

HOT INDICATIONS LIST

IMMUNOLOGY DEEP DIVE

**Top Three Indications
for Global Pharma R&D
Investment Intensity in Immunology
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(# OF 20) INDICATES TA RANK

\$990M

(#5 of 20)



2015 Cumulative
VC Funding

\$840M

(#12 of 20)



2015 Cumulative
IPO Amount

557

COMPANIES

(#5 of 20)

23,700

PUBLICATIONS

(#16 of 20)

219

**PHASE II & III
PROGRAMS**

(#6 of 20)

INDICATIONS IN TOP 100:

Rheumatoid arthritis/RA (#12)
Multiple sclerosis/MS (#36)
Lupus (#47)
Osteoarthritis (#77)

Ankylosing spondylitis (#78)
Scleroderma (#113)
Myasthenia gravis (#196)
Psoriatic arthritis (#197)

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In 2015, **rheumatoid arthritis (#12)**, **multiple sclerosis (#36)** and **lupus (#47)** retained the top three positions for pipeline activity within Immunology.

With 74 Phase 2 and 3 programs underway, and generating over \$400 million in VC funding in 2015, rheumatoid arthritis continues to lead as the indication receiving the most interest. Although anti-TNFs have altered the treatment paradigm, recent attention has been focused on developing alternative therapies such as JAK inhibitors, of which there are 7 in the pipeline. Examples of this emerging class include Eli Lilly's baricitinib (filed in Jan 2016), which if approved, will compete with Pfizer's approved JAK inhibitor Xeljanz. However, Xeljanz's associations with serious side effects suggest that further opportunities lie in developing drugs with fewer adverse reactions within this indication.

2015 marked Celgene's entry into the Immunology space; undeterred by an increasingly crowded multiple sclerosis marketplace, Celgene's acquisition of Receptos allowed it to gain rights to ozanimod. With 2 programs in Phase 3 for multiple sclerosis, ozanimod is expected to help Celgene further build upon its success with Otezla as they seek to establish a full Immunology portfolio across multiple hot indications.

MOVERS AND SHAKERS

The biggest mover in 2015 is **ankylosing spondylitis (AS)** – catapulting from #217 to **#78**. A rare, debilitating disease affecting mainly young males, there are no known cures at present. Large and small pharma players such as Celgene, Amgen and Innovent Biologics are continuing to focus on targeting TNF, with the latter notably receiving \$100 million in Series C funding for a number of its pipeline drugs, including its Phase 3 TNF blocker IBI303. Alternative targets, such as the IL-17 pathway, are also under scrutiny for a number of indications, in addition to AS. Novartis received FDA and EMA approval for Cosentyx (secukinumab) and is currently aiming for label expansion into rheumatoid arthritis and multiple sclerosis, while Eli Lilly's IL-17

inhibitor Taltz (ixekizumab) is also expecting to gain approval for AS and **psoriatic arthritis (#197)**.

Another indication that received increased attention is **myasthenia gravis**, jumping 70 places from #269 to **#196**. Lack of curative treatment options and the significant side effects of current therapies has led to both large and small pharma players to invest in this space. After huge success for treatment of **paroxysmal nocturnal hemoglobinuria (PNH, #129)** and **atypical hemolytic uremic syndrome (aHUS, #168)**, Alexion also had high hopes for Soliris to expand into the myasthenia gravis space in 2015. However, having missed its primary endpoint in a Phase 3 study in 2016, its approval is now in doubt. Recent Orphan Drug Designations for Phase 1 candidates ACT-101 (Alpha Cancer Technologies) and CV-MG01 (CuraVac) will hopefully see promising novel therapies in the future.

Scleroderma has also received a heightened level of interest in 2015, climbing from #152 to **#113**. In a disease with no current FDA-approved treatments, the race is on to become the first therapy to receive regulatory approval. Cytori was granted Orphan Drug Designation for its ECCS-50 cellular therapy in the EU, while Corbus

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Number of Programs by Stage of Development

RHEUMATOID ARTHRITIS (#12)

Preclinical (101) 

Phase I (59) 

Phase II (47) 

Phase III (27) 

MULTIPLE SCLEROSIS (#36)

Preclinical (65) 

Phase I (31) 

Phase II (36) 

Phase III (10) 

LUPUS (#47)

Preclinical (18) 

Phase I (22) 

Phase II (18) 

Phase III (10) 

OSTEOARTHRITIS (#77)

Preclinical (22) 

Phase I (10) 

Phase II (32) 

Phase III (9) 

ANKYLOSING SPONDYLITIS (#78)

Preclinical (7) 

Phase I (0)

Phase II (2) 

Phase III (2) 

SCLERODERMA (#113)

Preclinical (8) 

Phase I (6) 

Phase II (10) 

Phase III (4) 

MYASTHENIA GRAVIS (#196)

Preclinical (2) 

Phase I (2) 

Phase II (2) 

Phase III (2) 

PSORIATIC ARTHRITIS (#197)

Preclinical (4) 

Phase I (2) 

Phase II (4) 

Phase III (4) 

SOURCE: KAISER/BCIQ DATABASE

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gained fast-track status and FDA Orphan Drug Designation for its first-in-class oral therapy resunab. Upon approval, both of these have the potential to drastically change the treatment landscape.

DECLINING R&D INTEREST IN 2015

The biggest loser of the year is **psoriatic arthritis (PsA)**, which dropped 61 places from #136 to #197, marked by the competitive intensity of the marketplace and doubts over serious side effects of novel therapies. Celgene made its first foray into PsA with oral therapy Otezla in January 2015, joining major injectable players such as Johnson & Johnson's Stelara and AbbVie's Humira. In line with the trend in label expansion within this therapeutic area, Ote-

zla is also currently under investigation for the treatment of rheumatoid arthritis. Amgen & AstraZeneca's brodalumab showed potential in its Phase 3 trials; however, concerns over severe side effects resulted in Amgen ceasing their development collaboration of brodalumab with AstraZeneca. So far, it has debuted as a second line therapy in Japan, and is awaiting FDA approval.

CONCLUSION

Since the takeoff of blockbuster drugs Humira and Enbrel, Immunology has been a key area to watch. A further surge in innovation has already generated oral therapies, such as IL-17 and JAK inhibitors, and we can expect new research to unlock even more exciting curative therapies.

A NOTE FROM THE AUTHORS:

Indications are categorized based on the medical specialty most likely to treat patients with a disease or disorder. Autoimmune disorders have been 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. To see the top 200 Hot Indications List across all therapeutic areas, please go to <http://www.kaiserassociates.com/healthcare/hot-indications>



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 13,182 drug programs ongoing in 2015, categorized them into 577 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 2014 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 577 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 Immunology, whereas Multiple Sclerosis is included in Immunology due to the variety of symptoms it presents.

To see the full list, go to
<http://info.kaiserassociates.com/2016-hot-indications>

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ABOUT KAISER ASSOCIATES

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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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