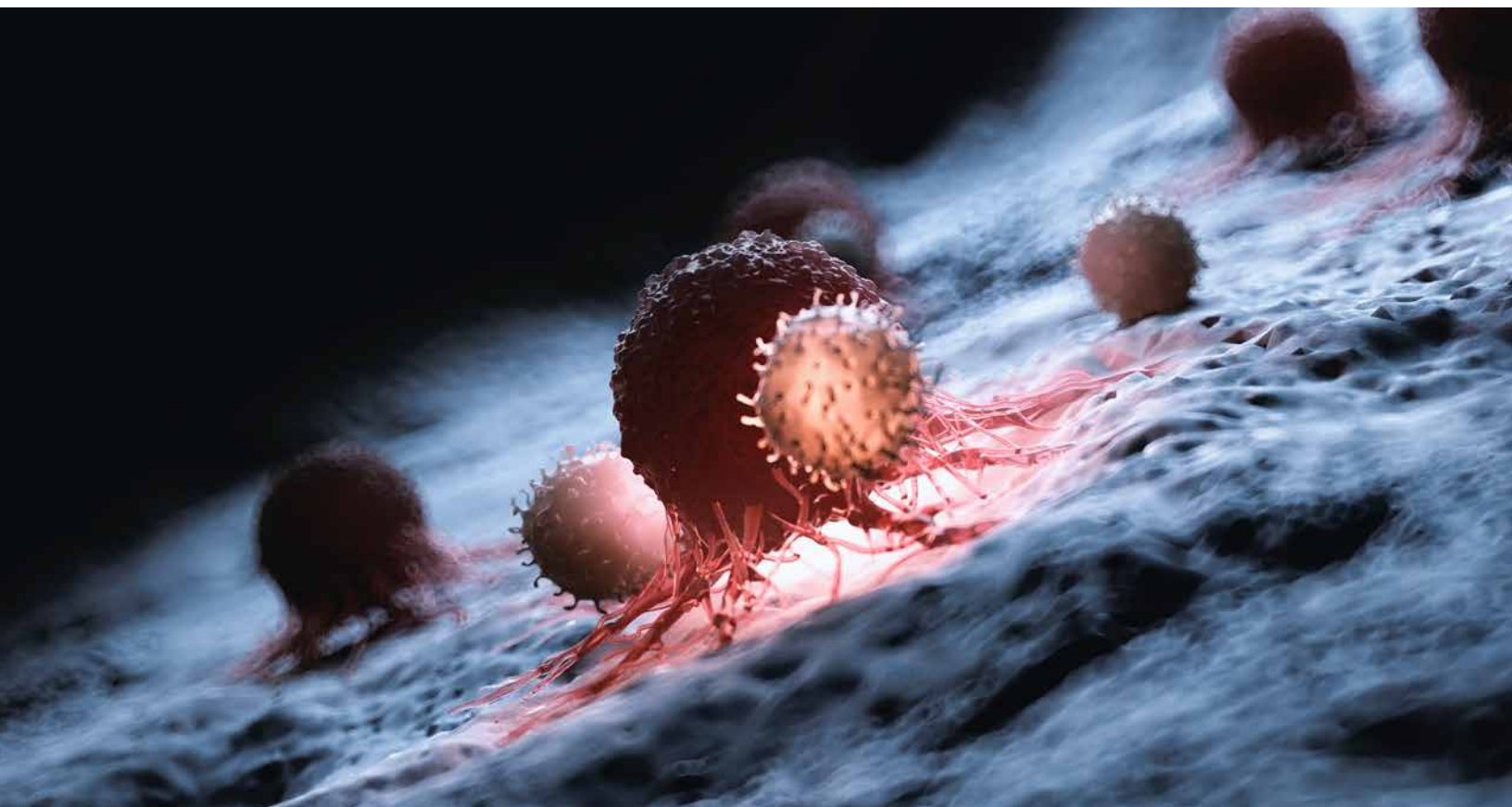


Pharmaceutical & Medical Products Practice

Delivering innovation: 2020 oncology market outlook

At the dawn of a new decade, we take stock of advances and unmet needs in the oncology pharmaceutical market. What will it take to deliver innovation to patients over the next ten years?

by Björn Albrecht, Simon Alfano, Harriet Keane, and Guang Yang



Over the past 50 years, the outcomes for people diagnosed with cancer have transformed. In 1970, of those diagnosed with cancer in the United States, approximately half would have been alive five years later. For those diagnosed in 2009, the figure was closer to 70 percent.¹ Such a transformation in outcomes has arrived through a combination of public-health measures (such as smoking education), improved healthcare (such as earlier diagnosis), and novel pharmaceutical therapies. This trifecta has turned select diagnoses, once considered terminal, into chronic conditions. For example, most patients now diagnosed with multiple myeloma or prostate cancer will have mortality tied to conditions other than their cancer. Furthermore, oncology therapeutics accounted for \$143 billion in branded pharmaceutical sales in 2019—approximately 20 percent of global pharmaceutical sales.² Analyst consensus figures indicate a robust 12 percent compound annual growth rate (CAGR), and global oncology therapeutics sales are forecasted to hit \$250 billion by 2024.

However, there is much more to do. For those who are receiving treatment, five-year survival rates for pancreatic cancer, glioblastoma, and non-small cell lung cancer (NSCLC, the most common form of lung cancer) remain below 50 percent. These three cancers collectively represent more than 250,000 new diagnoses each year in the United States alone.³ Despite substantial, justified excitement around the use of PD-(L)⁴ therapies in NSCLC, response rates remain below 50 percent.

Moreover, we see considerable variation in outcomes by geography. Recent EURO CARE-5 results show varying non-Hodgkin lymphoma (NHL)

five-year survival rates—63 percent in Northern Europe and 50 percent in Eastern Europe—and a gap in ten-year survival rates for breast cancer—76 percent in Northern Europe and 65 percent in Eastern Europe.⁵ While outcomes in China still lag behind those in developed markets, Chinese outcomes have dramatically improved; for example, the five-year survival rate across all cancers combined is estimated to be around 40 percent for those diagnosed in 2013, compared with approximately 30 percent for those diagnosed in 2003.⁶ Yet China still has ample opportunity to bring more innovations to its four million patients diagnosed annually (see sidebar, “China has four million new patients each year with substantial unmet need”).

Innovation in oncology is accelerating. Though it took about eight years between the first therapy for HER2-positive patients in 1999 and the next therapy, the gap between the first-to-market PARP inhibitor in 2013 and the next was less than two years. Globally, the next wave of innovation for patients is underway at an ever-increasing pace. Continued momentum and innovations for immunoncology treatments are expected, and more than 550 active cell- and gene-therapy agents are in clinical development.

We studied the current state of the global oncology pharmaceutical market to determine where investments are happening, where highest unmet need persists, and where competition is most intense. Our analysis also revealed five disruptive trends that could change oncology pharmaceutical leaders’ strategic focus—and perhaps even the face of the oncology market itself.

¹ Journal of the National Cancer Institute; Surveillance, Epidemiology, and End Results Program; see also the data visualization at Hannah Ritchie, “Cancer death rates are falling; five-year survival rates are rising,” Our World in Data, February 4, 2019, ourworldindata.org; Cancer Facts & Figures 2020, American Cancer Society, cancer.org.

² Product sales, EvaluatePharma@ July 2020, Evaluate Ltd.

³ Cancer Stat Facts, Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, seer.cancer.gov.

⁴ Refers to both PD-1 and PD-L1 therapies.

⁵ *Is Europe doing better in cancer care since the 90th?: The latest findings from the EURO CARE-5 study*, European Cancer Congress, Vienna, Austria, September 25–29, 2015, eurocare.it.

⁶ Peter Baade et al., “Changing cancer survival in China during 2003–15: A pooled analysis of 17 population-based cancer registries,” *The Lancet*, May 2018, Volume 6, Number 5, pp. 555–67, thelancet.com.

Oncology is the world's largest pharmaceutical therapeutic area and highly competitive

Advancements in oncology have significantly improved patient outcomes (Exhibit 1). But based on the extensive investment in oncology R&D across academia and industry, experts agree much work still remains. Oncology is a declared focus area for the ten largest pharmaceutical companies, with an estimated 1,700 clinical compounds in development (approximately one-third of the global clinical pipeline across all therapeutic areas).⁷ For NSCLC, around 100 active US Phase III studies represent approximately

75,000 patients. For acute lymphocytic leukemia, around 25 studies require more than 32,000 patients enrolled in clinical trials—more than the number of new diagnoses in a single year.⁸

In addition to abundant organic R&D at both large pharmaceutical companies and numerous clinical-stage biotechs, we have observed a spate of multibillion-dollar oncology-focused acquisitions (such as Pfizer's 2019 acquisition of Array BioPharma for \$11 billion) and partnerships (including a \$3 billion collaboration between AbbVie and Genmab on bispecific antibodies). Excitement about oncology targets has driven

⁷ Compounds in clinical development (Phases I–III) excluding reformulations and biosimilars, Pharmaprojects, 2019, pharmaintelligence.informa.com.

⁸ Accessed on Clinicaltrials.gov, October 24, 2019. Includes interventional trials where recruitment status is one of the following: recruiting, active, not recruiting, or enrolling by invitation.

China has four million new patients each year with substantial unmet need

Although China represents 18 percent of the global cancer burden, the country makes up more than 50 percent of hepatic cell carcinoma, gastric, and esophageal cancer patients.¹ And despite improvements in healthcare infrastructure, significant gaps remain; on average, China has 26 oncologists per million population versus 60 per million population in the United States, and many patients are diagnosed with advanced disease.

Given this opportunity, both local and multinational pharmaceutical companies have made substantial and growing investments in developing therapeutics for China. By 2025, 18 mechanisms of action are expected to be approved for non-small cell lung cancer and 13 for hepatic cell carcinoma,

compared with six and three available in the present day, respectively. We are also starting to see China garnering global-first approvals of new therapeutics, such as BeiGene's tislelizumab for Hodgkin lymphoma, which the National Medical Products Administration approved in December 2019. Approvals in China have historically been time-consuming, though the lag between those and global-first launches has gone down to 4.6 years in 2019 from 8.4 years in 2016. In this context, we expect to see increasing numbers of approvals in China (both of therapies developed in-country and those developed overseas).

In addition to its status as a crucial oncology market, China is increasingly a source for innovation. Some of the drugs

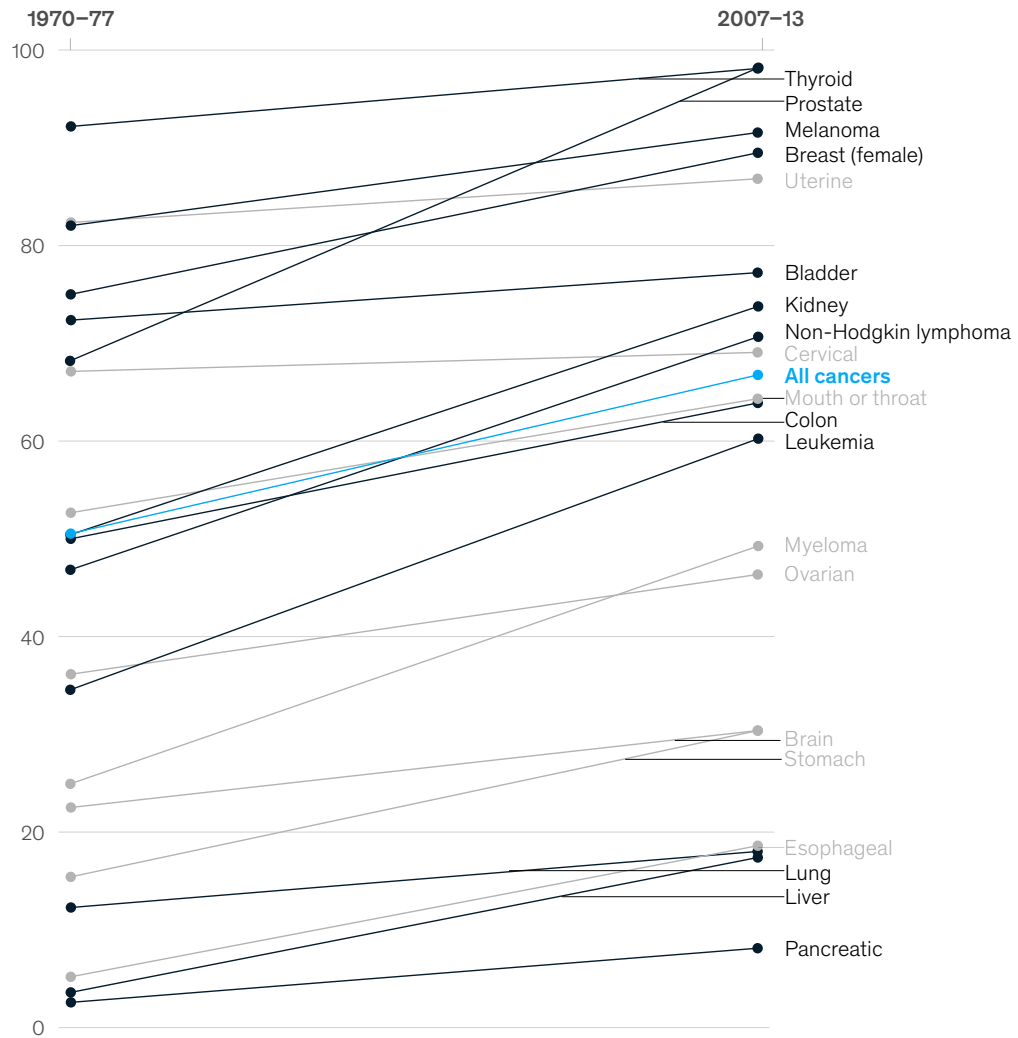
developed by Chinese biotechs have the potential to become global-first or best in class—such as savolitinib from Chi-Med—and pave the way for affordable innovation powered by China, as seen already in the PD-1 market. Innovent's PD-1 product got on the National Reimbursement Drug List in 2019, with total annual treatment cost for non-Hodgkin lymphoma patients at 102,000 renminbi (approximately \$14,600) per year. Unsurprisingly, global companies are making major investments in Chinese oncology R&D: over the past three years, AstraZeneca, Eli Lilly, Janssen, and Roche have all established or broadened their R&D footprint and partnerships in China.

¹ Tina Hou, Franck Le Deu, Yi Shao, and Jody Tian, "Managing China's growing oncology burden," August 26, 2020, McKinsey.com.

Exhibit 1

In the United States, outcomes across tumor types have improved significantly since the 1970s.

Average five-year survival rates from common cancer types in the United States, %¹



¹Percentage of people who live longer than five years following diagnosis.
 Source: Journal of the National Cancer Institute; Our World in Data; Surveillance, Epidemiology, and End Results (SEER) Program

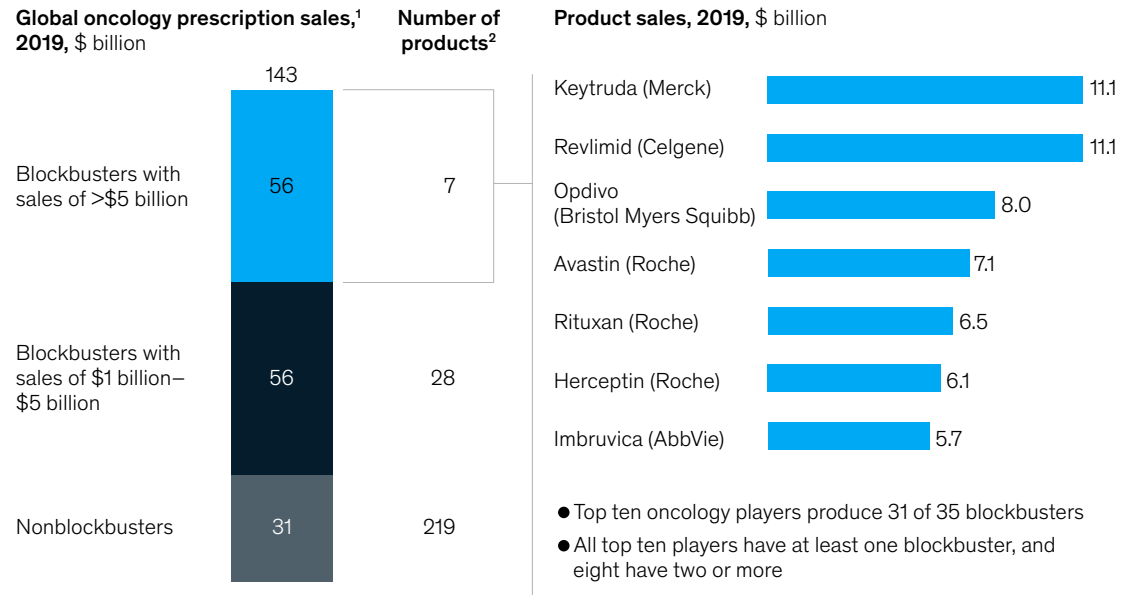
high deal premiums. Over the past five years, the median oncology acquisition premium was approximately 100 percent for transactions with a deal value of more than \$5 billion.

However, if past trends are repeated, a small proportion of these assets will shape the future market (Exhibit 2). Current success rates (from first-in-human to launch) are approximately 13 percent in oncology, with an average development timeline of 9.5 years.⁹ Even after launch, there is wide disparity

⁹McKinsey analysis of success rate based on oncology development projects excluding reformulations and biosimilars between 2008 and 2018; time-to-market based on average time in phase for successful phases based on oncology development projects excluding reformulations and biosimilars between 2010 and 2018; see Pharmaprojects, 2019, pharmaintelligence.informa.com.

Exhibit 2

A small number of very successful products represent a disproportionate share of the oncology market.



¹For branded and generic drugs, where data is reported.
²Only products with oncology prescriptions; excludes cancer prophylactic vaccines.
 Source: EvaluatePharma® July 2020, Evaluate Ltd.

in outcomes: seven products with more than \$5 billion in sales made up 39 percent of 2019 revenues, and more than half of the products launched over the past five years will generate less than \$500 million per year even at peak sales¹⁰ (Exhibit 3). While the clinical pipeline is crowded with promising prospects, it is likely that only a small number of these will have sufficiently transformative benefit-to-risk profiles to drive return on investment.

The oncology market covers a number of diverse indications

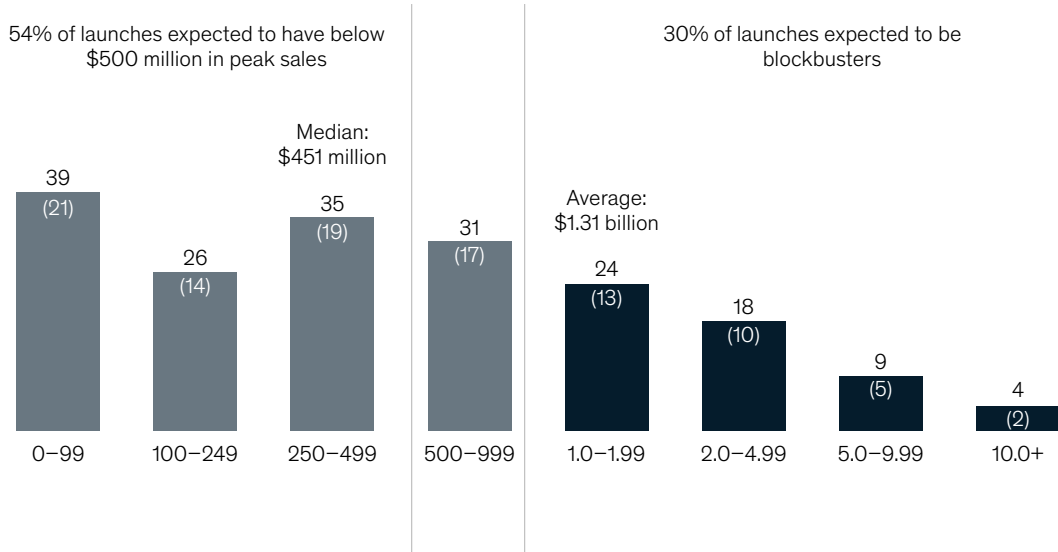
Although oncology is typically grouped as a single therapeutic area, it represents more than 20 different indications, and the majority of current sales stem from five of these indications. In 2019, breast cancer, multiple myeloma, NSCLC, prostate cancer, and NHL represented \$90 billion in sales (68 percent of the market). This is expected to

¹⁰ Product sales estimates, EvaluatePharma® July 2020, Evaluate Ltd.

Exhibit 3

Expected peak sales for the majority of launches are below \$500 million.

Peak sales range, 2010–20, number of oncology launches (% of total)¹ Peak sales ■ \$ million ■ \$ billion



¹n = 186; figures may not sum to 100%, because of rounding.

increase to \$141 billion in sales by 2024 (64 percent of the market), largely because of the growth in PD-(L)1 sales for NSCLC.¹¹ While each of these five indications has sizable incidence rates and unmet need, sales better correlate with the presence of a handful of breakthrough therapies (Exhibit 4).

In the commercial setting, most major pharmaceutical companies are focused on synergistic subsets of indications with overlapping call points and opinion-leader relationships. In the R&D setting, however, beyond their hypotheses, scientists don't know where a new therapy will

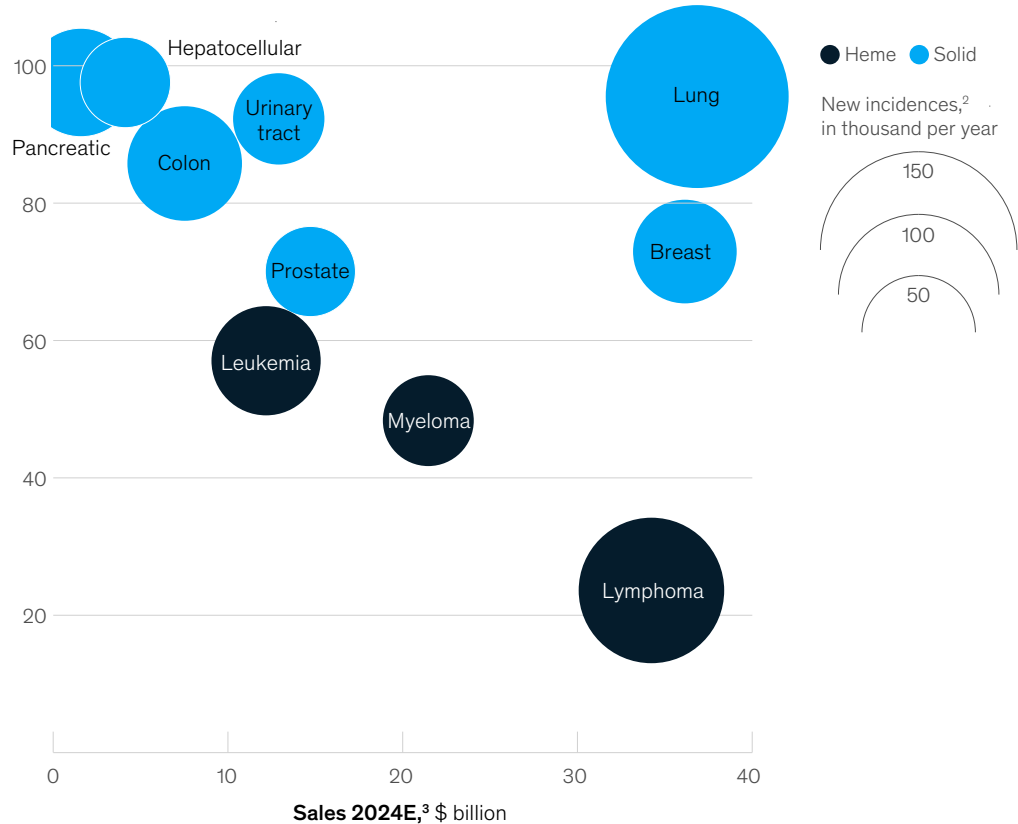
¹¹ Product estimates, EvaluatePharma® July 2020, Evaluate Ltd.

Global oncology therapeutics sales are forecasted to hit \$250 billion by 2024.

Exhibit 4

Sales do not strongly correlate with new incidences or mortality.

Five-year mortality rate¹ (overall for heme, metastatic for solid), %



¹Five-year mortality rate defined as one- minus five-year survival rate (overall for heme, metastatic for solid).
²Patient size calculated as annual incidence for heme, and larger of mortality and metastatic incidence for solid.
³Worldwide sales (all sales for cancer indications worldwide, does not include prophylactic treatment and symptomatic cancer indications).
 Source: EvaluatePharma@ July 2020, Evaluate Ltd.; Surveillance, Epidemiology, and End Results (SEER) Program

work. So we see most players exploring a wider set of indications by taking more “shots on goal”—the more indications they address, the greater the likelihood that their approach will yield a blockbuster product (Exhibit 5).

Oncology’s growth, status as a strategic focus area, and potential areas for focus are influenced by four high-level trends among indications and groups of indications:

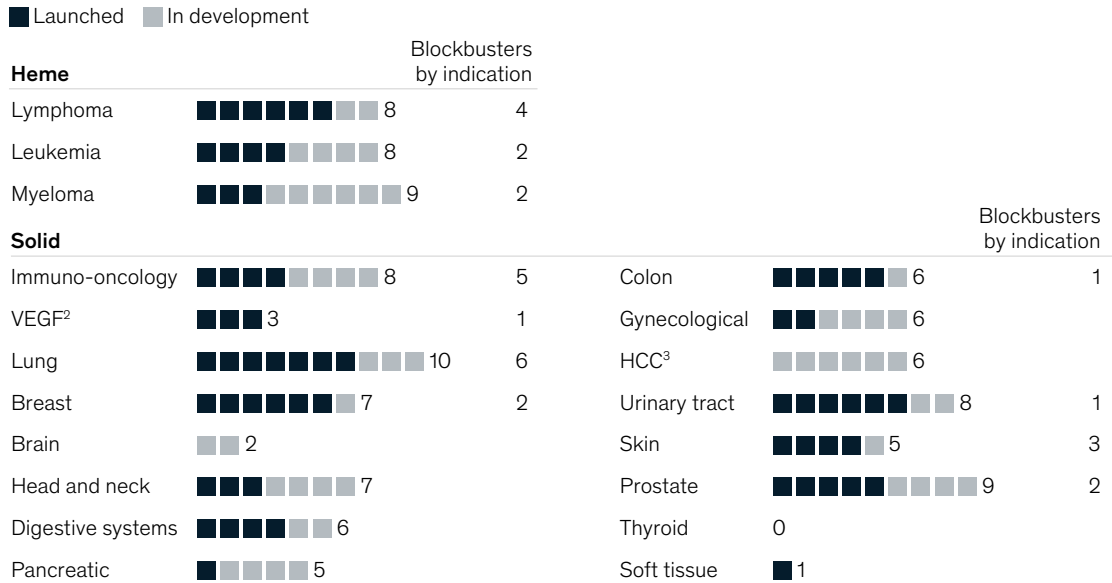
- *Growth potential in established markets.* In the short term, manufacturers are expected

to continue large market growth by expanding both geographic coverage and the settings in which these therapies are used—for example, moving into earlier lines of therapy as adjuncts to surgery. While unmet need remains (in many cases, five-year survival for metastatic patients is below 50 percent), the bar for standard-of-care is high, and true transformative therapies will be required for approval and access. Key indications include multiple myeloma, HER2 and ER+ breast cancer, prostate cancer, renal cell carcinoma, and anaplastic lymphoma kinase (ALK)- and

Exhibit 5

Indications with a larger presence of top ten pharmaceutical companies also see a higher share of blockbusters.

Number of top ten players with a presence in an indication¹



¹Most-advanced asset per top ten pharma company (ie, a pharma company with a marketed drug and drugs in development in a given indication is considered launched).

²Vascular endothelial growth factor.

³Hepatocellular cancer.

Source: EvaluatePharma® October 2019, Evaluate Ltd.; PharmaProjects, October 2019, Merck and J&J Phase I assets

epidermal growth factor receptor (EGFR)-driven lung cancer.

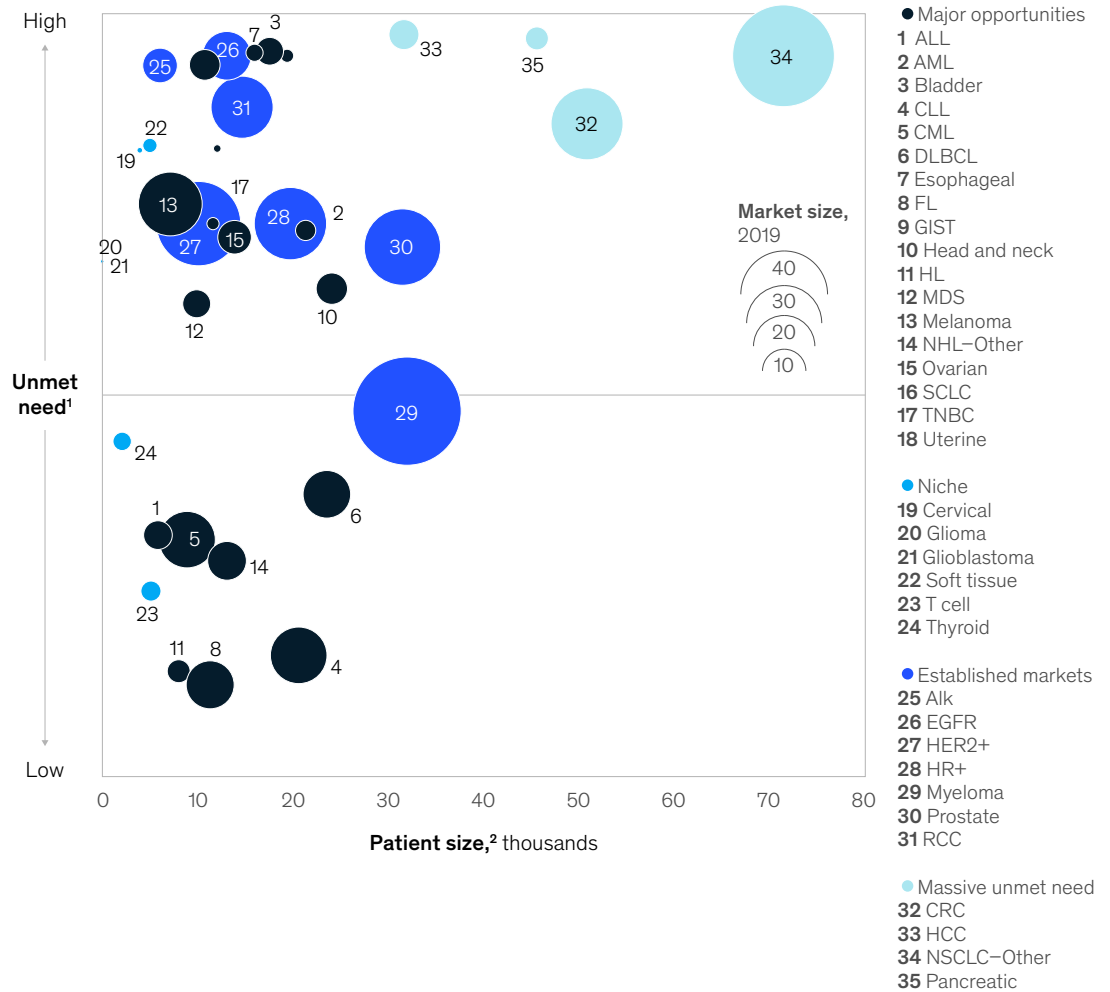
- *Continued poor patient outcomes.* Indications in this group are the holy grail of oncology R&D—characterized by poor patient outcomes (five-year survival below 15 percent) and very large patient populations (more than 30,000 new patients each year in the United States). Currently, these indications have limited therapies available, or existing therapies have low response rates. Hence, any effective therapy would represent an opportunity to transform standard-of-care, reshape cancer at a therapeutic-area level, and be very attractive from a commercial perspective.

Key indications include colorectal cancer, hepatic cell carcinoma, pancreatic cancer, non-ALK- and non-EGFR-driven NSCLC.

- *Large patient populations with remaining unmet need.* A large group of cancers present significant remaining unmet need (in most cases, five-year survival below 30 percent) and sizable patient populations—typically 5,000 to 30,000 new patients diagnosed each year in the United States (Exhibit 6). While the unmet need is relatively smaller, development of effective therapies is commercially attractive—for most patients, because more innovative treatments are not yet available, chemotherapy is still the standard of care.

Exhibit 6

Several tumor types with large patient population have persistently high unmet need.



¹Unmet need defined as one- minus five-year survival rate (overall for heme, metastatic for solid).

²Patient size calculated as annual incidence for heme, and larger of mortality and metastatic incidence for solid.

Key indications include soft tissue sarcoma, gastrointestinal stromal tumors, and triple negative breast, small cell lung, ovarian, uterine, and esophageal cancers.

- *Niche cancers.* Manufacturers could choose to target large groups of less common cancers, those with fewer than 5,000 patients per year. While unmet need is very high for

some indications, such as glioblastoma, smaller patient numbers require a new approach to develop and commercialize effective therapies. Such an approach might include site-agnostic approvals to group many niche cancers or orphan approvals to provide a rapid route to market. Key indications include T-cell cancers, thyroid cancer, glioma, and glioblastoma.

Oncology is at the vanguard of precision medicine: more than 160 oncology biomarkers were approved by 2019, and more than 90 percent of pivotal trials are against molecular targets.

Disruptive trends could shape oncology for years to come

The pharmaceutical industry's successful track record in oncology notwithstanding, broad unmet need must still be addressed. Five trends could disrupt an already-changing oncology innovation landscape.

New cell and gene therapies

The past five years have been characterized by a growing excitement about novel modalities including cell therapy, viral vectors, RNA therapy, and stem-cell therapies. In oncology, two chimeric antigen receptor T (CAR-T) cell therapies, Kymriah and Yescarta, were approved in acute lymphocytic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL) with unprecedented efficacy. While current CAR-T sales remain modest, several hundred active agents are being tested, with 2024 revenue forecast to surpass \$6 billion.¹² However, cell and gene therapies create significant disruptions to current healthcare approaches, with more complex manufacturing and supply-chain processes, especially for autologous therapies. These therapies

also have longer lead times and more challenging treatment protocols, and—due to the one-time curative potential of many therapies—more complex market-access considerations. If the cell- and gene-therapy spaces are to realize their promise, they will require fundamental shifts in the care paradigm and business models, including delivery systems that have economic incentives and an access model that captures and rewards long-term benefits.¹³

Precision medicine

Precision medicine—delivering the right drug to the right patient at the right time—is rapidly progressing. Oncology is at the vanguard of this trend: more than 160 oncology biomarkers were approved by 2019, and more than 90 percent of pivotal trials are against molecular targets.¹⁴ As more therapies target subpopulations, driving the uptake of biomarker testing and patient mapping and finding will become an important competitive advantage. For example, beyond the three most common mutations in NSCLC (those related to the ALK and KRAS genes and the EGFR protein), a plethora of less-frequent mutations represents

¹² Vanessa M. Hubbard-Lucey, Jun Tang, and Jia Xin Yu, "The global pipeline of cell therapies for cancer," *Nature*, May 30, 2019, nature.com.

¹³ Sarah Nam, Jeff Smith, and Guang Yang, "Driving the next wave of innovation in CAR T-cell therapies," December 13, 2019, McKinsey.com; Emily Capra, Jeff Smith, and Guang Yang, "Gene therapy coming of age: Opportunities and challenges to getting ahead," October 2, 2019, McKinsey.com.

¹⁴ *Table of pharmacogenomic biomarkers in drug labeling*, Food and Drug Administration, updated December 2019, fda.gov.

fewer than 3 percent of patients each.¹⁵ Ways to increase the adoption of testing can include collaborating with test providers and governments and furthering physician education. Once patients have been tested, several approaches can increase uptake of therapy; these include identifying prescription potential based on electronic health records, and engaging critical stakeholders such as patient advocacy organizations to better understand the patient-physician journey. Further, as pharmaceutical companies develop therapies for smaller groups of patients, exploring new clinical trial and commercial models will be critical to ensure costs are commensurate with the potential patient population.

Accelerating development timelines

As an increasing number of pharmaceutical companies focus on oncology, competition for key targets has become progressively more intense. We estimate that close to 80 percent of novel clinical assets are aimed at targets with either a marketed therapy or with four or more clinical competitors.¹⁶ Increased competition has shortened development cycles, and competitor therapies rapidly follow an initial launch. Success in this environment requires exploring new development paradigms including placing a greater emphasis on earlier trials (as 54 percent of approvals for assets with a breakthrough designation are based on Phase I or Phase II studies¹⁷), site-agnostic approvals (such as Keytruda for MSI-H or dMMR mutations and Vitkravi for NTRK mutations), and exploration of real-world evidence for expanding indications for a particular treatment (for example, prescribing Ibrance for male breast cancer or ongoing Opdivo ATTRACTION-2 study).

Immuno-oncology combination therapies

Companies have increased their investment in immuno-oncology combination studies, with more

than 200 mechanisms now being investigated as PD-(L)1 or CTLA-4 combination partners and immuno-oncology assets estimated to represent approximately half of top ten company pipelines (Exhibit 7). However, widespread use of combination therapies makes trial design more complex, particularly if neither combination partner is currently approved or if the additional costs of the combination partner must be purchased for clinical studies. When launched, these combination therapies are expected to drive increased treatment costs, potentially requiring new models for working with payers and demonstrating cost effectiveness.

New go-to-market model

The evolving development landscape requires pharmaceutical companies to fundamentally consider how they deliver medicines to physicians and patients. Treatment paradigms have become complex and patient populations have shrunk; for example, within NSCLC, there are multiple oncogenic driver mutations—such as ROS1, BRAF, NTRK, EGFR, HER2, and MET—each with its own targeted therapy. At the same time, greater and more-sophisticated decision-making tools and corresponding advanced analytical algorithms support prescribers by determining the right therapy for a given patient. Beyond determining the right treatment, pharmaceutical companies are increasingly providing “white glove” service to support patients as they undergo challenging treatment protocols. Nowhere is this more relevant than for emerging cell therapies. FDA-approved CAR-Ts are expected to increase from two in 2019 to 24 in 2024.¹⁸ These novel therapies face a combination of manufacturing and commercial challenges. The majority of assets—including all marketed CAR-Ts and about 75 percent of treatments in development—are autologous, which means they require a costly one-batch manufacturing approach. At the same time, only a few sites have the infrastructure in place and are certified for CAR-T, which requires a high-touch

¹⁵ Dara L. Aisner et al., “Multi-institutional oncogenic driver mutation analysis in lung adenocarcinoma: The Lung Cancer Mutation Consortium experience,” *Journal of Thoracic Oncology*, May 2015, Volume 10, Number 5, pp. 768–777, jto.org; Ethan Cerami et al., “The landscape of kinase fusions in cancer,” *Nature Communications*, September 10, 2014, Volume 5, nature.com; Julie M. Batten et al., “ROS1 rearrangements define a unique molecular class of lung cancers,” *Journal of Clinical Oncology*, March 10, 2012, Volume 30, Number 8, 863–70, ascopubs.org.

¹⁶ Pharmaprojects | Informa December 2017. McKinsey analysis based on number of novel assets pursued by MOA (based on primary target), excluding novel assets with undisclosed MOA; see Pharmaprojects, 2017, pharmaintelligence.informa.com.

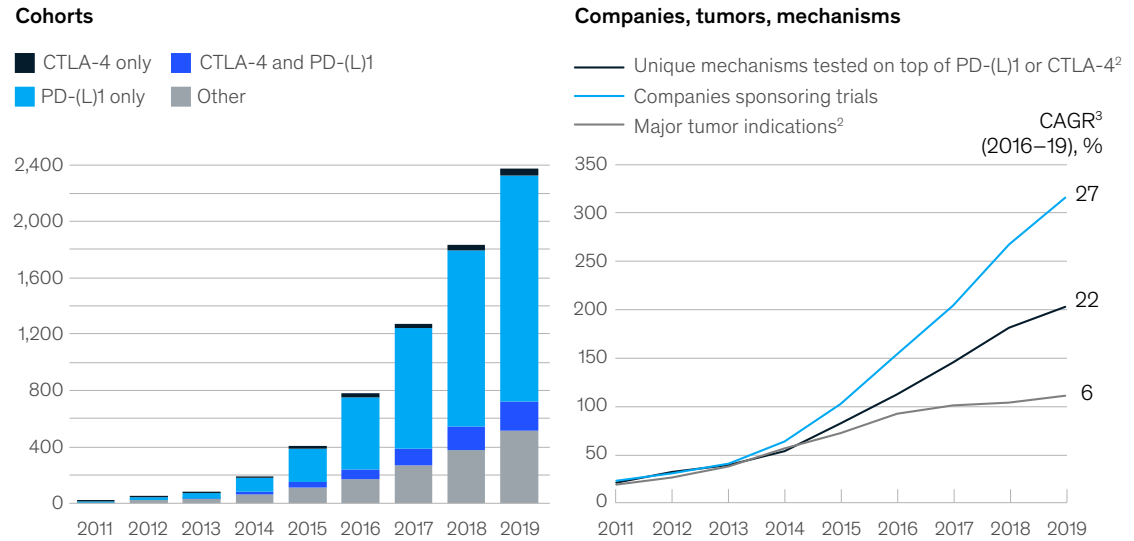
¹⁷ Based on assets approved between 2013 and 2019 with breakthrough designations, Breakthrough Therapies, Friends of Cancer Research, updated June 2020, focr.org.

¹⁸ Sarah Nam, Jeff Smith, and Guang Yang, “Driving the next wave of innovation in CAR T-cell therapies,” December 13, 2019, McKinsey.com.

Exhibit 7

Immuno-oncology has experienced unprecedented diversity, scale, and complexity.

PD-(L)1 and CTLA-4 clinical activity, cumulative count¹



¹By September of the respective year.
²Each tumor indication is a unique combination of tumor type (eg, prostate, NSCLC, etc) and tumor subtype (adenocarcinoma vs squamous, mutation type, etc).
³Compound annual growth rate.
 Source: McKinsey MIOSS; McKinsey curated clinicaltrials.gov database as of September 2019

commercial model to bring these novel therapies to patients, providers, and payers.

Overall, we expect that the therapeutic area of oncology will continue to have a meaningful and transformative potential for patient outcomes. Many indications continue to have significant unmet need, both in the United States and globally. There is tremendous potential for innovation as

measured both by the number of new medicines being tested and the investment made by the pharmaceutical industry. Precision medicine and novel modalities, including cell therapy, offer huge potential to transform the lives of patients. However, capitalizing on this potential will require pharmaceutical companies to work in new ways as they accelerate development timelines, develop combination therapies, and—critically—find effective routes to bring these therapies to market.

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