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Investment Insights:

Catalysts Strengthen Our Outlook for Healthcare

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Early Signs of Exciting Innovation Cycle

At the end of August, we continue to see evidence of the transformative innovation cycle in healthcare. Two key catalysts in particular confirm the advancement and validation of CAR-T/TCR and new therapies that harness the immune system.

On August 28, Gilead (GILD) announced it would acquire Kite Pharma (KITE), an innovator in cell therapies that has a robust pipeline of treatments for blood-based cancers and is far along in the development of treatments for solid tumors. In late November, it expects FDA approval for its most advanced drug, Axi-cel, which treats the most common type of non-Hodgkin's lymphoma and has the potential to generate $1.4 billion in revenues by 2023.

On August 30, Novartis (NVS) announced that it received FDA approval for the first individualized immunocellar therapy, Kymirah. This first-to-market cell therapy uses the patient's own T-cells to fight cancer and provides a much-needed option to pediatric and young adult cancer patients unresponsive to other treatments.

CAR-T and TCR Immunotherapies

These announcements are the first of an exciting pipeline of immunotherapies to treat cancer through adoptive cell transfer where immune cells (T-cells) are removed from a patient's blood and then genetically modified. The patient's T-cells are engineered in a lab to express chimeric antigen receptors (CAR) or T-cell receptors (TCR) that allows them to hone in on that individual's particular cancer cells. The CAR or TCR expressing T-cells are infused back into the patient where they hunt and kill tumor cells. (The key difference between CARs and TCRs is that CARs can only recognize targets found on the surface of tumors, whereas TCRs can detect intracellular targets.)

Robust data is emerging from several other CAR-T focused companies. For example, Celegene (CELG) is collaborating with bluebird bio (BLUE) on developing a CAR-T therapy for multiple myeloma patients, focused on anti-B-cell maturation antigen (BCMA CAR) treatments. Myeloma is the second-most common blood cancer that most often affects the aged. As presented at American Society of Clinical Oncology in June, 8 out of 11 relapsed / refractory patients that have had many lines of prior treatment achieved a complete response (CR). Of note, all patients who achieved a CR remain relapse free ranging from 2 to 7.4+ months.

Demographic studies indicate the global population over the age of 65 will grow 20% to 30% over the next decade. This growth will accelerate the demand for more oncology therapies and extend the growth runway for CAR-T type therapies.

Innovation Opens M&A Spigot

With cellular therapies becoming mainstream, we expect to see a solid growth path ahead for biotech companies focused on oncology immunotherapies. There are over 60 publicly traded small- and mid-cap companies focused on cancer treatments. Many of these have disruptive stand-alone therapies that can be compelling acquisition targets for large-cap biotech companies seeking to augment their R&D pipelines.

Healthcare:
A Long-Term, Secular Growth Cycle

Aging Population

The US Census Bureau projects that 20% of US residents will be over the age of 65 by 2020. This will fuel strong demand for healthcare services, including immunotherapies and other drugs.

Innovation

CAR-T type cell therapies are radically changing the way we harness the immune system to treat cancer. CRISR/Cas9 gene-editing techniques to target and modify DNA with ground-breaking accuracy are accelerating therapies to eradicate gene-caused diseases, with broad potential applications.

Favorable Regulatory Environment

FDA productivity is near an all-time high as commissioner streamlines process to close a backlog of generic approvals and to accelerate approvals of treatments for rare diseases with currently unmet needs.

We believe the Gilead and Kite deal signals a long-anticipated positive inflection for M&A. We expect to see more M&A activity over the next 12 to 18 months as companies seek to develop combination therapies and large-cap companies, who have essentially outsourced riskier R&D to small- and mid-cap companies, seek to roll up promising technologies on their formidable distribution platforms.

M&A activity could also increase significantly with US tax reform, specifically a holiday on the repatriation of cash held outside of the US.

Exhibit 1: Foreign Cash Balances

	Tax Holiday	2Q 2017 Cash Balance ($b)	Foreign Cash Balance ($b)
AMGN	Amgen	$39	$37
GILD	Gilead Sciences	$37	$31
CELG	Celgene Corp.	$10	$8
BIIB	Biogen, Inc.	$6	$4

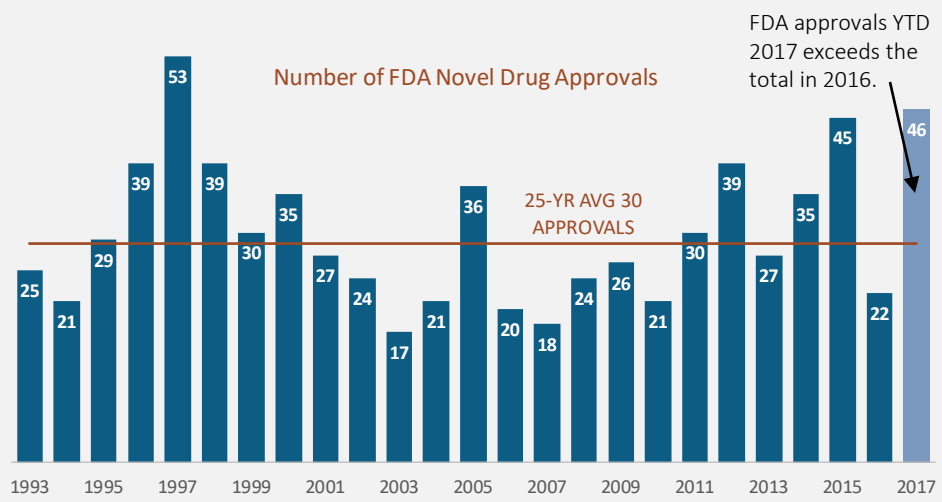
As of June 30, 2017. Source: FactSet and Company 10Qs

Streamlining FDA Approvals Could Be Another Growth Lever

Dr. Scott Gottlieb, the recently appointed FDA Commissioner, has streamlined the FDA approval process. Dr. Gottlieb has committed to adding more FDA resources and is especially focused on reducing the backlog for approvals of generics, which potentially can lower healthcare costs overall, and on prioritizing promising treatments for rare diseases without any good therapeutic options available.

The approval of the first CAR-T therapy, expedited under a designation called "Priority Review and Breakthrough Therapy", is significant as it seems like only two years ago that people thought CAR-T was science fiction and unlikely to become commercial ready. But now it is a reality.

Exhibit 2: FDA Approvals Likely to Increase



As of Oct. 2, 2017. Source: Barclays Capital and www.fda.gov

Specialization and Selectivity Are Key

With healthcare undergoing a transformative innovation cycle, we believe it is key to do research specifically on the emerging technologies and resulting therapies and to identify companies further along the development path with strong therapy pipelines. These companies should benefit from the secular tailwind of a rapidly aging population and the need for innovative approaches to cancer and other age-related diseases.

Notably, these types of companies are available to public-market investors. In contrast to other sectors, particularly technology, biotechnology companies must come to the public markets sooner to fund the huge costs of drug development and regulatory approval. Most of the upside can be experienced later in a company's lifecycle, and—importantly—after much of the uncertainty around the technology and management team has been has de-risked.

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Yet even with rigorous company-specific research, we expect there to be volatility within this overarching positive trend. Investors may experience volatility around pivotal data releases and in the short-term when broader geopolitical tensions could cause a de-risking away from biotech companies.

That being said, we believe that this is an exciting time for this space and encourage you to evaluate whether an allocation to a dedicated healthcare strategy is appropriate for your portfolio.

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