

HOT INDICATIONS LIST

ONCOLOGY DEEP DIVE

Top Indications for
Global Pharma R&D
Investment Intensity in Oncology

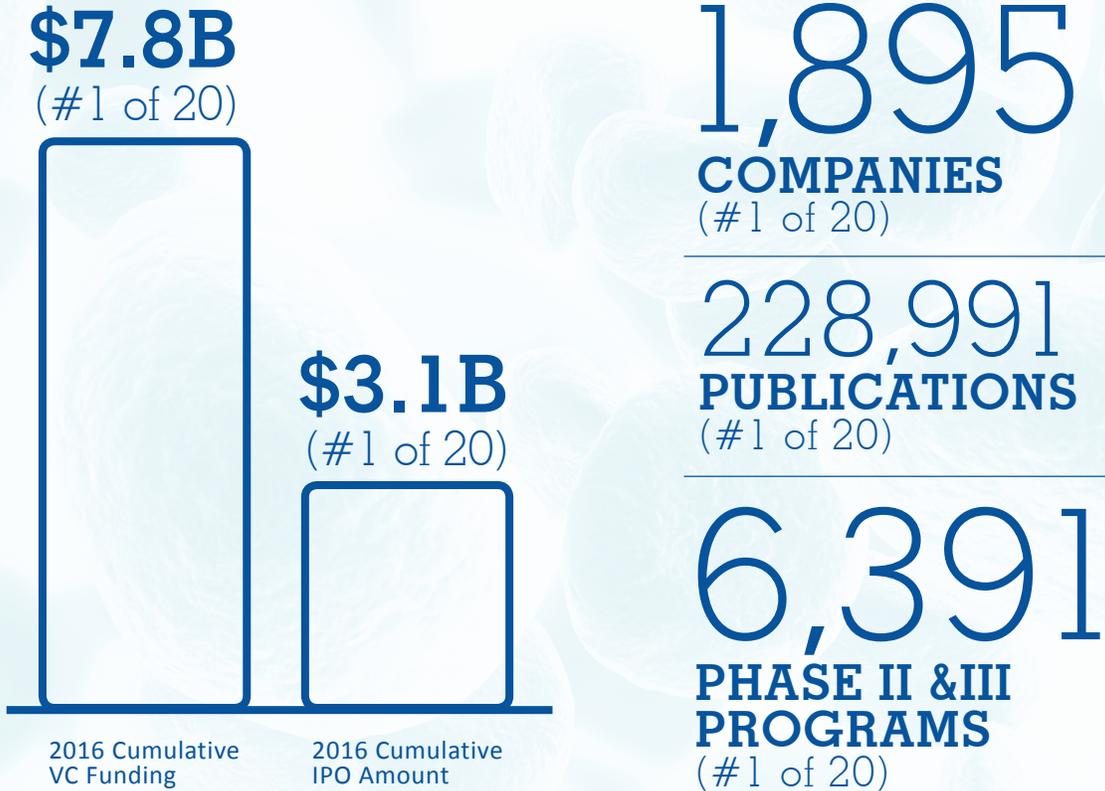
Published July 2017



HOT INDICATIONS LIST

ONCOLOGY DEEP DIVE

(# OF 20) INDICATES TA RANK



INDICATIONS IN TOP 100:

- | | | |
|------------------------------------|--|---|
| Breast cancer (#1) | Chronic lymphocytic leukemia (#14) | Glioma (#53) |
| Non-small cell lung cancer (#2) | Liver cancer (#15) | Hodgkin's disease (#54) |
| Non-Hodgkin's lymphoma (#4) | Multiple myeloma (#16) | Chemotherapy-induced side effects (#55) |
| Prostate cancer (#5) | Renal cancer (#21) | Esophageal cancer (#71) |
| Melanoma (#6) | Head and neck cancer (#22) | Neuroendocrine tumors (#81) |
| Colorectal cancer (#7) | Myelodysplastic syndrome (#26) | Bladder cancer (#82) |
| Pancreatic cancer (#8) | Gastric cancer (#27) | Sarcoma (#83) |
| Ovarian cancer (#11) | Lung cancer, general (#31) | Chronic myeloid leukemia (CML) (#85) |
| Glioblastoma multiforme (#12) | Acute lymphoblastic leukemia (ALL) (#38) | Waldenström's macroglobulinemia (#89) |
| Acute myeloid leukemia (AML) (#13) | Small cell lung cancer (#43) | Fallopian tube cancer (#93) |

HOT INDICATIONS LIST

ONCOLOGY DEEP DIVE

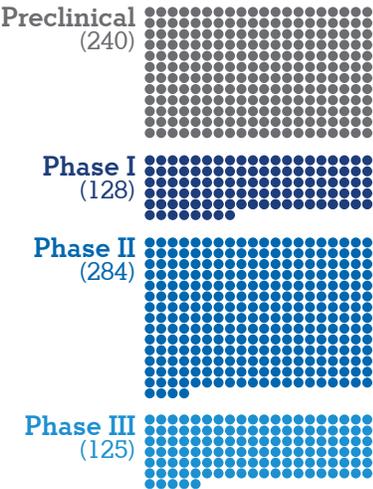
Given the scale of the opportunity and the high unmet need for innovative cancer treatments, it is no surprise that Oncology is the top-ranked Therapeutic Area for the third year in a row, and that **7 of the top 10** Hot Indications are in Oncology.

For many years, the level of investment in Oncology R&D has been higher than any other therapeutic area, underlying the success of many blockbuster cancer treatments (e.g. Herceptin for **breast cancer (#1)**). Looking

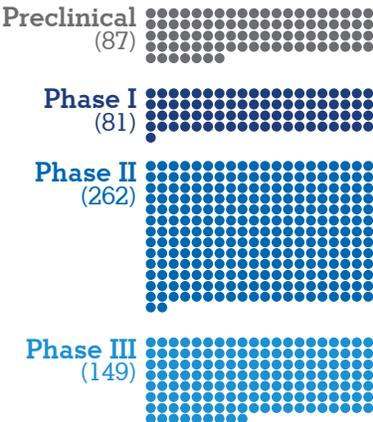
within the therapeutic area, investment can be dynamic: this year, **colorectal cancer (#7)** re-entered the Top 10 after falling to #25 in 2015, and **chronic lymphocytic leukemia (CLL) (#14)** jumped from #30 in 2015.

Number of Programs by Stage of Development

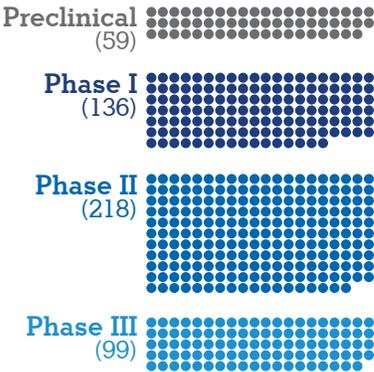
BREAST CANCER (#1)



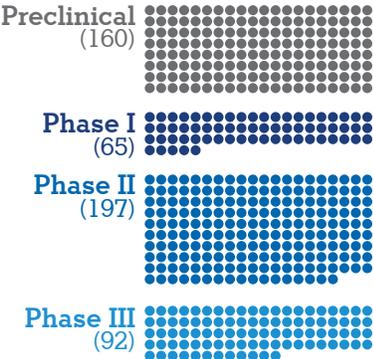
NON-SMALL CELL LUNG CANCER (#2)



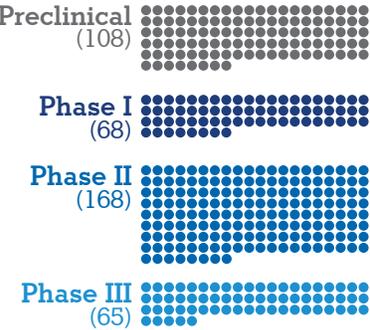
NON-HODGKIN'S LYMPHOMA (#4)



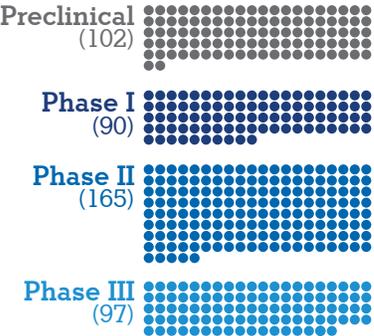
PROSTATE CANCER (#5)



MELANOMA (#6)



COLORECTAL CANCER (#7)



SOURCE: KAISER/EVALUATEPHARMA DATABASE

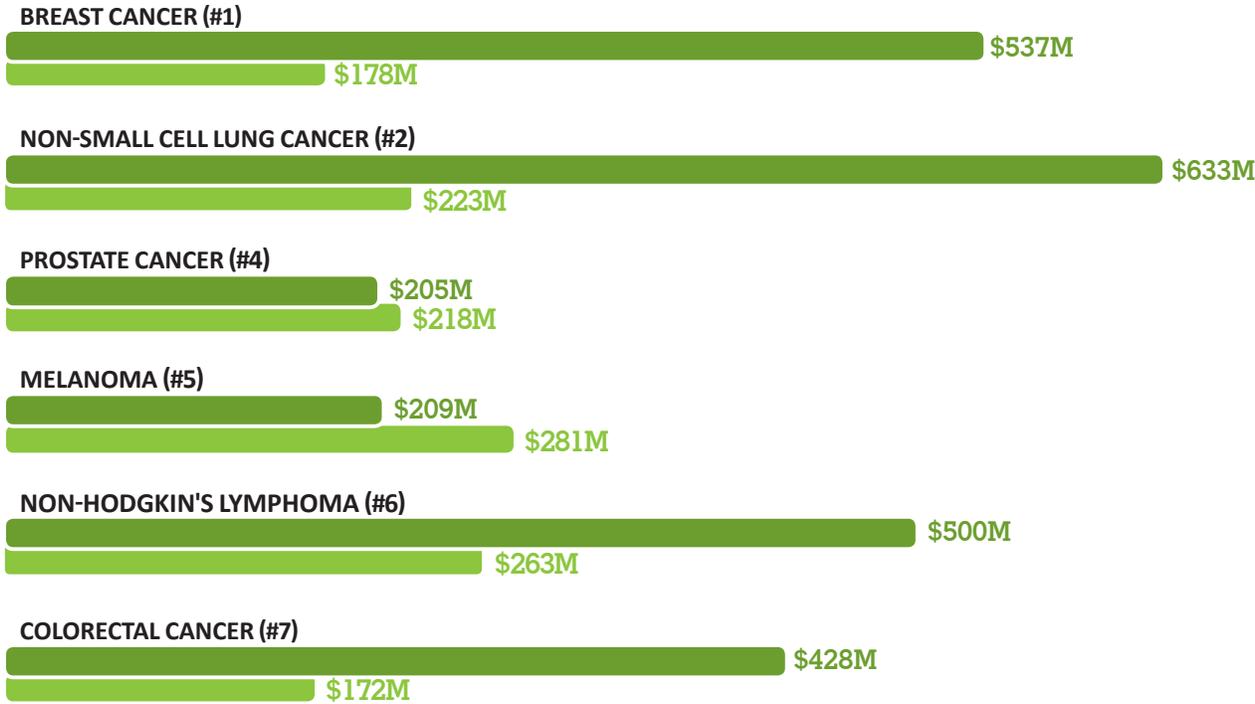
HOT INDICATIONS LIST

ONCOLOGY DEEP DIVE

Funds Raised from IPOs and VC in 2016, by Indication

Sum of funds raised by companies with at least one program

VC AMOUNT
 IPO AMOUNT



SOURCE: KAISER/EVALUATEPHARMA DATABASE

The rise of particular indications can be attributed to investment in innovative candidates such as NOXXON Pharma’s NOX-A12, which targets the tumor microenvironment and may work synergistically with other cancer therapies. Currently in Phase 2 trials for **multiple myeloma (MM) (#16)** and CLL, NOXXON’s \$44M IPO will enable further late-stage trials planned for metastatic **colorectal and pancreatic (#8) cancers** and **glioblastoma (#12)**, for which NOX-A12 has been granted Orphan Drug Status.

Combination therapies have long been a focus of Oncology drug development, but have been particularly attractive in the post-genomic area, as our understanding of the combinations of genetic mutations driving cancer has expanded. Examples of successful combination therapies include Merck KGaA’s EGFR inhibitor Erbitux and DNA damaging agent irinotecan in **colorectal cancer**, and GSK’s dual HER2/EGFR inhibitor Tykerb / Tyverb and capecitabine in advanced **breast cancer**.

HOT INDICATIONS LIST

ONCOLOGY DEEP DIVE

In 2016, the focus was on immuno-oncology combinations, which have driven collaboration between big pharma and biotech.

As an example, Syndax Pharmaceuticals has entered into partnerships with Pfizer, Merck, and Genentech for late-stage trials of entinostat in combination with Aromasin (for HR+ **breast cancer**), Keytruda (for **NSCLC (#2)** and **melanoma (#6)**) and Tecentriq (for triple-negative **breast cancer**). A Phase I trial for **ovarian cancer (#11)** with Merck KGaA and Pfizer's immunotherapy candidate avelumab is also underway. In March 2016, Syndax raised \$53M via its IPO.

Another notable example is Genentech's expanded partnership with Corvus Pharmaceuticals to take Corvus' adenosine A2A receptor inhibitor CPI-444 into a Phase Ib/II **non-small cell lung cancer (NSCLC) (#2)** trial in combination with immunotherapy Tecentriq. Corvus' March 2016 IPO raised \$78M, although the combination trial will be managed by Genentech as part of their MORPHEUS immunotherapy platform, which aims to increase the speed and efficiency of immunotherapy combination development.

The largest biotech IPO of 2016 involved a less evident partnership: Myovant's \$218M offering was driven both by its promising testosterone inhibitor Relugolix, in Phase III development for androgen-sensitive

prostate cancer (#5), and Pfizer's \$30M interest in the company. Pfizer will have first negotiation rights to acquire Myovant or its pipeline candidates.

Outside of immunotherapy combinations, there are other pharma-biotech collaborations supporting innovation in Oncology. Moderna Therapeutics, which raised a record-breaking \$450M in funding in August 2016, is developing mRNA therapeutics for multiple cancers in partnerships with Merck and AstraZeneca. Although these candidates are currently preclinical, AstraZeneca was sufficiently convinced by the results coming out of its earlier partnership across cardiovascular and other conditions to expand the partnership into immuno-oncology in January 2016.

Looking back at Oncology within Kaiser's first Hot Indications List in 2014, 50% of the top 10 Oncology indications have seen new drug approvals in 2015-2016. These include major launches such as Pfizer's Ibrance for **breast cancer**, which achieved over \$2B in worldwide sales in 2016. With a number of major approvals so far in 2017, such as Pfizer and Merck KGaA's Bavencio immunotherapy for Merkel cell carcinoma, Novartis' Kisqali for HR+/HER2- **breast cancer**, and Tesaro's Zejula for **ovarian, fallopian tube (#93)** and peritoneal cancer, this year is likely to be another blockbuster for the Hot Indications within Oncology.



HOT INDICATIONS LIST

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 36,538 drug programs ongoing in 2016, categorized them into 626 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 pre-clinicals 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 Funding Score 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 2016 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 626 indications, the overall ranking score is calculated by a weighted average of Pipeline Score (50%), R&D Funding (40%) and Academic Focus (10%). Throughout this analysis, the rank number from the final Hot Indications List is denoted in parentheses immediately following first mention of the indication in each section.

Therapeutic Areas & Ranking

The Therapeutic Area Ranking is an index of R&D investment intensity that synthesizes and normalizes the Hot Indications Ranking scores for all indications within a Therapeutic Area.

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

Systemic diseases, such as autoimmune 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 Autoimmune, whereas Multiple Sclerosis is included in Autoimmune due to the variety of symptoms it presents.

HOT INDICATIONS LIST

ABOUT KAISER ASSOCIATES

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.

ABOUT THE AUTHORS

Jenna Riffell

Jenna is a Manager in Kaiser Associates' Global Healthcare Practice based in London, UK.

You may contact her by email at jriffell@kaiserassociates.com

Bob Serrano

Bob is a Vice President in Kaiser Associates' Global Healthcare Practice based in Washington, D.C.

You may contact him by email at bserrano@kaiserassociates.com

Dan O'Neill

Dan is a Senior Vice President in Kaiser Associates' Global Healthcare Practice based in Washington, D.C.

You may contact him by email at doneill@kaiserassociates.com

Special thanks to Jay Howard for his contributions to this analysis.

Design and Graphics by Kelly Martin Design

