
Newsletter

**Fundamental Growth
and Core Equity**

October 2021

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Quality Will Prevail



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As we sail into the final leg of a blustery year for equity markets, the global economic recovery has remained in place, albeit with signs that the breakneck pace at which it set off is abating.

The resurgent recovery appears to have lost some of the momentum spurred by the reopening of economies amid the spreading delta variant and worrying data emerging from China. The global equity rally forged its way on the path of least resistance through August, defying a growing list of worries — apart from the aforementioned COVID-19 variant, these worries included high inflation, supply chain disruption, imminent central bank tapering, China market volatility, and a scaled back fiscal package in the United States. Signs that these issues were beginning to catch up on investor sentiment became evident in September, when share prices took a tumble from their highs. Growth stocks have largely led markets higher, but as vaccinations have accelerated and the number of virus cases appeared to peak, the reopening trade reasserted itself.

Among the positives, corporate earnings have continued to increase and the market has underestimated this rise. This has allowed the consensus forward valuations to fall significantly this year despite the advance of markets — this is the “benign derating” we referenced last quarter. Despite this, valuations are still on the high side by historical standards. Looking forward, our primary considerations going into year-end are interest rates and inflation, COVID, the potential for new taxes weighed against potential infrastructure spend in the US, and a continued progression of earnings growth.

The market three-way tug-of-war between reopening cyclical, risk-off, and long-duration growth persists as investors jostle to find balance in the wake of the global economic recovery. In this environment, we believe it is especially important to focus on the long term and that quality will win out over the extended period. We continue to invest in companies with strong management teams, resilient business models, and solid financials that reflect quality and trade at reasonable valuations.

In this edition of our quarterly newsletter, our first piece discusses two deep technologies that we believe are key for radical innovations in healthcare that will tackle key challenges such as access and outcomes. In the second piece, one of our research analysts takes a deep dive into a transformative industrial gas company, APD (Air Products). APD’s opportunistic long-term growth potential is driven by the goals of management to enable sustainability through strategic investment in ‘clean’ technology that reduces the carbon emission intensity for its customers.

Healthcare Innovation — The New Frontier in Finding Cures

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Rapid advancements in technology have led to significant innovation in healthcare in recent years. This has resulted in improvements in treatment for cancer, rare diseases, and, of course, viruses such as COVID-19. In the medical equipment space, robotic-assisted surgery has delivered improved outcomes and a better surgery experience at a cost that is declining. In this article, we take a look at some of these advancements and consider the implications for investors.

**Biopharmaceuticals
— Driving Innovation**

Decades of progress in foundational biomedical research leveraging artificial intelligence (AI) and machine-learning technologies have led to a golden era of innovation for biopharmaceutical companies. Many of the new technologies build on basic science discoveries as well as the sequencing of the human genome. It's not that long ago that targeted antibodies and protein-based injectable therapies were viewed as being at the forefront of the innovation cycle, but now genes delivered to a patient through viral vectors with the intention of a single-shot cure for some diseases spearhead biomedical development.

As noted in Figure 1, gene-editing technologies called CRISPR / CAS-9 allow for correction of genetic mutation using machinery in the cell. This technology has evolved from a technique used in the laboratory to a low-risk therapy for patients with sickle cell anemia and beta-thalassemia (orphan disease). It could be approved by FDA within the next 18–24 months. Gene therapy is immensely effective against orphan diseases such as SMA (spinal muscle atrophy) and possibly providing a cure for Hemophilia as early as next year.

Another recent innovation, mRNA-based therapies have been center stage due to the rapid development, approval, and global rollout of mRNA-based vaccines developed for COVID-19. The typical timeframe for clinical development of any vaccine is usually 10–12 years, but mRNA technologies shortened this to 12 months for the COVID-19 vaccine. An estimated three billion people across the globe could benefit from mRNA vaccines developed both for COVID-19 and other diseases, such as cancer.

Figure 1

Breakthrough Technologies

Platform Technology	Therapeutic	Selected Companies	Lead Indication	Clinical Trial Stage	Launch
Gene editing — Curative	CTX001	CRISPR	β-thalassemia/sickle cell anemia	Phase 1/2	2023
Gene editing — Curative	NTLA-2001	Intellia	Transthyretin (ATTR) Amyloidosis	Phase 1/2	—
Gene therapy — Curative	AVXS-101	Novartis	Spinal muscular atrophy	Approved	—
Gene therapy — Curative	Luxturna	Roche/Spark	Retinal dystrophy	Approved	2017
mRNA therapeutics	mRNA-1273	Moderna	COVID-19	EUA	Dec. 2020
mRNA therapeutics	BNT162b2	Pfizer/BioNTech	COVID-19	Approved	Dec. 2020
Targeted protein degradation	KT-474	Kymera	AD and HS	Phase 1/2	2025
Targeted protein degradation	ARV-110	Arvinas, Inc.	Prostate cancer	Phase 2	—
Targeted oncology	Verzenio	Eli Lilly	HR+, HER2- breast cancer	Approved	2017
Targeted oncology	Alectinib	Janssen	mNSCLC	Approved	2017
CAR-T	Cilta-cel	JNJ/Legend	Multiple myeloma	Regulatory review	—
CAR-T	Abecma	Bristol Myers Squibb	Multiple myeloma	Approved	2021
CAR-T	Breyanzi	Bristol Myers Squibb	B-cell lymphoma	Approved	2021
DNA therapeutics	INO-4800	Inovio	COVID-19	Phase 2/3	2022
DNA therapeutics	HEPLISAV-B	Dynavax	Hepatitis B	Approved	2017

Source: Company Reports as of September 2021.

Novel cell therapies for cancer indications have also exploded in the past several years, primarily based on CAR (chimeric antigen receptor) technology for T-cells. Several CAR-T approaches have been approved for several blood cancers, including multiple myeloma and lymphomas which show a long-lasting clinical benefit and very good tolerability. For example, patients with multiple myeloma treated with CAR-T cells may live 1, 2, or even 3 years longer than those using conventional chemotherapy. In the coming years, we could witness curative approaches to various blood cancers and solid tumors such as lung and breast cancer, which continue to have a large unmet need.

Breakthroughs in Unmet Medical Needs

Not only has there been an impressive evolution of technologies utilized in biotech/ pharmaceutical research and development (R&D), but there have been major breakthroughs in some of the biggest areas of unmet medical need. The most topical example is the recent approval of Biogen's Aduhelm for Alzheimer's disease, the first major new therapy in more than 20 years. The US Food and Drug Administration (FDA) felt that the benefit/risk profile was acceptable enough to grant approval as a new option for millions of Alzheimer's patients, thereby sending a strong signal for companies to continue innovating in this complex disease. The development of Aduhelm, and the potential for others Alzheimer's drugs to follow, was aided by breakthroughs in imaging agents — this is where a patient's brain can be directly scanned for the presence of beta-amyloid, thought to be the causative agent in Alzheimer's. There are dozens of companies that could use this approach, which uses PET imaging to determine whether a drug can reduce plaque burden on the brain, likely slowing cognitive decline over time.

In the area of specialty medicine and the field of rare and orphan diseases, cystic fibrosis existed as a large unmet medical need with decades of failures for drugs that aimed to help improve patients' lung function. However, Vertex utilized new technologies in lung disease models to significantly improve lung function, as well as development of better chemical targeting in searching for a cure to this life-threatening disease.

Innovation in the field of immuno-therapy has led to advances in patient survival. With significant development by many leading pharmaceutical companies, including Merck, Bristol, and Roche, this has led to dramatic improvements in survival due to the re-programming of the immune system to recognize and kill the primary tumor and related sites where the cancer metastasized. Immuno-therapy in many cancers including lung, melanoma, and kidney cancer, has evolved from single drugs to novel doublets and triplets which could enhance the benefit's duration and improve the safety and tolerability profile.

We expect the innovation based on new technologies to continue. As shown in Figure 2, there are many diseases which are ripe for rapid progress in their treatment, ranging from cancer to heart disease to inflammation.

Figure 2

Breakthrough Indications

Lead indication	Therapeutic	Status	Selected companies
Alzheimer's disease	Aducanumab	Approved	Biogen
Alzheimer's disease	Donanemab	Phase 2 and 3	Eli Lilly
Alzheimer's disease	Gantenerumab	Phase 2 and 3	Roche
Alzheimer's disease	BAN2401	Phase 3	Biogen/Eisai
Triple negative breast cancer	Trodely	Approved	Gilead
Triple negative breast cancer	Keytruda	Approved	Merck
Cystic Fibrosis	Trikafta	Approved	Vertex
Type 1 Diabetes	Tirzepatide	Phase 3 completed	Eli Lilly
HIV	Biktarrvy/LA	Approved	Gilead
Lung cancer	Opdivo	Approved	Bristol Myers Squibb
Lung cancer	Keytruda	Approved	Merck
Lung cancer	Lumakras	Approved	Amgen
Atopic Dermatitis	Dupixent	Approved	Sanofi
Atopic Dermatitis	Lebrikizumab	Phase 3	Eli Lilly
Bladder cancer	Padcev	Approved	Seagen
Psoriatic arthritis/psoriasis	Skyrizi	Approved	Abbvie
Psoriatic arthritis/psoriasis	Deucravacitinib	Phase 3 completed	Bristol Myers Squibb

Source: Company Reports as of September 2021.

Biopharmaceuticals: Investment Perspective

From an investment point of view, we seek high-quality companies that are likely to deliver long-term sustainable growth, which are trading at reasonable valuations. To evaluate Quality, we use a framework called Confidence Quotient (CQ), which includes a measure of Market Position, Management, Transparency, Financial Condition, and Fundamental Momentum.

In the Biopharmaceutical space, we believe that this proprietary framework captures innovation in the form of Market Positions and Strength that are further fortified by proprietary technology and healthy drug pipelines driving sustainable growth. Additionally, we value Management teams that invest prudently for future growth, and Transparency enhanced by clear and open updates, as this underpins our ability to find investment opportunities and generate sustainable alpha and robust returns.

Robotic-assisted Surgery

Healthcare systems are always striving for better and more predictable outcomes, an improved experience for the patient and care team, and a lower cost. Robotic-assisted soft-tissue surgery enables the first two objectives, while the cost equation is gradually improving.

There are three types of surgical procedures: open, laparoscopic, and robotic.

- Open is the traditional and still predominant form of surgery. It requires a large incision, creating more trauma and infection risk, and often requires a longer hospital stay (more trauma = more time needed to heal).
- Laparoscopy was introduced in the 1980s and provides a minimally-invasive alternative to open surgery. Three or more small incisions (1.0–1.5 cm) are made, allowing access for instruments and a camera (endoscope). The endoscope's video feed allows the surgeon to manipulate the instruments and perform the procedure. While laparoscopy is less invasive and traumatic, it's technically challenging. It requires a highly-skilled surgeon, and the instruments are limited in their functionality (surgery is basically performed with two sticks via a tv screen).
- Robotic surgery was introduced in 1999. It uses a minimally-invasive approach like laparoscopy while addressing some of the former's limitations. The anatomy is still accessed via small incisions, but the robot adds computational and imaging technologies, along with robotically-assisted instruments that provide greater dexterity and precision (Intuitive's robot can peel the skin off a grape). As such, it does not require as much technical skill as laparoscopy, while delivering a similar, minimally-invasive outcome.

The World Health Organization estimates almost 400 million surgical procedures are performed annually.¹ The vast majority of these are open surgery. Outcomes are highly variable, depending in part on the skill of the surgeon. Robotics has the potential to become the standard of care in general surgery, given greater consistency, reduced pain and discomfort, faster recovery times, and less scarring.

In 2020, about 1.2m robotic-assisted soft-tissue surgeries were performed (i.e., approx. 0.3% penetration rate). Currently, however, only 6m of the 400m annual procedures are approved for robotic surgery, putting robotic surgery penetration closer to 20% (1.2m/6m). Future technological advancements and indication expansions are expected to bring the number of approved robotic procedures to 20–50m, implying a penetration rate of 2–6% based on today's figures.²

Prostatectomies and malignant hysterectomies provide good, illustrative examples of robotic surgery's potential. Over a 10-year period in the United States, these procedures went from 100% open to 75–85% robotically-assisted (i.e., standard of care). Not all procedure types will enjoy this degree of penetration, but this experience indicates that several can.³

Intuitive (ISRG) is the dominant provider of surgical robots. Having commercialized in 1999, the company now has a global installed base of 6,335 of its da Vinci systems. They've had the market largely to themselves for the past 20 years, but Medtronic (MDT) launches a competing robot this year, and Johnson & Johnson's (JNJ) offering should be available in the next 12–24 months.

Intuitive has a clear first-mover advantage and has used that time to continue innovating and improving its offering. Da Vinci Xi is a fourth-generation system with a non-trivial competitive moat. How will the capabilities from Medtronic and J&J's first-generation systems compare? While displacing Intuitive will likely prove very challenging, Medtronic and J&J have the resources to compete. And given the large total addressable market, there is certainly room for multiple providers.

One of the largest barriers to adoption has been cost. A da Vinci system requires an upfront capital investment of about \$2.25m, along with replacement instruments every ten procedures. However, with competition imminent, Intuitive has allowed more flexible purchasing arrangements (e.g., operating leases instead of an upfront capital payment), reduced the price of instruments for more mature procedures, and recently introduced extended-use instruments that last for 12–18 procedures instead of 10. This should help reduce the cost per procedure, encouraging greater adoption and increased utilization. The ultimate objective is to achieve cost parity with open surgery, although this is several iterations away. Cost parity with laparoscopy is not too far off.

Robotic surgery is a large, under-penetrated market that will likely enjoy double-digit growth for the foreseeable future. In our CQ framework, companies like Intuitive and Medtronic score well based on the strength of their market positions. Which are driven by significant barriers to entry, innovation, and high switching costs for their customers.

Air Products: Enabling Sustainability

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The market for industrial gases is dominated by a handful of key players, one which is the US-based Air Products. Supported by its competitive position and strong demand for its products across the consumer, medical and industrial sectors, the company is also to the fore in using innovative techniques to reduce carbon emissions and is already a leading producer of hydrogen in the commercial market.

Industrial gas companies use advanced technologies to supply gases like nitrogen, oxygen, hydrogen and even carbon. We come across their applications in our everyday lives. Some are easily recognizable, like the carbon-infused beverages or helium used in the party balloons. Others might not be as well known, but are essential in industries like refining (CO₂ or nitrogen for enhanced oil recovery), healthcare (medical oxygen or helium used in MRIs), electronics (nitrogen used in manufacturing of semi-conductors and flat-screen TVs) and metals (oxygen in steel furnaces). Altogether, the commercial industrial gas industry is sized at over \$90 billion and is expected to grow 5–6% annually.

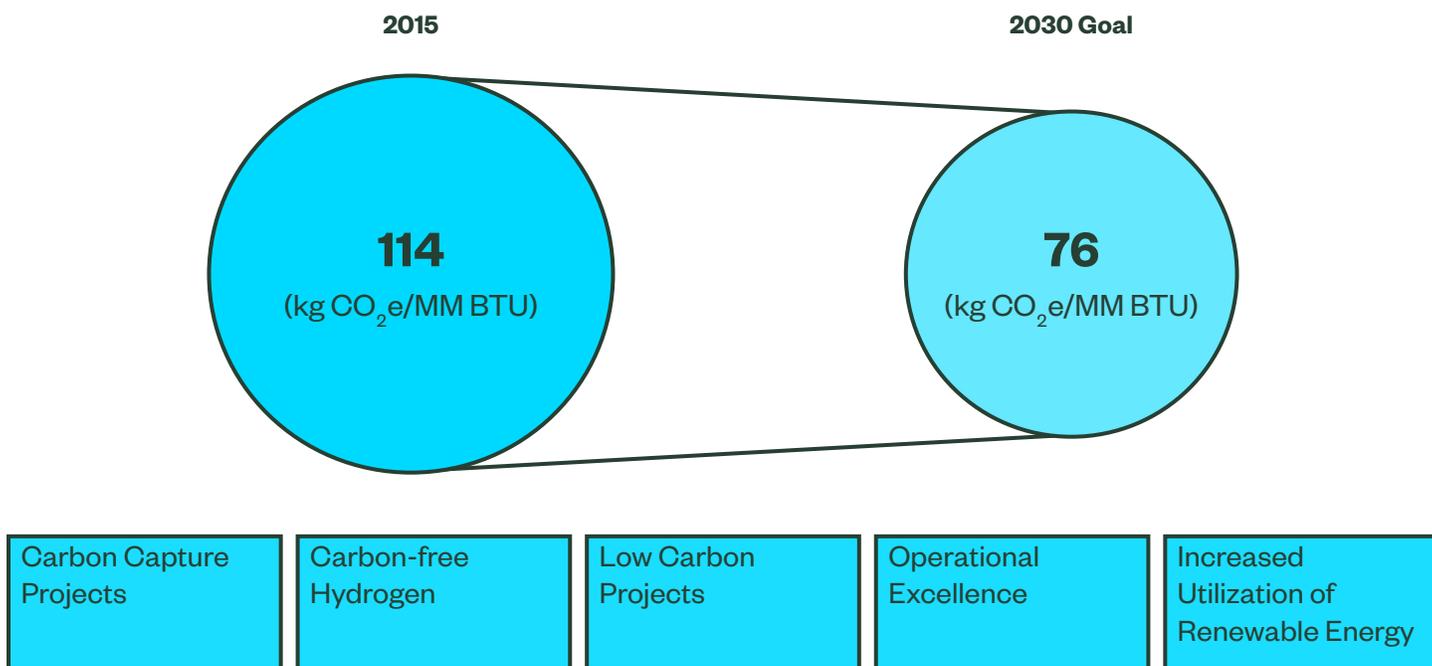
The companies that operate in this industry have a business model that is considerably different to that of the broader chemicals industry. Consolidation has led to an oligopolistic market, with the top three players controlling over two thirds of the market. And while demand can rise and fall with the economic cycle, long-term 'take-or-pay' contracts allow the companies to act defensively during downturns.

Air Products: An Introduction

APD (Air Products) is the smallest of the three global industrial gas companies. Activist involvement led to Board Member Seifi Ghasemi becoming CEO in 2014 and he has since divested non-core assets, expanded margins, grown earnings by 11% and outperformed the S&P 500 by more than 2% annually.⁴ The company's growth strategy also supports the UN Sustainable Development Goals, aligning with nine of the 17 objectives, thus setting it up for potential long-term outperformance.

3X. That is the ratio of emissions avoided by APD’s customers using the company’s coal gasification versus burning coal. They can do that because in their coal gasification plants, for example, coal is reacted with oxygen and steam at high temperatures and pressure, rather than combusted. The process is much more efficient, enables use of carbon capture, and results in lower SOx and NOx emissions. In 2020, their customers avoided 72m tons of CO₂, which is equivalent to emissions from 16m cars. This underpins APD’s view of sustainability as a tailwind for its business. Their growth platforms align well with their sustainability initiative, “Third by 30”, that aims to cut CO₂ emissions intensity by one third by 2030 compared to 2015.⁵

Figure 3
“Third by ‘30” Carbon Intensity Goal



For illustrative purposes only.

The challenge for APD is their carbon intensity. Whether on an absolute level, or relative to total revenue, industrial gas companies have a high carbon profile across sectors. This is because they use natural gas to make hydrogen (which drives up Scope 1 emissions) or use electricity in the process (which drives up Scope 2 emissions). Recognizing the importance to be viewed as ‘enablers of energy transition’ as being key to sustainable growth, they have aggressively committed to sustainability goals and to provide better than average disclosures.

APD’s Growth Platforms

The three main growth platforms for Air Products are:

- 1 Carbon Capture** The International Energy Agency (IEA) considers carbon capture as a core technology and expects it to grow from about 40mt (metric tons) today to over 7,600mt by 2050 in their net zero scenario.⁶ For APD, the Valero refinery in Port Arthur, Texas, has been capturing approx. 1m tons of carbon dioxide annually since 2014.⁷ The rising price of carbon will enhance the economic case for this growth platform.

- 2 Hydrogen** Growing awareness, and a need to decarbonize hard-to-electrify end markets such as steel and cement industries and the heavy-duty vehicle market, is leading to renewed enthusiasm around hydrogen. APD has been involved in the full value chain of hydrogen for decades and is already one of the largest producers of hydrogen in the commercial market. The company's NEOM project in Saudi Arabia, which will produce 650 tons per day of green hydrogen, will be the world's largest production facility and is big enough to eliminate 3m tons of CO₂, which is equivalent to emissions from over 700,000 cars.⁸
- 3 Gasification** This enables the use of carbon-intensive feedstock like coal into useful chemicals or energy, while reducing pollutants like sulphur oxide. In 2020, at a time when spot methanol prices were low, APD signed a coal-to-methanol project in Indonesia, something identified as a strategic priority by the country's government. The facility will offer a better and cleaner use for coal, and the methanol produced will be capable of being converted into higher-value 'green' products like biofuels. Carbon capture and alternative feedstock like biomass are pathways to reduce emission intensity of this growth platform.

APD follows a multi-pronged approach in sourcing renewable energy to reduce their Scope 2 emissions. This includes installing solar arrays at operating sites, signing long-term renewable power purchase agreements directly with developers of renewable energy, and purchasing certificates linked to renewable power of specific renewable assets. They estimate 24% of their electricity purchases in 2020 were from renewable sources.⁹

Water conservation is also an important area of focus, since use of water is closely tied to the hydrogen-making process. APD has saved over 200m gallons in its North American cooling towers, in collaboration with Suez. This enabled them to reduce water consumption by 26% in 2020 versus the 2015 baseline, which was ahead of its 5% reduction goal.¹⁰

Sustainability at APD, however, goes beyond just the 'E' in ESG. For a company operating with heavy machinery and with potentially hazardous gases, they have received numerous awards for their safety performance. Being perceived as a good corporate citizen is also important, and the company has goals around diversity, talent management and employee well-being.

Investment Assessment

Within our team's proprietary Confidence Quotient (CQ) framework, which we use to assess company quality, APD stands out relative to the broader chemical industry group. We like the forward-thinking approach of the Management team and believe they will continue to create long-term shareholder value. We also like the Market Position of the company, operating in an oligopolistic market and with technology leadership in its growth platforms of gasification, carbon capture and hydrogen. Furthermore, and of particular importance, APD has the financial flexibility to invest in transformational projects. We realize that abundant natural resources are prevalent in emerging economies, where the legal and political climate can change, but we believe this risk is manageable and more than offset by the company's advantageous position in the value chain.

In conclusion, we think that the energy transition trend is going to be disruptive for the chemicals sector. However, in our view, the core strength of enabling efficient use of natural resources, along with leadership in newer technologies of carbon capture and hydrogen, will lead to long-term success for the Air Products company and its shareholders.

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Endnotes

- 1 Source: World Health Organization, Sanford C. Bernstein, March 2021.
- 2 Source: Intuitive Surgical Inc. Company presentation, January 2021.
- 3 Sanford C. Bernstein research paper, March 2021.
The "TAM"inator: Sizing markets, fears, and dreams — Intuitive: Five reasons robotic surgery may be poised for explosive growth.
- 4 Source: APD company reports, Bloomberg Finance L.P., as of September 2021.
- 5 Source: Air Products 2021 Sustainability Report.
- 6 Source: International Energy Agency Technology Report, April 2021.
- 7 Source: Air Products 2021 Sustainability Report.
- 8 Source: Air Products 2021 Sustainability Report.
- 9 Source: Air Products 2021 Sustainability Report.
- 10 Source: Air Products 2021 Sustainability Report.

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