

Crohn's Disease

We analyzed our expertly curated clinical and biological data at Intelligencia AI to generate a high-level view of the current and potential future state of drug development for Crohn's disease.



Crohn's disease is a chronic inflammatory bowel disease (IBD) characterized by recurrent episodes of intestinal inflammation¹.



It is believed to be caused by a dysregulated immune response to gut bacteria, though the exact mechanism is unknown².



Symptoms may be non-specific and progress gradually, often delaying diagnosis. Organs such as the skin and joints can also be affected.



Genetic, environmental, and immunological factors influence Crohn's disease. Genetic predisposition can play a significant part, with first-degree relatives having a five-fold increased risk. Smoking and processed food diets can also increase risk¹.



While on its own, it is not a life-threatening disease, it can cause complications that reduce life expectancy (e.g., cancers, osteoporosis, heart problems). The prevalence of Crohn's disease is 300 per 100,000 in the U.S.³

HOW IS CROHN'S DISEASE CURRENTLY TREATED?

Commonly used types of treatment⁴:

- Anti-inflammatory medicines
- Immune system suppressors
- Biologics
- Janus kinase (JAK) inhibitors
- Antibiotics
- Surgery
- Diet and nutrition

In the past five years, the following drugs are the only ones that have received regulatory approval from the FDA: Rinvoq, Skyrizi, and the subcutaneous form of the previously approved Entyvio.

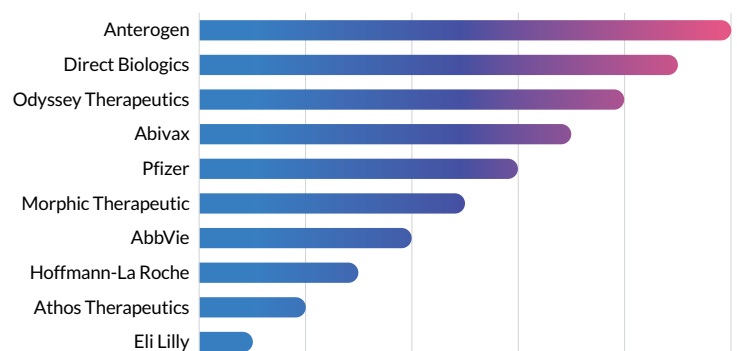
Rinvoq is a small molecule inhibitor (SMI) targeting JAK. Skyrizi is a monoclonal antibody (mAb) that targets interleukin 23 (IL-23). Entyvio is a mAb that targets Integrin alpha-4/beta-7. All three act by modulating immune response.

DETAILS IN THE DATA: HERE'S WHAT WE LEARNED ABOUT DRUG DEVELOPMENT FOR CROHN'S

In analyzing our data⁵, we identified:

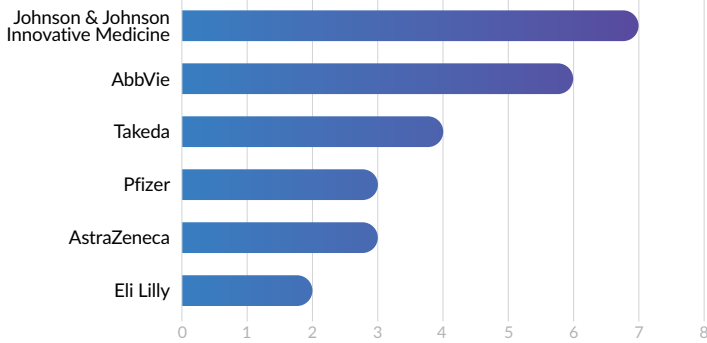
- 41 ongoing industry-led, FDA-track interventional clinical development programs* among which:
 - 5 are in Phase 1 or 1b,
 - 18 are in Phase 2 or 1/2 and
 - 18 are in Phase 2/3 or Phase 3.
- The programs mentioned above are conducted by 22 different primary sponsors and correspond to 33 investigational drugs/drug combinations, covering 7 different drug modalities/modality combinations.

Top 10 Sponsors in Crohn's Disease - Ranked by Intelligencia AI Pipeline Performance Score



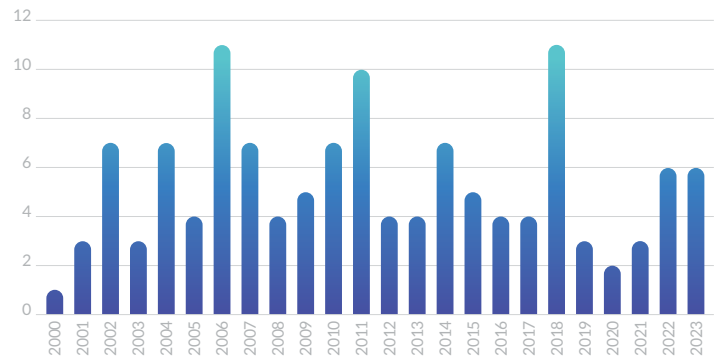
Our pipeline performance score leverages our patented AI-driven probability of technical and regulatory success (PTRS) assessments.

Sponsors With the Highest Number of Active Crohn's Disease Clinical Programs



These are the top sponsors based on the number of ongoing Crohn's disease clinical programs*.

Distribution of Crohn's Disease Clinical Programs by Year of Initiation Since 2000



Over the past two decades, Crohn's disease clinical development has been quite irregular, alternating between highs and lows. The relatively small number of programs for most years might be able to justify this level of deviation.

- Among our industry-led, FDA-track historical programs, 69% transitioned from Phase 1 to Phase 2 and 24% from Phase 2 to Phase 3.
- There have been six drugs (run by six different sponsors) that have not received prior FDA approval in Crohn's and are being tested in Phase 3 trials.
- These drugs referenced above are either mAbs or SMIs.
- Regarding Mechanism of Action (MoA), the most common targets would be IL-23 for the mAbs, and sphingosine-1-phosphate (S1P) receptor for the SMIs.

PERSPECTIVE: WHAT DOES THIS ALL MEAN?

Since 2000, less than ten separate drugs have received regulatory approval for the treatment of Crohn's disease. None of them are an effective cure for the disease, and in a best case scenario can result in disease remission. Out of the 18 previously mentioned drugs, currently ongoing Phase 3 clinical development programs, almost half are testing the same drug, Guselkumab, in different population subsets.

Taking this data and trends into account, as well as the disease's prevalence rate, Crohn's disease indeed constitutes

an unmet need for the patients. However, it is a disease that the pharmaceutical industry does not seem eager to address – likely due to the lack of lethality and varied intensity among patients – which is evident considering that there are only six non-approved assets in late-stage development. It's imperative that biomarkers must be identified for early detection and treatment in advanced stages. In the foreseeable future, the industry's focus is projected to be limited.

About Intelligencia AI

Intelligencia AI™ leads the way in leveraging proprietary data, biomedical expertise and artificial intelligence (AI) with its patented technology to address significant challenges in the pharmaceutical industry. These challenges include lengthy drug development timelines, excessive costs, and unsustainable return on investment (ROI). Its suite of AI-powered solutions delivers actionable insights crucial in mitigating risks and enhancing decision-making associated with drug development by providing an accurate, unbiased assessment of a drug's probability of success. Founded in 2017, Intelligencia AI is headquartered in New York, NY, with offices in Athens, Greece, and employs 110 individuals globally. Visit intelligencia.ai to discover more.

References

- Roda G, Chien Ng S, Kotze PG, Argollo M, Panaccione R, Spinelli A, Kaser A, Peyrin-Biroulet L, Danese S. Crohn's disease. *Nat Rev Dis Primers*. 2020 Apr 2;6(1):22. doi: 10.1038/s41572-020-0156-2. Erratum in: *Nat Rev Dis Primers*. 2020 Apr 6;6(1):26. doi: 10.1038/s41572-020-0172-2. Erratum in: *Nat Rev Dis Primers*. 2020 May 20;6(1):42. doi: 10.1038/s41572-020-0183-z. Erratum in: *Nat Rev Dis Primers*. 2020 Jun 19;6(1):51. doi: 10.1038/s41572-020-0193-x. PMID: 32242028.
- Mowat AM, Agace WW. Regional specialization within the intestinal immune system. *Nat Rev Immunol*. 2014 Oct;14(10):667-85. doi: 10.1038/nri3738. Epub 2014 Sep 19. PMID: 25234148.
- Weisman MH, Oleg Stens, Seok Kim H, Hou JK, Miller FW, Dillon CF. Inflammatory Bowel Disease Prevalence: Surveillance data from the U.S. National Health and Nutrition Examination Survey. *Prev Med Rep*. 2023 Mar 9;33:102173. doi: 10.1016/j.pmedr.2023.102173. PMID: 37223580; PMCID: PMC10201824.
- <https://www.mayoclinic.org/diseases-conditions/crohns-disease/diagnosis-treatment/drc-20353309>
- Data as of December 3, 2024



*A program (also known as clinical pipeline or drug pipeline) is the clinical development of a drug (or a set of drugs in case of combination therapies) by a pharmaceutical company (alone or in collaboration with other partners) for an indication. A program consists of a set of clinical trials with the ultimate goal of approval for marketing. Each program has unique and specific parameters that can potentially justify a separate regulatory approval. Specifically, the definition of a clinical program is one of unique drug(s), drug dosage, mode of administration, adjuvant state, indication, sponsor, disease severity (e.g. stage of disease), line of treatment and biomarker information used as inclusion criteria.