KAISER ASSOCIATES

HOT INDICATIONS

# Oncology Deep Dive

PUBLISHED OCTOBER 2018

**2017 CUMULATIVE VC FUNDING**

**$2.8B**
(#1 of 20)

**2017 CUMULATIVE IPO AMOUNT**

**$5.6B**
(#1 of 20)

**2,810**
**COMPANIES**
(#1 of 20)

**770,960**
**PUBLICATIONS**
(#1 of 20)

**1,712**
**PHASE II &III PROGRAMS**
(#1 of 20)

(# OF 20) INDICATES TA RANK

## INTRODUCTION

# In Kaiser's 4th annual Hot Indications List, Oncology retains the top spot as the highest ranked Therapeutic Area (TA), with 6 of the top 10 Hot Indications in this TA.

2017 was a year marked by major innovations: we witnessed a number of novel drug approvals, such as the FDA Breakthrough Therapy CDK4/6 inhibitors Kisqali (Novartis) and Verzenio (Lilly) for HR+/HER2- **breast cancer (#2)** and the first CAR-T therapies.

Hailed as a revolutionary cancer treatment, CAR-T was undoubtedly the biggest talking point in 2017. Novartis' Kymriah and Gilead's Yescarta were approved for B-cell precursor acute lymphoblastic and adult patients with relapsed and/or refractory large B-cell lymphoma, respectively. However, side effect management and pricing will be challenges for the CAR-T class, as both anti-CD19 therapies may cause severe side effects such as cytokine release syndrome and neurotoxicity. Controversial price tags of $373,000 to $475,000 per course of therapy have already resulted in Yescarta's rejection by UK's National Institute for Clinical Excellence, while Kymriah was only approved upon offering an undisclosed discount[1]. It remains to be seen whether both therapies will live up to commercial expectations, especially if Novartis and Gilead experience similar reimbursement challenges in other global markets.

Given the hype surrounding CAR-T, the race to develop second-generation therapies is driving continued M&A and partnership activities. After forking out nearly $12 billion to buy Kite in October 2017, Gilead Sciences acquired Cell Design Labs in that December, in a deal worth up to $567 million to further cement its position in cellular therapy[2]. Just a month later, Celgene swiftly followed suit by snapping up Juno Therapeutics for an estimated $9 billion[3].

## FUTURE HOT INDICATIONS IN A CROWDED ONCOLOGY MARKET

While Oncology continues to be the most competitive TA, and large markets like breast, **prostate (#4)** and **lung cancer (#64)** are saturated with major players and continuing innovation, there are untapped pockets of opportunity in rare and neglected cancers.

As an example, rare forms of **non-Hodgkin's lymphoma (NHL, #5)** have recently been a focus of development. Mantle cell lymphoma (MCL) is a particularly aggressive subtype, which represents 3-10% of all NHL cases in the US, but current chemotherapy and targeted therapy options (e.g. proteasome or Bruton's tyrosine kinase (BTK) inhibitors) tend to fail within 18 months, and 10-year survival is currently only 5-10%[4]. There is hope that CAR-T may provide potential curative therapy for MCL; Yescarta is currently being assessed in Phase II for patients with relapsed/refractory MCL. The market for therapies for T-cell lymphoma, which accounts for approximately 12% of NHL cases, is also growing quickly. After receiving the green light for primary cutaneous anaplastic large cell lymphoma last year, Seattle Genetics' Adcetris (FDA Breakthrough Therapy, Orphan Drug and Priority Review) may also be on the cusp of approval for patients with CD30-expressing peripheral T-cell lymphoma after meeting its primary Phase III endpoint of progression-free survival and achieving significant improvement in all key secondary endpoints.

Our Hot Indications analysis reveals major development activities in **gastrointestinal stromal tumors (GIST)**, jumping from **#250** in 2017 to **#90** in 2018. Most GIST patients develop resistance to first-line therapy Gleevec within 2-3 years, and second (Sutent) and third line (Stivarga) therapies have limited efficacy. Major unmet needs include therapies for tumors driven by mutations in c-KIT or PDGFR-α D842V, which are highly refractory to approved tyrosine kinase inhibitors. Notable programs seeking to address these needs include Blueprint Medicine's avapritinib (FDA Breakthrough, Orphan Drug and Fast Track designations), which selectively inhibits PDGFR-α D842V and c-KIT exon 17 variants, in Phase III development for third-line GIST treatment. Arog Pharmaceutical's crenolanib (FDA Fast Track and EMA Orphan Drug designations), a FLT3 and PDGFR-α D842V inhibitor, is also in Phase III development. In June 2017, Deciphera raised $52 million to take DCC-2618, a pan-KIT and PDGFR-α inhibitor, into Phase III trials[5].

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**Biliary cancer** (also known as bile duct cancer or cholangiocarcinoma) has also made a notable rise from **#198** in 2017 to #117 in 2018's Hot Indications List, driven by a high unmet need for effective treatments. A rare cancer with an incidence of 0.35 to 3 per 100,000 in the Western world, surgical removal is the only curative option available today. As the majority of patients present with unresectable disease, mortality is high, with a 5-year survival rate of only 30% for early-stage disease. The race is on to become the first therapy to win regulatory approval: competitors include big pharma (Lilly's merestinib), biotech (RedHill Biopharma's Yeliva, PCI Biotech's fimaCHEM, ASLAN's varlitinib), and new entrants. The intensity of development and number of mechanisms of action under investigation, including FGFR inhibitors, pan-HER inhibitors, and others, demonstrates the potential of a market that is expected to double in size by 2023, reaching over $300 million globally[6].

Other rare cancers with promising clinical programs in development include **glioblastoma multiforme (GBM, #33)**, which affects less than 10 per 100,000 globally. The key treatment challenge is developing therapies that cross the blood-brain tumor barrier. The success of vaccines in other cancers has led to considerable excitement regarding its potential for GBM. Northwest Biotherapeutics' DCVax (Phase III) is currently in the lead, and has shown survival extension by as much as 7 years, and MimiVax's SurVaxM is in Phase II development; both have been granted FDA Orphan Drug Designation. **Mesothelioma (#116)** is another indication to watch out for: it is notoriously difficult to treat, due to frequent recurrence, and an annual incidence of ~3,330 per year in the US resulted in an empty pipeline since Lilly's Alimta was approved in 2004. However, there may be hope on the horizon: Eisai's amatuximab (EMA Orphan Drug designation; Phase II) is aiming for approval in 2020, while Epizyme's tazemetostat (Phase II) is planned to launch in 2022 as a potential first-in-class EZH2 inhibitor.

## NO RISK, NO REWARD IN ORPHAN CANCERS

While rare and neglected cancers offer attractive opportunities, with high market potential and the possibility of Orphan Drug and other priority designations to smooth development, companies need to be well-prepared to combat challenges associated with the development and commercialization of orphan drugs. Even with smaller pivotal trial sizes, companies must tackle the unique issue of recruitment from rare patient populations. Pressure on pricing and the need for market development and HCP education, particularly for cancers where surgery is currently the only option, present commercialization challenges that will need to be addressed for success in these niche opportunities.

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## LIST OF INDICATIONS IN TOP 100

| INDICATION | RANK |
|---|---|
| **Breast Cancer** | **2** |
| **Prostate Cancer** | **4** |
| **Non-Hodgkin's Lymphoma (NHL)** | **5** |
| **Non-small cell lung cancer (NSCLC)** | **7** |
| **Acute myelogenous leukemia (AML)** | **8** |
| Liver cancer | 9 |
| Colorectal cancer | 14 |
| Melanoma | 17 |
| Head & neck cancers | 22 |
| Ovarian cancer | 23 |
| Multiple myeloma | 26 |
| Pancreatic cancer | 27 |
| Glioblastoma multiforme (GBM) | 33 |
| Small cell lung cancer | 38 |
| Skin cancer | 53 |
| Lung cancer | 64 |
| Glioma | 66 |
| T-cell leukemia | 67 |
| Bladder cancer | 69 |
| Chronic lymphocytic leukemia (CLL) | 80 |
| Gastrointestinal stromal tumors (GIST) | 90 |
| Acute lymphoblastic leukemia (ALL) | 102 |
| Myelodysplastic syndrome (MDS) | 106 |
| Gastric cancer | 112 |
| Mesothelioma | 116 |
| Biliary cancer | 117 |

## METHODOLOGY

# Kaiser Associates' methodology is designed to assess investment intensity of drug development for each indication through a comprehensive and balanced analysis of the key drivers and metrics.

Our Hot Indications analysis framework considers the volume of ongoing scientific investigation, as well as the types of companies and level of funding supporting these trials. Kaiser's analysis evaluated 20,087 drug programs ongoing in 2017[7], categorized them into 572 unique indications, and compared available data for these indications across three main criteria:

### 1. PIPELINE SCORE

The Pipeline Score measures the overall level of drug development activity for an indication. The score gives greater value to later-stage programs, higher volumes of programs overall, and indications with greater numbers of companies with programs.

### 2. R&D FUNDING

R&D Funding estimates the availability of financing to support the development of each drug program to its reasonable endpoint. For some programs, this endpoint will be FDA approval, while for others it will be discontinuation in preclinicals or Phase I.

The score measures availability of funds and willingness to invest based on two main inputs for each indication. First, the R&D FundingScore quantifies the historical track record of sponsor companies, based on the number of drugs each company has successfully developed. Second, the score measures initial public offering and venture capital investment fundraising activity in 2017 for each indication, with the expectation that the financing from such events will be major contributors in supporting ongoing R&D programs.

### 3. ACADEMIC FOCUS

Academic Focus measures the overall publication activity for each indication, based on the absolute number and the one-year change in publications citing the indication for the evaluation period.

### HOT INDICATIONS RANKING

For each of the 572 indications, the overall ranking score is calculated by a weighted average of Pipeline Score (50%), R&D Funding (40%) and Academic Focus (10%).

### THERAPEUTIC AREAS

Each indication is categorized into one of 21 TAs, which include 20 major fields of medicine and an "Other" group. In general, indications are categorized based on the medical specialty most likely to treat patients with a disease or disorder.

Systemic diseases, such as automimmune disorders, or TAs representing a variety of medical specialties, such as Musculoskeletal, are grouped on a case-by-case basis. For example, Crohn's disease and ulcerative colitis are included in Gastroenterology rather than Immunology, whereas Multiple Sclerosis is included in Immunology due to the variety of symptoms it presents.

## REFERENCES

[1]*Astellas, October 10, 2017*
[2] *Gilead Sciences, December 7, 2017*
[3]*Celgene Corporation, January 22, 2018*
[4]*MedicineNet*
[5]*Deciphera Pharmaceuticals, June 1, 2017*
[6]*ASCO, via Cancer.Net*
[7]*EvaluatePharma*

## ABOUT KAISER

Founded in 1981, Kaiser Associates is an international strategy consulting firm that serves as a key advisor to the world's leading companies. We provide our clients with the unique insight to drive critical decision-making and solve their most pressing problems.

Kaiser's Global Healthcare Practice engages with executives at leading Life Sciences companies, including pharmaceutical, medical device, clinical diagnostics, consumer health, and health IT. We work with our clients to identify new growth markets, develop long-term portfolio strategies, and maximize commercial success.

The foundation of Kaiser's service offering is its world-class "outside-in" methodology, which involves delivering critical facts and insights from the complex external environment to drive strategic decision making. Kaiser possesses the unique ability to generate insights across physicians, thought leaders, patients, competitors, partners, regulators, suppliers, and payers. Kaiser uses its deep industry experience and analytical tools to synthesize this diverse set of insights and develop high-impact solutions.

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*Special thanks to Ricardo Espinosa and Jonathan Eary for their contributions to this analysis.*

*Design and Graphics by Kelly Martin Design*