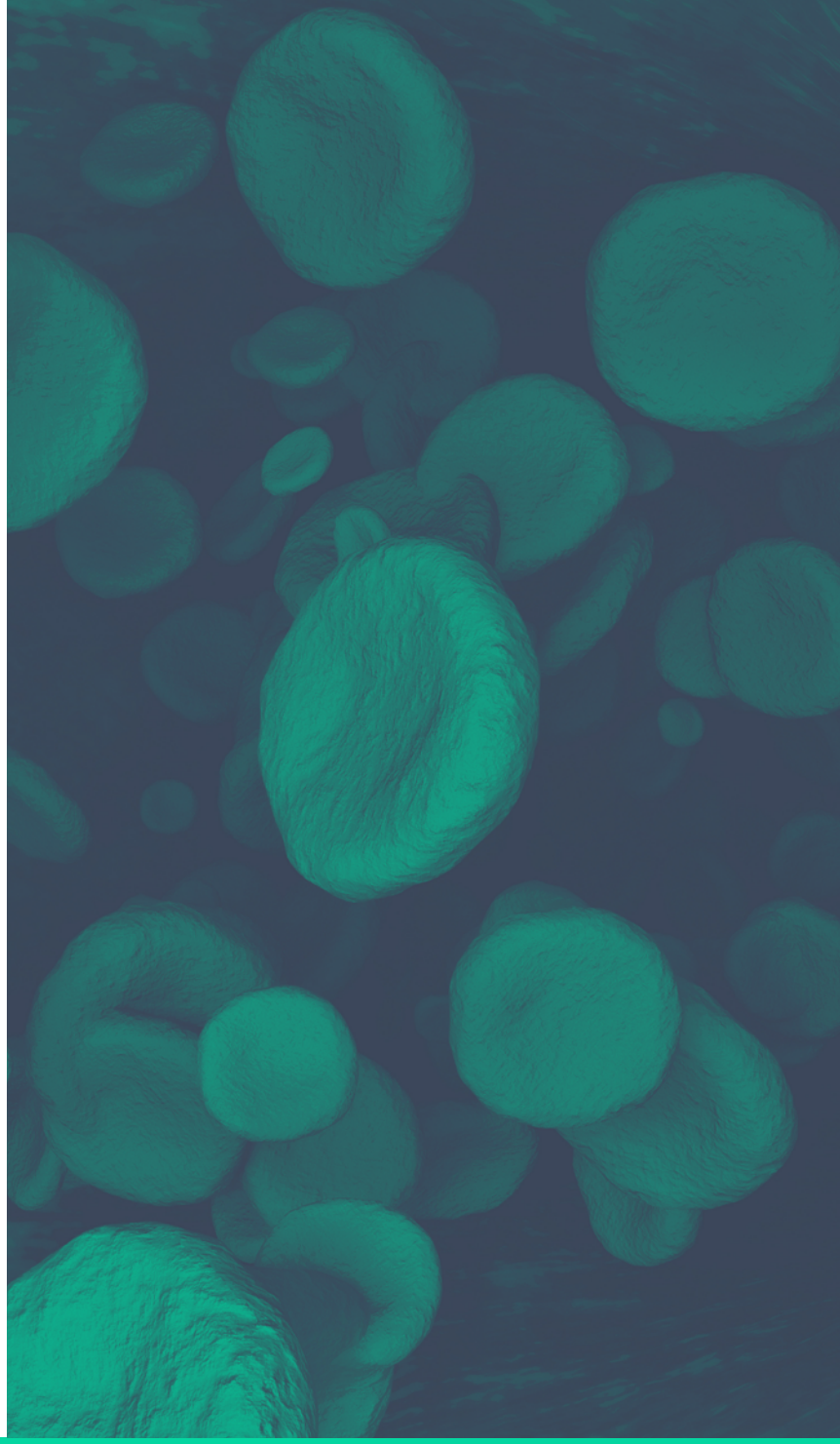
PKR activators are small molecules targeting the red blood cell's energy metabolism and increasing the cells energy levels.

- Activating the PKR pathway should have a more upstream effect and is expected to affect both the oxygenation levels as well as the pain episodes.
- An oral small molecule is still the easiest to adopt and would be the first line treatment option.

The newcomers in the race

Forma Therapeutics and Agios, will both be presenting early data from their PKR programs, which have the potential to be a game changer in this indication.

- Forma, ahead in the development race, should present data from a study investigating higher doses, having already shown intriguing hemoglobin response after a single dose.
- Agios already reported top line data from their ph.1/2 and should provide more granular data, important for its competitive positioning.



Non-Hodgkin Lymphoma – Overview

A broad encompassing term

Non-Hodgkin Lymphoma (NHL) is a type of blood cancer that affects specific white blood cells called lymphocytes. NHL is a general term used for various types of T-cell and B-cell lymphomas.

- The most common types are Diffuse Large B-cell Lymphoma (DLBCL) and Follicular Lymphoma (FL), representing about 60% of the ~77k people diagnosed with NHL annually in the U.S.
- The risk of these malignancies increases with age and most diagnoses are with older patients – aging population is likely to increase the incidence of this condition.

NHL is a fertile ground for research breakthroughs

The research on cancer cells in the blood has yielded an array of scientific innovations in oncology, from precision medicine to immunotherapies. Drug makers consider this field strategic given the higher chances for positive outcomes.

- Cancerous blood cells are far easier to access when compared to solid tumors, which are tissue specific, hence often facilitate proof of mechanism with a lower precision hurdle.
- Rituxan and Imbruvica, the two current first line treatments in this setting, were two of the top-selling oncology drugs in history, with peak sales north of $8bn each.

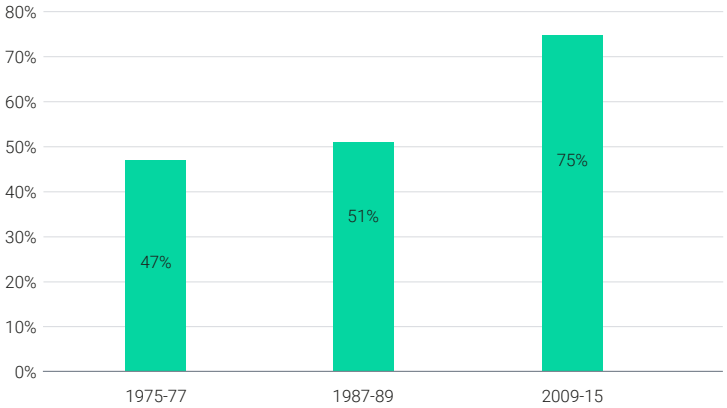
Clinical outcomes are still sub-optimal

The introduction of new treatments has improved NHL prognosis to non-fatal in many cases, but tolerability is still an issue. Pharmaceutical efforts in recent years have focused on relapsing patients with diminishing options.

- Evolution of targeted therapies, anti CD-20 antibodies such as Rituximab and BTK inhibitors like Imbruvica, are being used as front-line treatments (in combination with Chemo) and demonstrate robust efficacy.

ESTIMATED NEW CASES, 2020
NON-HODGKIN LYMPHOMA, BY SEX

CHANGE IN 5-YEAR SURVIVAL



Source:
American Cancer Society
Cancer Statistics Center

Non-Hodgkin Lymphoma – Innovative treatments (1/2)

Bispecific antibodies

Bispecific antibodies are molecules engineered to have the ability to bind to two different tissues simultaneously, which open the door for various biological, tumor-killing effects.

- In hematology (and specifically NHL) these antibodies, also called T-cell engagers, bind to a cancer antigen on one side and a T cell on the other, promoting a direct, tissue-specific anti tumor activity through different mechanisms.
- Amgen's Blincyto is the first (and only) bispecific approved to date, gaining regulatory endorsement based on impressive efficacy data on B-cell Leukemia.

A potentially lucrative market opportunity

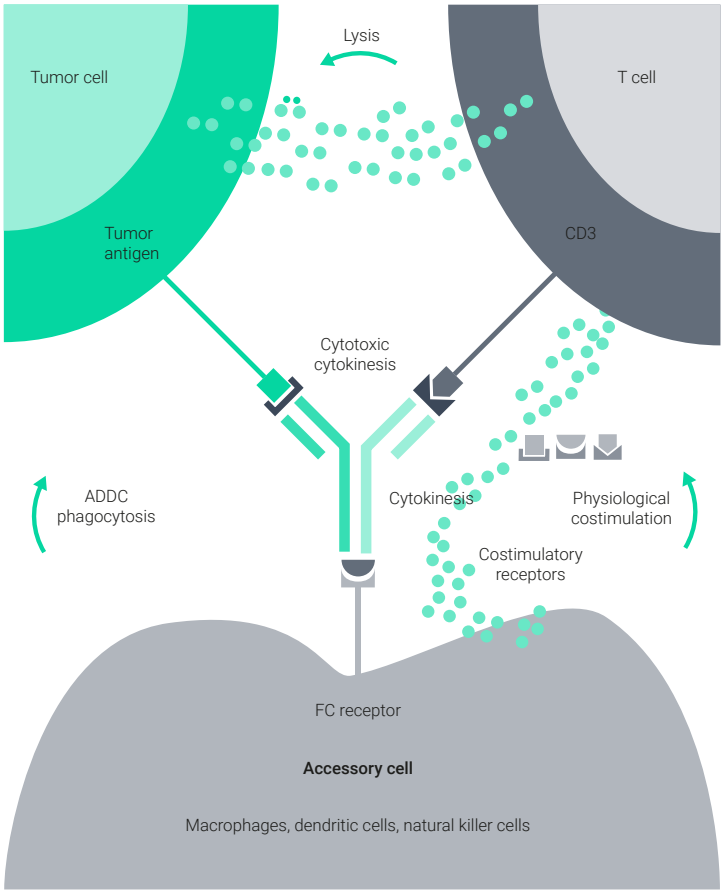
As is often the case in oncology for emerging technologies, bispecific antibodies currently address last line patients*, however the market opportunity is likely to grow substantially as these drugs are adopted earlier in the treatment algorithm.

- The NHL T-cell engagers market opportunity is estimated to reach peak sales of $5bn by 2035, however this assumes most sales to be for last lines, which is likely conservative.
- As a point of reference, Kite Pharma, which developed one of the first cell therapies for relapsing NHL patients, was acquired by Gilead in 2017 for $12bn.

What's in the clinics?

The CD20xCD3** T-cell engagers race is one of the most competitive in the industry. The approach, aiming at generating cell-therapy-like efficacy in a relatively easy to manufacture drug, with fewer side effects, has yet to be fully validated.

- Efficacy to date looks impressive (>90% response rate in indolent forms for last line patients). More patient data and larger safety-data base should help validation.



*patients that relapsed on all other therapies.
**CD20 is an antigen commonly expressed on B-cells and CD3 is a T-cell receptor with validated anti-tumor activity.

Non-Hodgkin Lymphoma – Innovative treatments (2/2)

Cell therapies promise has yet to fully materialize

The first cell therapies approved, notably Kymriah from Novartis and Yescarta from Gilead, were transformative, however commercial success was not that straight forward given significant logistical liability and a consequential hefty price tag.

- Approved therapies are autologous (derived from own blood), and therefore require a personalized process.
- Next generation cell therapy pipeline is predominantly allogenic (off the shelf), which should compensate for the biggest downfall of current cell therapies.

Simultaneously pursuing alternative targets

Additional immune system targets is a large area of industry focus, most notably Natural Killer (NK) cells. These are potent cytotoxic cells which play a key role against cancer and infectious diseases, both in antigen killing as well as signaling to other cells in the immune system.

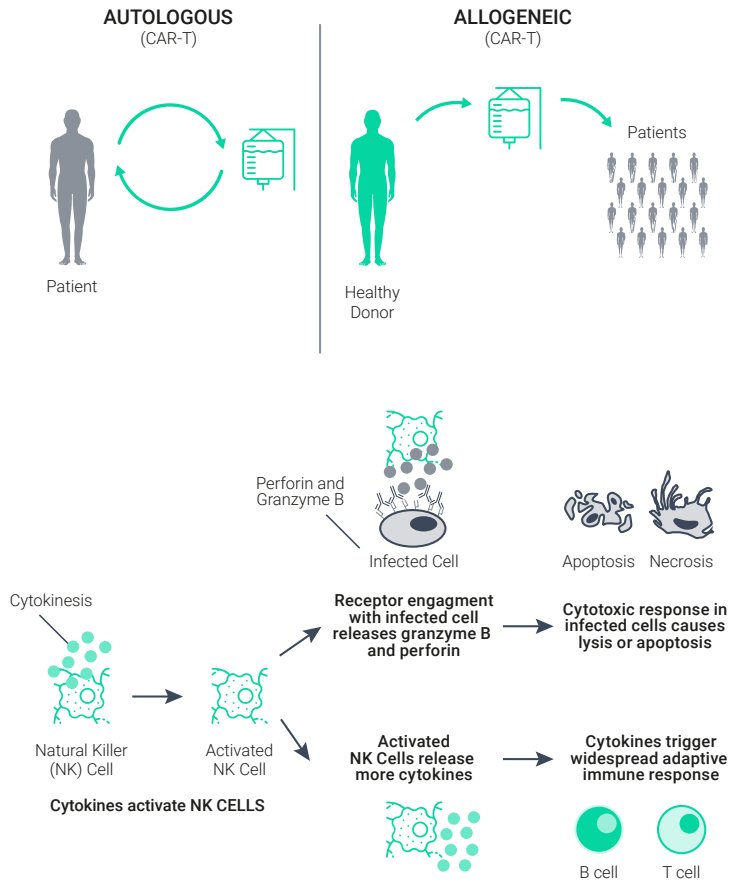
- Engineered NK cells are produced from healthy donors (and are therefore allogenic), expanded and engineered prior to administration, and are believed to provide similar efficacy with a better safety profile (another downfall of current CAR-T's).

Early results generated strong interest

First results published last year validated the hypothesis of targeting this part of the immune system, with impressive efficacy and none of the safety issues previously witnessed.

- There are currently several runners in the race that differ on several features such as the origin of the cell and the mutation that is being targeted.
- In focus at this year's conference is Fate's off-the-shelf multi-targeted NK cell therapy, which is thought to generate strong efficacy through direct tumor killing, in addition to augmenting anti-cancer activity of parallel treatments.

*Source: Company Filings and JP Morgan Estimates



Catalysts

- **Data presentations at ASH.** Upcoming data presentations during ASH, will help preliminary validation of mostly novel technologies and biological pathways, across therapeutic areas.
- **Label expansion.** We think these technologies are more a platform story than a single drug/indication and can be utilized across different diseases and earlier treatment lines, increasing market opportunity several folds.
- **M&A.** Most of the innovation in hematology is still coming from clinical-stage companies, and further validation will make them target for collaboration and consolidation.

Risks

- **Biological risk.** Despite promising early data, efficacy data tends to inclemently diminish with larger data sets, and safety risk is stress tested across broader populations.
- **Competition.** The successes in this space during the past decades made the hematology drug development market a premier venue for validating technologies, making it a particularly competitive market.
- **Trial disruption due COVID-19.** A risk emphasized in this setup, as mostly are early-stage studies, with mainly at-risk patient population (age >65) with other treatment options.

Bottom Line

- The hematology market has experienced substantial growth and demonstrated the crucial value of innovation, which also contributed to its highly competitive dynamic. Within these lines we believe that a profound understanding of the underlying science of each program and market application is crucial for picking the technologies and companies with a real potential to differentiate.
- As outlined in the article, we are focusing on the antibody space, notably on the bi-specifics, as well as on the cell therapy space, offering sizeable market opportunities for novel technologies. We have been building exposure to these segments in our portfolios over the past months and are looking to increase it depending on the data that will be provided at the upcoming ASH conference.

Companies mentioned in this article:

Agios (AGIO US), Fate Therapeutics (FATE US), Forma Therapeutics (FMTX US), Regeneron (REGN US)

CREDIT CARD COMPANIES DOOMED TO REINVENT THEMSELVES

The Road To A New Business Model

A gloomy future for credit card networks

Compared to traditional payment cards, new payment solutions are operationally more efficient, cheaper and more secure. Payment cards are losing market share and suffer margins contractions. Major card networks have an impellent need to reinvent themselves.

- Universal credit cards appeared in the 1950s and have lacked major innovation since then.

A thin line between long and short

Acquiring the next cash cow is not straightforward, as the payment networks face many legal obstacles in their quest for change. But no matter the ongoing legal inquiries, credit card networks will have to continue their M&A activities.

- Visa and Mastercard are under the antitrust radar of the Department of Justice.

Strong M&A activities benefiting the whole fintech industry

We believe the above-average growth in revenues experienced in the last decade by credit card titans will not last. To change their business model, card networks have been multiplying acquisitions and investments in promising fintech companies.

- Mastercard and Visa have publicly announced respectively 23 and 15 deals since the beginning of 2019.

SOURCE:
Encyclopaedia Britannica, Companies' reports, AtonRâ Partners

A Story Of Disruption

A payment method largely exposed to fraud

In early 2000s, at the birth of online payment, Visa and peers decided to rely on the "unguessable" credit card numbers, instead of developing a more adequate system. Frauds pushed to add several security layers but with limited success.

- Nilson Report projects the total amount of fraud to reach $37.3bn in 2025, almost 6% of the total volume processed.
- With over 270'000 reports, credit card fraud was the most common identity theft in 2019 in the United States.

Open banking era not designed for payment cards

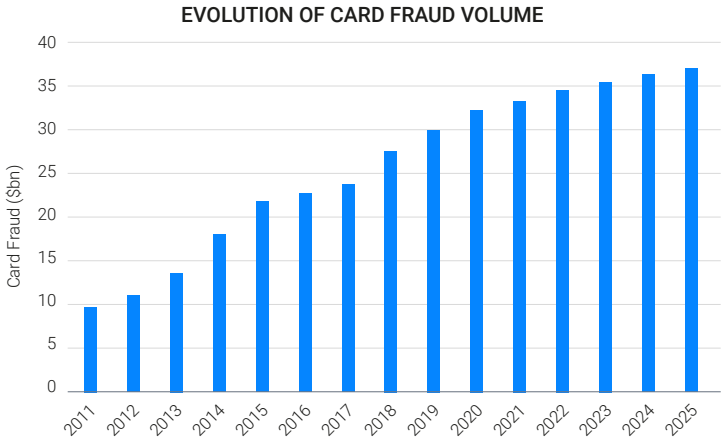
Thanks to open banking, any authorized organization or app can instruct a payment from a bank account, without the need of an intermediary like a card network. E-wallets facilitate P2P payments and new technologies, e.g., blockchain-based payments, are emerging too.

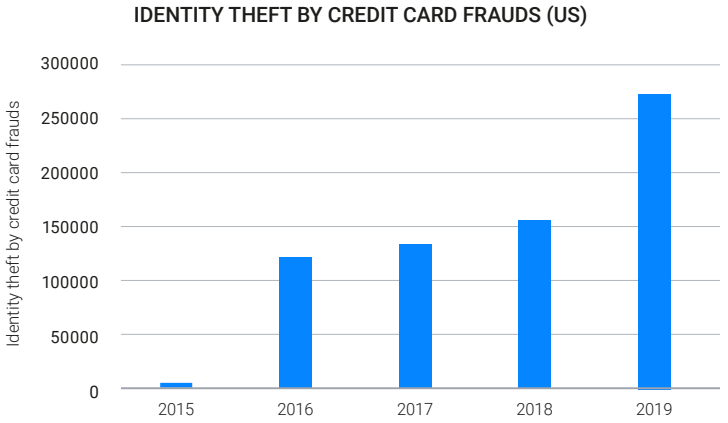
- In Europe, the EU directive PSD2 opened the financial services market.
- We wrote an introduction to open banking in this article.

Towards mass-adoption of new payment means

The new generation of alternative payment solutions offer all the advantages that were once only offered by credit cards, like rewards or deferred payment options. Millennials are heavy users of these new payment means, and older generations have been transitioning to these new apps during COVID-19.

- People over 50 accounted for the fastest growing segment from March to April 2020 on PayPal.





SOURCE:
Nilson Report, Federal Trade Commission, PayPal

Technology Acquisitions To Remain In The Race

The deployment of war chests

Competition in the payment industry has been intensifying thanks to the arrival of fintech companies. For historical players, the debate about technology boils down to build or buy. The latter was an obvious choice given the available war chests.

- Visa should generate free cash flows of $13bn in 2021, Mastercard $8bn.
- Their net debt/EBITDA is <0.25x, thus increasing leverage is not an issue.
- American Express is having a more difficult year due to its travel and hospitality industries exposure, but also has resources for acquisitions.

Open banking apps provide new sets of data

The most significant acquisitions are related to data. Visa acquired Plaid, which provides APIs to fintech firms and will eventually facilitate payments without payment cards. Through Plaid, Visa will have access to financial data of millions of people. Mastercard follows the same direction through the acquisition of Finicity, an open banking API provider and data aggregator.

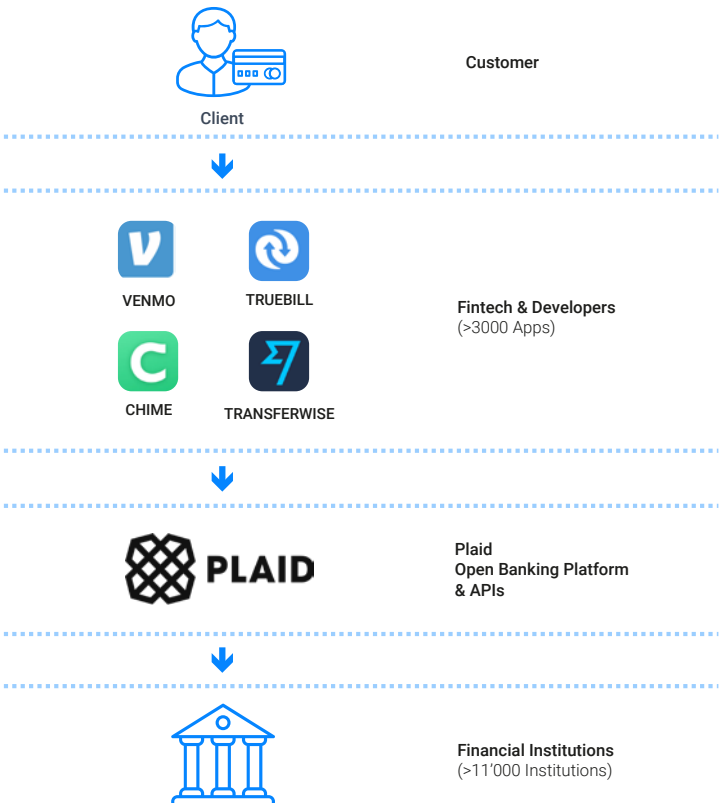
- Visa acquired Plaid for $5.3bn, almost 50 times the sales. For Finicity, the offered $985mn also represents more than 50 times the sales.

The shopping list is broad

Other technology investments have focused on increasing the security of the payment networks to reduce fraud, and on next generation payment platforms like cloud-based payments as well as fintech services, not related to payments.

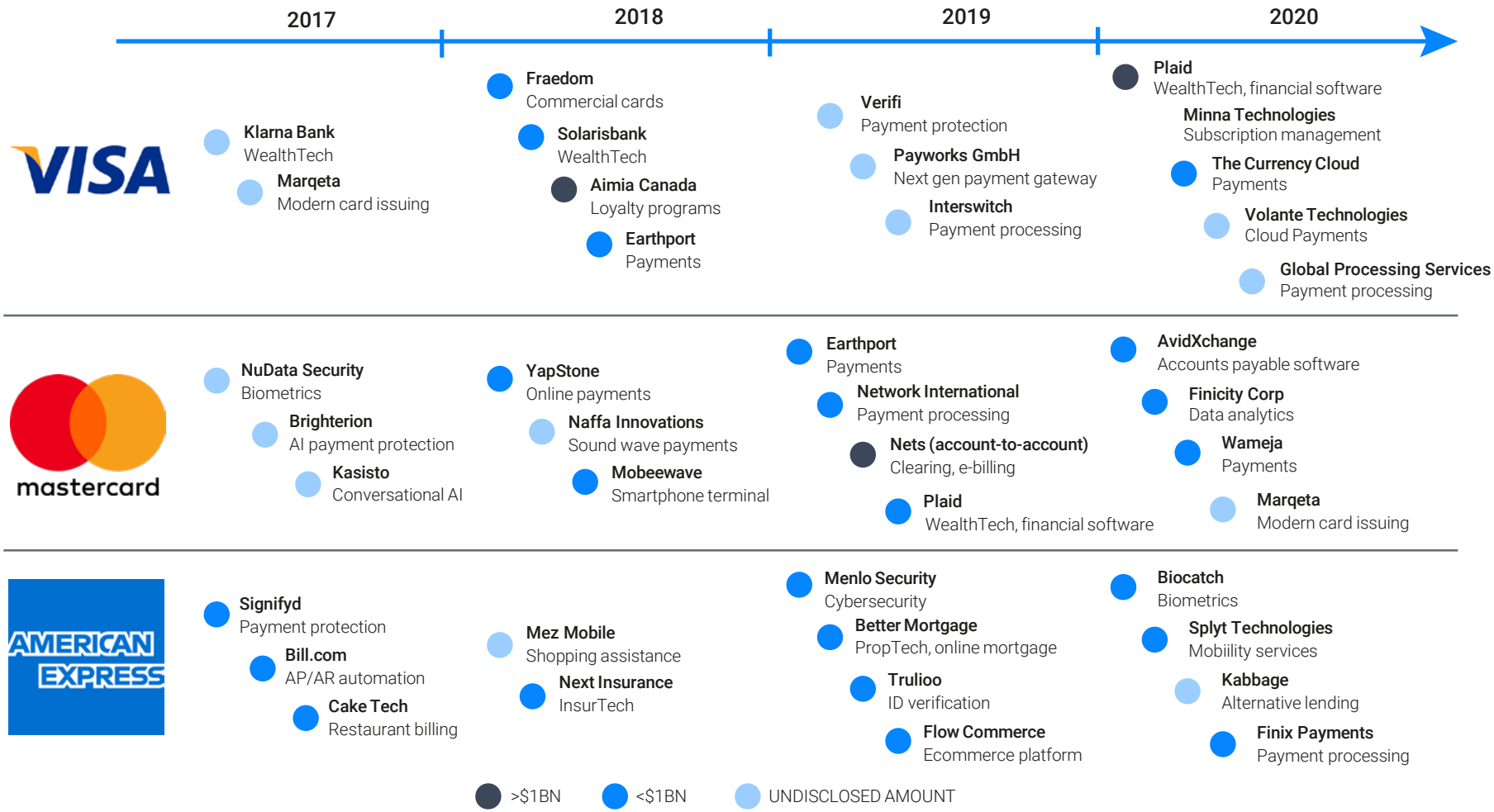
- American Express is diversifying its activities by investing in platforms for account payables, alternative lending, or insurtech.

PLAID, THE TECHNOLOGY SUPPLIER TO FINTECH



SOURCE:
Companies' financial statements, AtonRâ Partners

Selected Fintech Investments And Acquisitions



SOURCE:
Companies' reports, Reuters, AtonRâ Partners
Data as of 5 November 2020

Legal Difficulties On The Horizon

Antitrust scrutiny

The payment card industry is only composed of a handful of companies. The US Justice Department (DOJ) sees the recent M&A activities as the elimination of a nascent competitive threat going against innovation and savings for customers.

- The DOJ filed a lawsuit on Visa's Plaid acquisition in November 2020.
- Regulators are also looking at Mastercard's bid for Finicity.
- It follows a series of inquiries on the big tech acquisitions and activities.

The defense line for Visa

Visa argues Plaid is not a payment company. Negotiations between card networks and the DOJ will be difficult. A solution would be to lower fees on credit cards, dismantle the activities of the group, or guarantee that Plaid' services will remain available and affordable to fintech. This remains speculation so far.

- It is not the first time DOJ attacks Visa and Mastercard on their dominant positions.

A threat to long-term growth

Even if the current acquisitions fall apart, payment card tycoons will not disappear overnight. We believe they will keep acquiring promising technology to maintain long-term growth prospects and their leading market positions.

- According to the DOJ, Visa has a 70% market share of online debit services, Mastercard 25%.

SOURCE:
Department of Justice

Catalysts

- **Consumer protection.** New regulations in favor of consumers are likely to accelerate the transition to other payment means. The exclusivity agreements between banks and card networks could also be challenged.
- **User-friendly apps.** Credit and debit cards are easy to use. Developers try to make the new generation of e-wallets and payment apps as user-friendly as cards.
- **Scalability of blockchains.** The technology behind distributed ledgers is evolving to reach the same number of transactions per second as credit card networks. The nascent Ethereum 2.0 is a good example of a protocol that could revolutionize the payment industry.

Risks

- **Barriers to entry.** The oligopoly power of credit card companies represents significant barriers to entry for competitors and new technologies. We could be overestimating the impact on the top line of Visa or Mastercard if they do not modify their business model.
- **Habits take time to change.** The silver generation is not as tech savvy as millennials and will remain important clients for the traditional payment means for the next two to three decades.
- **Antitrust regulations.** Regulators may put an end to the shopping frenzy of credit card companies.

Bottom Line

- Credit and debit card companies are destined to lose market shares against other payment means. Forced to review their business model, they have multiplied investments and acquisitions in promising fintech companies to keep up with the competition. We believe that despite the current DOJ inquiries, credit card networks will have to continue their shopping spree.
- We see this M&A activity as highly positive for the entire fintech industry. Our exposure to credit card majors in our portfolios will evolve based on the eventual success of current and future deals.

Companies mentioned in this article:

American Express (AXP US), Finicity (not listed), Mastercard (MA US), PayPal (PYPL US), Plaid (not listed), Visa (V US)

ELECTRICITY SUPPLY: KEEP THE SPARK ALIVE

An Evolving Power Sector

Growing electrification driven by renewables

Growing electrification is happening in both developed and emerging economies with many sectors being increasingly reliant on electricity. Additionally, the power mix is shifting to a more significant share of variable renewable energy sources.

- The share of electricity in final energy consumption grew from 15% to 20% today and is to reach 31% by 2040 in a 2° scenario (source: IEA).
- Wind and solar are to supply 56% of global electricity by 2050 (vs. 9% today), while power demand is to rise +60% worldwide over the same period.

The electricity system is facing new challenges

The ongoing energy transition towards more variable renewable generation, combined with the growing adoption of digital technologies and the increased impact of climate change is putting electricity systems under new threats.

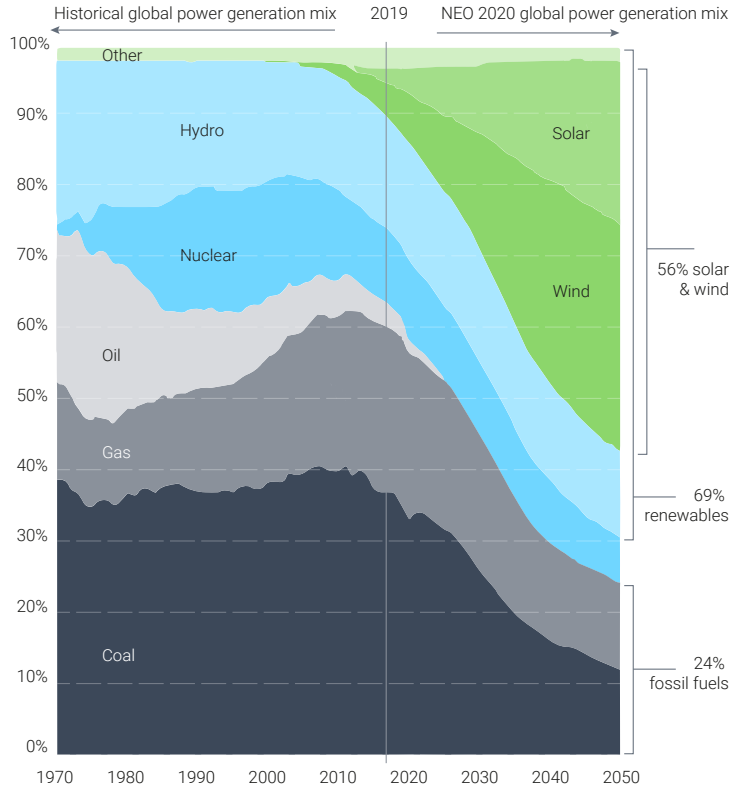
- Generation variability increases uncertainty & complexity of electricity systems.
- Digitalization expands the vulnerability to cyberattacks.
- Extreme weather events is the leading cause of power outage in the U.S.

Technology to the rescue

To cope with these imminent challenges threatening electricity security, the power sector has no choice but to develop and deploy new technologies & policies. It is the role of policy makers, regulators and operators to co-operate and make sure the required actions are implemented.

- Growing share of variable renewables requires increased system flexibility.
- Digital technologies must be standardized and secured.
- Power grid infrastructure must be made more climate-resilient.

GLOBAL ELECTRICITY GENERATION MIX



SOURCE:
Power systems in transition, IEA 2020,
Utility Outages Spur Legislative Changes During Challenging Extreme Weather Events

Ensuring Continuity During The Energy Transition

Power systems need to be more flexible

New distributed generation sources require more flexible systems to cope with their higher variability (wind and solar are not available 24/7). This flexibility can be provided by deploying other low-carbon sources (e.g., biomass/biogas, hydrogen, etc.), demand response, batteries, and improved interconnection of regional systems.

- A diversified generation mix mitigates the risk of supply disruption.
- A more intelligent use of energy storage and dispatchable generation will be essential to maintaining security of supply during peak demand.

New investments are needed

The need for system flexibility increases as the generation mix shifts to variable renewable energy. Government policies & spending need to focus on building renewables but also on providing solutions that enable grid stability.

- Policymakers should start incentivizing flexibility resources, demand-response technologies and energy storage (short, medium and long duration).

Improve grid flexibility to integrate more variable renewables

Grid flexibility is in essence its ability to handle power variability and balance demand & supply. This can be done at the demand side (e.g., behind-the-meter storage, or smart charging, where consumer adapts the amount of power he injects into the grid), at the supply side (e.g., standalone batteries, or hydrogen storage, compressed air, etc. to help balance grid supply), or at the transmission & distribution levels (microgrids, community storage, aggregated loads, etc.).

- Tesla is working on several fronts by providing home batteries (powerwall) and commercial & utility scale storage (powerpack/ megapack).

SOURCE:
New Energy Outlook 2020, BNEF

Improving Cyber Resilience

Cyberattack surface is expanding

An increasing use of connected devices & distributed resources such as distributed renewables, home batteries, electric vehicles, or smart devices, results in expanding the cyberattack surface & cyber vulnerability of electricity systems.

- While the number of "significant" cyber attacks (damages >$1mn) remains low, energy remains one of the U.S. top 3 targeted sector for cyberattacks.
- In winter 2015, a cyberattack targeted several power providers in Ukraine, leaving >230'000 people without access to electricity for several hours.

Regulations and innovation are key to mitigate cyber risk

Governments must put in place new standards to enable better traceability throughout the supply of key grid components. Innovative technologies aim to detect anomalies on networks, spot intrusions, and develop real-time response.

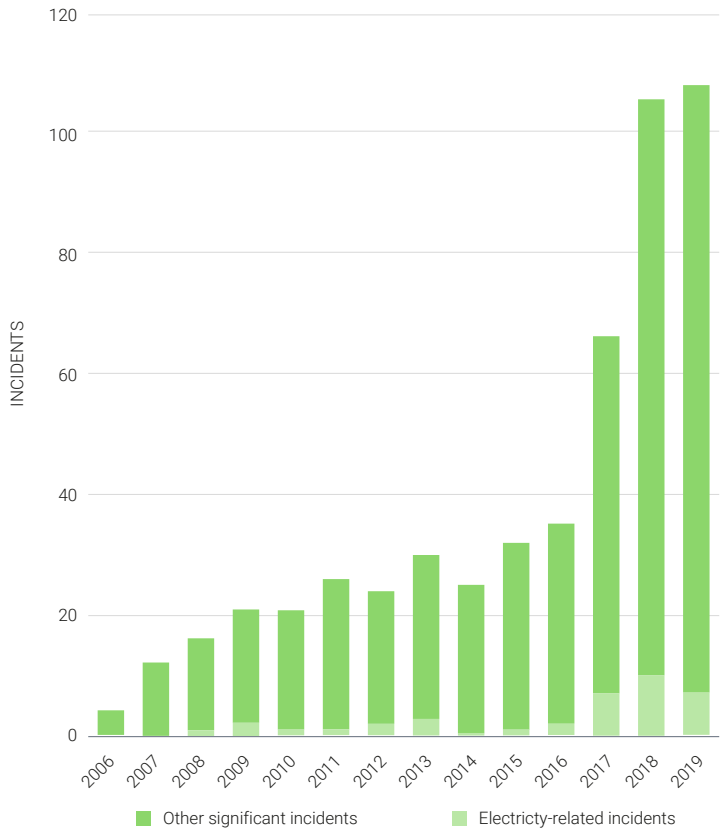
- Blockchain can be used to improve traceability through components' supply.
- Earlier this year, Trump signed an executive order aimed to limit the use of foreign components in the U.S. grid, mentioning "extraordinary threat to national security".

Standards and tech to minimize cyber risk

Standards exist to set up the basis for power grids cybersecurity, e.g., the North American Electric Reliability Corporation Infrastructure (NERC CIP) or the European Programme for Critical Infrastructure Protection (EPCIP). Since security threats keeps on evolving, utilities must constantly improve measures & processes.

- Schneider Electric developed the EcoStructure Cybersecurity Admin Expert software to manage cybersecurity of electrical network's operation technology through a set of tools (define & assign system rules, users' permissions, etc.).

SIGNIFICANT CYBER INCIDENTS WORLDWIDE, 2006-2019



Note: "Significant" cyber incidents are defined here as cyberattacks on government agencies, defence and high tech companies, or economic crimes with losses of more than a USD 1 million.

SOURCE:
Power systems in transition, IEA 2020
Managing cyber risk in the electric power sector, Deloitte 2019
Executive Order on Securing the United States Bulk-Power System

Mitigating Climate Risk (1/2)

Climate change is directly threatening power systems

Climate hazard is threatening electricity systems by impacting both supply (generation, transmission and distribution infrastructures) and demand patterns (heating/cooling needs).

- Recent heatwave in California spurred air conditioning demand causing rolling blackouts for up to 4mn people during several hours across several days.
- In the U.S., about 90% of large-scale power outages (affecting >50'000 people) in the past 20 years were caused by extreme weather events.

Investing in resilient system is profitable on the long run

To avoid enormous economic losses associated with climate-related damages, governments must make climate resilience a top priority. Supportive incentives should be introduced to facilitate utilities' long-term investment in resilient technologies.

- It is estimated that for every dollar invested in climate-resilient infrastructures, six dollars are saved.

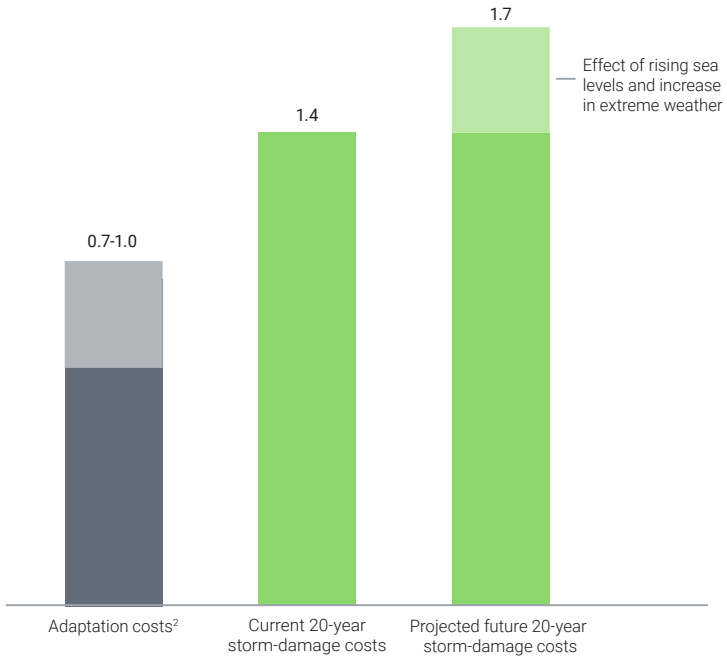
Modern and smart infrastructures to improve climate resilience

More accurate climate projections and weather predictions (by using AI&ML, satellite data, etc.) are key to help utilities anticipate and respond faster. Additionally, some structural measures can be taken on the infrastructure itself, e.g., build higher transmission/distribution towers, use stainless steel material, etc.

- Trimble provides solutions to help with utility network design, maintenance, optimization, & outage management, including digital twin features providing a virtual replica of the power network's real-time condition.

TAKING ACTION ON RESILIENCY CAN BE COST-EFFECTIVE, ESPECIALLY WHEN CLIMATE-CHANGE RISKS ARE TAKEN INTO ACCOUNT

Adaptation Costs Compared With 20-year Strom-damage Costs[1]
For A Typical Utility In Southeastern United States. Estimate, $bn



[1]Storm-damage costs include lost revenue (currently $0.1 billion), in addition to damage repair.
[2]Adaptation involves "hardening the infrastructure" ie, reinforcing the transmission and distribution infrastructure.

SOURCE:
For Every Dollar Invested in Climate-Resilient Infrastructure Six Dollars Are Saved, Secretary-General Says in Message for Disaster Risk Reduction Day,
Redefining the power industry,
Power systems in transition, IEA 2020

Mitigating Climate Risk (2/2)

EXAMPLES OF ADAPTATION MEASURES FOR ENERGY INFRASTRUCTURE

	Climate impacts on infrastructure	Management measure	Structural Measure
Generation	• Inundation of coastal infrastructure, such as generation plants • Reduced efficiency of solar energy • Insufficient cooling water • Temperature of cooling water before and after use • Reduced output from hydropower generation	• Model climate impacts on existing and planned assets in collaboration with meteorological service • Revise maintenance schedules • Update hydropower operating • Update hydropower operating rules	• Fortify coastal, off-shore and flood-prone infrastructure against flooding • Increase cooling system capacity • Locate new facilities outside high-risk zones
Transmission and distribution	• Flooding of electricity substations • Damage to transmission lines from climate extremes	• Implement program for pruning and managing trees near transmission and distribution lines • Create disaster mitigation plans • Train emergency response teams for quick repair and restoration actions	• Adjust design criteria for transmission lines, e.g.: ◦ Increase transmission tower height ◦ Bury distribution lines ◦ Use stainless steel material to reduce corrosion from water damage
Consumption	• Change in energy demand patterns (e.g. increased demand for cooling and reduced demand for energy for heating)	• Undertake load forecasting using climate information • Promote behavioural change measures to reduce peak consumption	• Improve building and industrial energy efficiency

SOURCE:
For Every Dollar Invested in Climate-Resilient Infrastructure Six Dollars Are Saved, Secretary-General Says in Message for Disaster Risk Reduction Day.
Redefining the power industry.
Power systems in transition, IEA 2020

Catalysts

- **Supportive regulations.** Policymakers can stimulate investments in the required safety technologies/ infrastructure by setting-up supportive incentives & regulatory frameworks.
- **Rising public awareness.** The increasing frequency of power outages is rising public awareness and adding pressure on companies & politics to take the appropriate actions.
- **Technology breakthrough.** Breakthrough in battery technologies or renewable synthetic fuels could provide the required system flexibility and allow intermittent renewables to considerably increase their share in the power mix.

Risks

- **Uncontrolled growth.** An uncontrolled growth of renewables share in the power mix without proper investments in flexible resources could threaten system' stability.
- **Climate change denial.** Lack of political interest on climate change impacts could lead to insufficient spending in power resiliency.
- **Cyberwar.** Geopolitical tensions could spark new major cyber attacks on electricity systems, resulting in irreversible damages.

Bottom Line

- Electricity plays a central role in all modern economies with implications in many critical sectors (e.g., banking, healthcare, transportation), hence securing reliable electricity supply is a top priority. The increasing share of renewables, combined with new cyber risks associated with digitalization, as well as climate-change related impacts are all new challenges that power systems need to cope with.
- In our Sustainable Future portfolio we have a broad exposure to key technologies enabling the security, stability and resiliency that are required by power systems.

Companies mentioned in this article:

Schneider Electric (SU FP), Tesla (TSLA US), Trimble (TRMB US)

CHARTS FOR THOUGHTS

Will Medical Innovation Impact Supply?

Healthcare spending drives innovation

Developed countries with remarkably good healthcare systems are also those where the per-capita spending is highest. It can be argued that high compulsory and government health spending is related to medical innovation.

- Taking the Nobel Prize in Medicine as a simplified indicator, the leading spender, the U.S., has by large the highest number of Prizes.
- But Switzerland, Denmark and Sweden, all smaller countries by population, do lead in terms of number of Prizes per-capita as well as in terms of spending.

Inflation Disparity

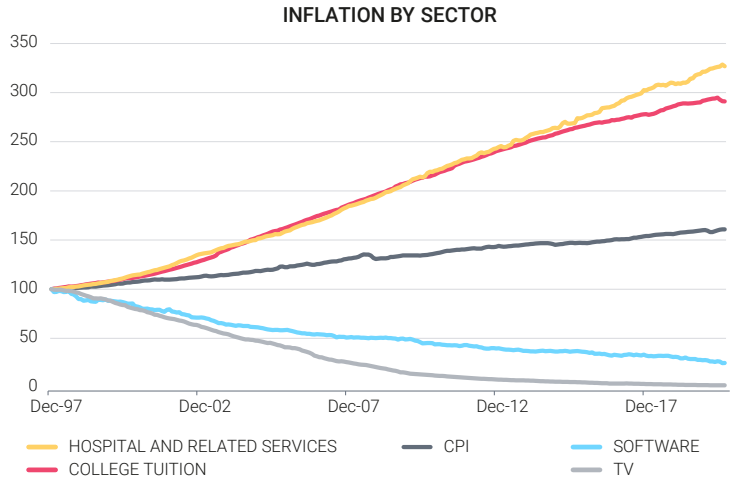
As discussed here, the disparity in inflation across U.S. sectors relates to pricing power. Where innovation drives supply to match or exceed demand, inflation turns negative.

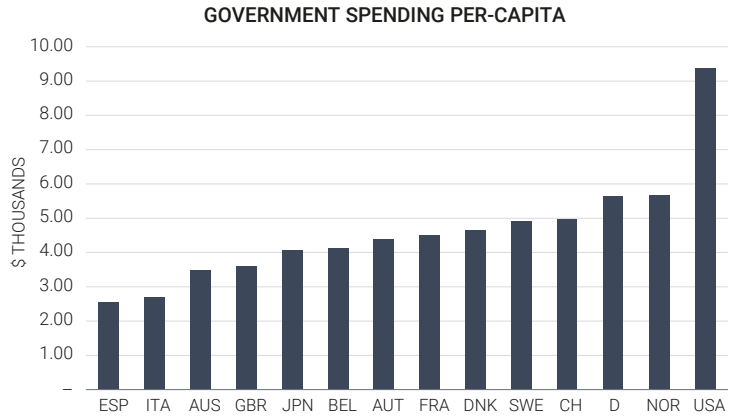
- Software or TV are sectors where innovation allows supply to lead demand.

Innovation to help supply catch demand?

For healthcare related services, costs inflation has been remarkable, indicating how supply has not been able to match demand. No wonder, innovation is being promoted and incentivized by public powers.

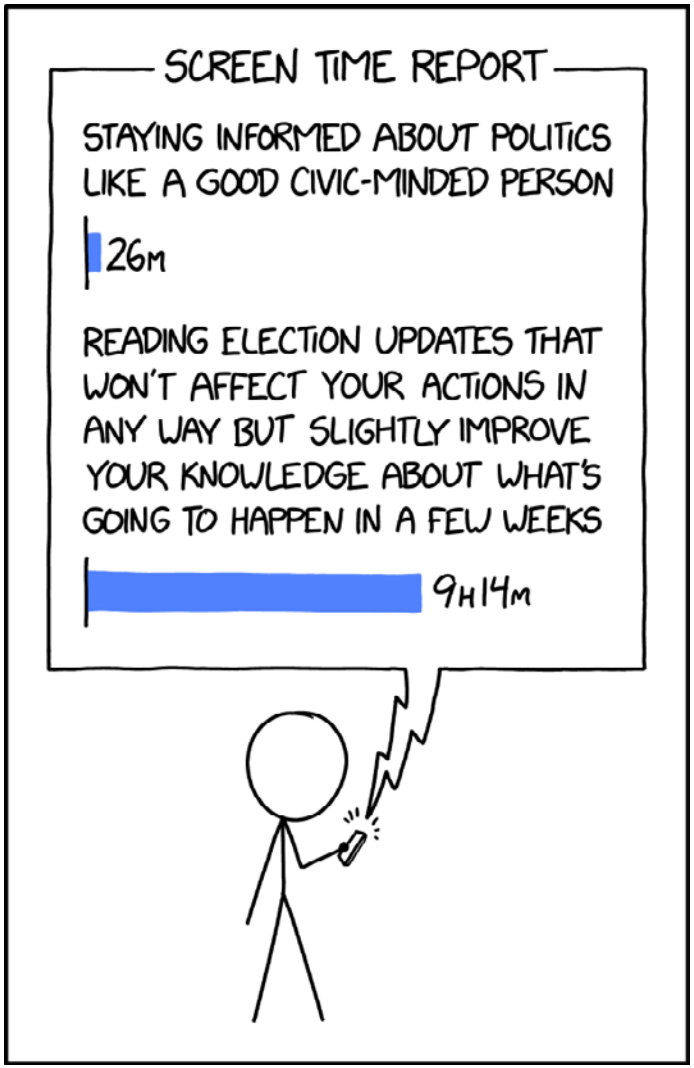
- Healthcare services costs increased >300% over the past 20+ years.
- Is healthcare innovation simply unable to impact supply? Or are we at the very beginning of healthcare innovation?





SOURCE:
Health spending

CASUAL FRIDAY



SOURCE:
https://xkcd.com/2371/

Invest Beyond The Ordinary

Explore our investment themes:
www.atonra.ch/investment-themes/








HEALTHCARE M&A	SUSTAINABLE FUTURE	BIOTECHNOLOGY	AI AND ROBOTICS	FINTECH	SECURITY AND SPACE	MOBILE PAYMENTS	BIONICS

About AtonRâ Partners

AtonRâ Partners is an asset management company, founded in 2004 with head office in Geneva, incorporated under Swiss law, duly approved by the Swiss Financial Market Supervisory Authority (FINMA) under the Swiss Collective Investment Schemes Act.

AtonRâ Partners is a conviction-driven asset manager combining industrial and scientific research with financial analysis. AtonRâ Partners focuses on long-term trends powerful enough to be turned into thematic equity portfolios.

Disclaimer

This report has been produced by the organizational unit responsible for investment research (Research unit) of AtonRâ Partners and sent to you by the company sales representatives.

As an internationally active company, AtonRâ Partners SA may be subject to a number of provisions in drawing up and distributing its investment research documents. These regulations include the Directives on the Independence of Financial Research issued by the Swiss Bankers Association.

Although AtonRâ Partners SA believes that the information provided in this document is based on reliable sources, it cannot assume responsibility for the quality, correctness, timeliness or completeness of the information contained in this report.

The information contained in these publications is exclusively intended for a client base consisting of professionals or qualified investors. It is sent to you by way of information and cannot be divulged to a third party without the prior consent of AtonRâ Partners. While all reasonable effort has been made to ensure that the information contained is not untrue or misleading at the time of publication, no representation is made as to its accuracy or completeness and it should not be relied upon as such.

Past performance is not indicative or a guarantee of future results. Investment losses may occur, and investors could lose some or all of their investment. Any indices cited herein are provided only as examples of general market performance and no index is directly comparable to the past or future performance of the Certificate.

It should not be assumed that the Certificate will invest in any specific securities that comprise any index, nor should it be understood to mean that there is a correlation between the Certificate's returns and any index returns.

Any material provided to you is intended only for discussion purposes and is not intended as an offer or solicitation with respect to the purchase or sale of any security and should not be relied upon by you in evaluating the merits of investing in any securities.