File No. CT-2024-006

COMPETITION TRIBUNAL

IN THE MATTER OF the *Competition Act*, R.S.C. 1985, c. C-34 (the "**Act**");

AND IN THE MATTER OF an application by JAMP Pharma Corporation for an order pursuant to section 103.1 of the Act granting leave to bring an application under section 79 of the Act;

AND IN THE MATTER OF an application by JAMP Pharma Corporation for an order pursuant to sections 79 of the Act;

BETWEEN:

JAMP PHARMA CORPORATION

Applicant

– and –

JANSSEN INC.

Respondent

AFFIDAVIT OF AMÉLIE FAUBERT
(Pursuant to section 103.1 of the *Competition Act*)

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AFFIDAVIT OF AMÉLIE FAUBERT

(Pursuant to section 103.1 of the *Competition Act*)

I, AMÉLIE FAUBERT, of the City of Boucherville, in the Province of Quebec, **MAKE OATH AND SAY**:

1. I am employed by JAMP Pharma Corporation ("**JAMP**") as a Vice-President, in charge of the BioJAMP Division, and as such I have personal knowledge of the matters herein deposed, except where I rely on information provided by other persons, in which case, I believe that information to be true.

2. This affidavit is sworn in support of an application being brought by JAMP for an order pursuant to section 103.1 of the Competition Act ("**Act**") for leave to bring an application against the Respondent under section 79 of the Act.

I. CURRICULUM VITAE

3. I was originally hired by JAMP in 2022. Among other things, I oversee all of BioJAMP's operations (including sales) and the operation of JAMP's patient support program, JAMP Care. My responsibilities also include the launch, marketing and sales of new biosimilar products. I am a member of JAMP's executive committee and I report directly to Mr. Louis Pilon, who is the President and Chief Executive Officer of JAMP.

4. Prior to joining JAMP, I worked for a number of other pharmaceutical companies. For approximately 9 years, I worked in clinical, medical and scientific roles for different pharmaceutical companies. Starting in 2016, I began working in different business roles, including sales, marketing and corporate development.

5. I hold four university degrees: a Bachelor of Science degree from Université de Montréal in 2000; a Master of Science degree from Université de Montréal in Immunology; a Doctor of Philosophy from McGill University in Experimental Medicine; and an Executive Master of Business Administration and Management from McGill University and HEC Montréal.

I. INFORMATION ABOUT USTEKINUMAB

6. The affidavit of Sukhad Juneja describes ustekinumab drugs in detail. Capitalized terms in this affidavit have the meaning ascribed to them in the affidavit of Mr. Juneja, unless otherwise indicated herein.

7. Once a patient begins taking an ustekinumab drug, the drug proves effective and is well tolerated, a prescriber is not likely to switch the patient to another drug (including in response to a small price increase) and these patients will be maintained on the drug for many years.

8. Among customers for ustekinumab, there are a number of identifiable segments. Those segments are created by the different formats in which ustekinumab biologics are offered and the rules of different public drug plans and private insurance plans, among other dynamics. Those segments include:

(a) Vials (Infusion Clinics) and Pre-Filled Syringes (Pharmacies) – Ustekinumab biologic drugs are sold in two formats – vials and pre-filled syringes. To administer a vial, a sterile syringe must puncture the vial to draw the drug, the drug is added to an infusion bag, and the drug is then administered to the patient using intravenous infusion. These infusions are typically performed by a medical professional, sometimes at "infusion clinics" mostly operated by a patient support program (which are described in more detail below). Vials represent less than 5% of units sold of ustekinumab. By contrast, the vast majority of ustekinumab is sold in the format of a pre-filled syringe. Typically, patients are supplied with syringes and inject themselves under the skin. Patients are typically dispensed these syringes from pharmacies.

(b) New Patients and Existing Patients – Ustekinumab is a maintenance drug – that is, once a patient begins taking an ustekinumab drug, the drug proves effective and is well tolerated, the patient requires administration of the drug over the long-term

and, absent a valid medical reason, a prescriber is not likely to switch the patient to another drug. This means that competition to supply ustekinumab for new patients and existing patients differs. Competition for new patients involves a drug manufacturer convincing a prescriber as to the quality of its product and the effectiveness of its patient support program. Competition for existing patients involves a drug manufacturer identifying to a prescriber why a switch would be in the patient's best interest (e.g., the similar safety and efficacy of the drug, insurance requirements, lower overall costs, the relative similarity or superiority of a patient support program, etc.). In addition, competition for new patients and existing patients can differ due to rules adopted by insurance plans; for example, an insurer may require that new patients be prescribed a biosimilar, but not require that existing patients be switched to a biosimilar.

(c) Public Drug Plans and Private Insurers – The cost of ustekinumab is frequently reimbursed by different types of insurers. Drug manufacturers compete for their products to be listed on the formularies of insurers, but that competition can differ by type of insurer. Public drug plans, for example, may have a range of policy objectives in mind when deciding whether to list a drug on a formulary and the amount they are willing to reimburse for the drug. For example, a public drug plan may consider the incremental efficacy of a drug compared to alternatives on the formulary; its willingness to list a new drug and pay for that new drug may correspond to that incremental efficacy. By further example, a public drug plan may require a "most-favoured-nation" provision regarding pricing in any agreement with a drug manufacturer (because that plan's policy is to require such provisions).

By contrast, a private insurer may consider if other private insurers reimburse a drug, to ensure the private insurer remains a competitive and attractive option for customers (such as employers) that are selecting a private insurer. By further example, a private insurer may be interested in the lowest possible reimbursement cost for a drug (regardless of what other considerations may apply).

9. In addition to differences in competition among segments of customers, there are also some differences in competition between different geographies within Canada. This is largely attributable to the fact that public drug plans are operated by provincial/territorial governments, and the rules of those drug plans vary slightly. That said, there are numerous similarities in the rules of those provincial-level drug plans, and the differences in competition between the provinces/territories are not significant.

10. Between 2008 (when a Notice of Compliance for Stelara was issued by Health Canada) until March 1, 2024 (when both JAMP and Amgen Canada Inc. ("**Amgen**") began marketing ustekinumab biosimilars), the only supplier in Canada of ustekinumab was the Respondent, Janssen Inc. ("**Janssen**"). Throughout that period, I understand that Janssen's wholesale price for Stelara was virtually unchanged (i.e., in excess of $4,000 per dose). On March 1, 2024, each of JAMP and Amgen began marketing ustekinumab biosimilar products in Canada that, to the best of my knowledge, were priced at significant discounts to Stelara. In the month of May 2024, according to data I reviewed from IQVIA, Janssen's share of unit volumes and revenues for ustekinumab in Canada remained above 99.8%. I do not have reason to believe that Janssen's shares of ustekinumab have changed in any significant way since that time.

II. MARKETING AND DISTRIBUTING BIOLOGIC DRUGS

a. Certain Marketing Activities Directed at Prescribing Physicians, and Prevalence of Non-Disclosure Agreements

11. I understand that drug manufacturers seek out ways to engage with prescribing physicians as part of their broader marketing activities for individual biologic drugs. For example, drug manufacturers may invite physicians to participate in so-called "advisory boards." I have attached as Exhibit "F1" a description of advisory boards prepared by a consultancy that facilitates the operation of such boards; it describes those boards as "laboratories" for "key message development." By further example, drug manufacturers may sponsor academic research papers and invite prescribers to participate in their preparation. I have attached as Exhibit "F2" and "F3" two research papers regarding ustekinumab that were funded by Janssen, in which Canadian prescribing physicians were listed as co-authors; each paper explains that Janssen "was involved in the design, interpretation, and reporting of study results." By final example, drug manufacturers may provide honoraria to prescribers, invite and pay prescribers to speak at conferences the manufacturers have organized, or fund the prescribers' research efforts, among other things. It is my understanding that a drug manufacturer will frequently require that prescribers who participate in these types of marketing activities enter into non-disclosure agreements.

b. Distribution of Biologic Drugs and Patient Support Programs

12. I understand that the administration of biologic drugs can be complex. For example, some biologics must be administered chronically through infusion. I understand that, historically, the Canadian healthcare system has not supported the administration of drugs. To support

the adoption of drugs with complex administration requirements, I understand that drug manufacturers have established so-called "Patient Support Programs" ("**PSP**"). I understand that PSPs may provide a number of services to patients. It is my understanding that, typically, at the time a prescriber prescribes a biologic drug to a patient, the prescriber will also enroll the patient in the PSP of the drug's manufacturer. A representative of the PSP will typically contact the patient for the purposes of establishing a schedule for the administration of the drug and to facilitate reimbursement of the drug's cost for the patient (if available through a public drug plan or a private insurance plan). From time-to-time, a PSP may decide to supply the drug to a patient for free (e.g., in the event the patient is in the process of switching insurers, or in the event the patient's insurer is still in the process of reviewing an application to reimburse the drug or will only pay a portion of the cost of the drug). These efforts by the manufacturer ensure the patient is administered the drug in the prescribed manner, which improves health care outcomes. These efforts also reduce the likelihood of the patient avoiding the drug for administrative reasons or financial reasons. These efforts also support and increase the drug's volume of sales.

13. The process of enrolling a patient in a PSP and the PSP overseeing the administration of its biologic drug gives manufacturers very extensive information about the identity and practices of the physicians who prescribe their biologic drug and the patients to whom it is administered. During the period of time when an innovative biologic is protected from competition, the biologic's manufacturer will obtain such information for every prescriber and patient of the drug in Canada. When a manufacturer of a biosimilar enters, it does not possess any such detailed information about prescribers or patients (but faces a rival that does).

14. The process of enrolling a patient in a PSP and the PSP overseeing the administration of its biologic drug also gives manufacturers a means to contact and communicate with physicians and patients. As described in more detail below, Janssen operates a PSP called BioAdvance. It is my understanding that, from time to time, Janssen uses BioAdvance to communicate with prescribers or patients directly regarding rival biosimilar drugs (rather than simply about the administration of Janssen's biologic drugs). For example, I understand that in 2018 a private insurance company in Canada announced a new policy requiring that its insured patients switch from Janssen's Remicade to a lower priced biosimilar. I attach as Exhibit “F4" a letter that I understand that Janssen sent directly to patients insured by that company; among other things, the letter explains that Janssen does "not support" the insurer’s policy, warns that Janssen will not provide financial support to patients covered by the insurer’s policy, and warns that its BioAdvance PSP will not be available to patients covered by the insurer’s policy. The letter concludes by suggesting that patients contact the insurer about its policy.

15. Over time, physicians and patients can become familiar with an individual PSP. For example, a physician (or their staff) may become experienced at enrolling new patients in an individual PSP, and the services offered by that PSP. By further example, a patient may become experienced at accessing the services offered by an individual PSP, including the points of contact with the PSP. During the period of time when an innovative biologic is protected from competition, physicians and patients can become familiar with the innovative company’s PSP. This familiarity can make it challenging for a biosimilar company to convince physicians and patients to switch to its biosimilar drug, because the switch requires that both the physician and the patient become familiar with a new PSP.

III. THE BIOJAMP BUSINESS

16. As described in the affidavit of Sukhad Juneja, JAMP's activities are organized through a number of different divisions, and JAMP created a new division, BioJAMP, for the sale of all of its biosimilar products in early 2022. The BioJAMP division is independent and separate from JAMP's other divisions. In the subparagraphs below, I describe some of the ways that BioJAMP is independent and separate from JAMP's other divisions.

(a) Dedication to Selling Biosimilars. BioJAMP offers biosimilar products. None of JAMP's other divisions sell biosimilars. Indeed, some of JAMP's other divisions sell products that have no material commercial connection to biosimilars at all, such as Cosmetic Import (which sells cosmetic products) and Wampole (which sells over-the-counter nutritional supplements).

(b) Unique Strategic Relationship to Alvotech. BioJAMP is largely able to operate as a result of JAMP having entered into a series of exclusive agreements with Alvotech, a manufacturer of biosimilars. No other division of JAMP has any contractual relationship with Alvotech.

(c) Dedicated Personnel. BioJAMP has a team of employees whose responsibilities are dedicated exclusively to BioJAMP and its products. These dedicated personnel include a sales director, 10 other sales staff located across Canada and two brand managers, among others. These personnel have no responsibilities at all related to JAMP's other divisions. I am responsible for overseeing all of these employees. Attached as Exhibit "F5" is an organizational chart for BioJAMP, which shows the

lines of reporting within the BioJAMP division; I serve in the Vice-President role as the head of the division.

(d) Unique Branding, Trademark and Website. BioJAMP operates under the BioJAMP brand. JAMP has registered a trademark for BioJAMP. BioJAMP has a dedicated website, www.biojamp.com, and domain name for email addresses, @biojamppharma.com. None of JAMP's other divisions utilize the BioJAMP brand, the BioJAMP trademark, the BioJAMP website or the BioJAMP domain name to promote their respective products.

(e) JAMP Care. To support the administration of BioJAMP's biosimilars, JAMP established a patient support program called JAMP Care. JAMP Care's services are offered to patients who are prescribed BioJAMP biosimilars as well as a handful of JAMP Pharma specialty products whose administration benefits from support. JAMP Care's costs related to Simlandi and Jamteki (which represent the large majority of JAMP Care's costs) are allocated to BioJAMP. I am responsible for overseeing JAMP Care.

(f) Segregated Cost Centre. BioJAMP calculates its own selling, general and administrative ("**SG&A**") expenses (including the costs of dedicated personnel and JAMP Care), separate from the SG&A costs of other JAMP divisions. BioJAMP's calculated SG&A costs are allocated exclusively to its biosimilar drugs (and not to any other products of other JAMP divisions).

17. As described in the affidavit of Sukhad Juneja, BioJAMP currently sells two drugs – Simlandi, a biosimilar to Humira (adalimumab) and Jamteki, a biosimilar to Stelara

(ustekinumab). BioJAMP does not prepare its own profit and loss statements. As described below, BioJAMP maintains profit and loss statements at the level of individual drugs. However, I can advise that once Jamteki has penetrated the market for ustekinumab, BioJAMP anticipates that [redacted] of its revenues will be generated from sales of Jamteki (which I discuss in more detail at paragraph 39, below).

IV. JAMP'S INVESTIGATION OF USTEKINUMAB AND THE LAUNCH OF JAMTEKI

18. At JAMP, a decision to launch and market a new prescription drug is made on a drug-by-drug basis through careful analysis of the drug's potential revenue, costs and profit. In this manner, each drug is its own separate business.

19. In particular, when a potential new drug is identified, JAMP prepares a "bottom-up" and detailed demand forecast to estimate the revenues the potential drug might generate for JAMP. JAMP has extensive experience preparing these types of forecasts, which it prepares for every product. Those demand forecasts are carefully calibrated to, among other things, account for the amount of the drug sold to different customer segments in different provinces, the total amount of the drug sold in Canada (and likely to be sold in the coming years), the number of other competing suppliers of the drug, and different potential developments in the market (e.g., a decision by a public drug plan to pay for a drug or not). Those demand forecasts permit numerous different scenarios to be identified, evaluated and contrasted.

20. The demand forecast's estimate of revenues that a potential drug might generate for JAMP is an input into another document JAMP prepares when evaluating a potential new drug –

a drug-specific profit and loss statement. Subtracted from the estimated revenues are all of JAMP's projected costs for the drug, including: costs that are incurred directly from the sale of the drug (e.g., costs of goods sold); SG&A costs, which are a portion of common overhead costs that are allocated to the drug; and other costs (e.g., royalty payments). The difference between the projected revenues and the projected costs is JAMP's profit (e.g., EBITDA).

21. Prior to the launch of Jamteki, BioJAMP prepared a detailed forecast of expected demand for Jamteki. I supervised the preparation of that forecast, which is attached as Exhibit "F6". The forecast is informed by objective facts and is conservative in a number of different ways. Among other things, I note the following:

a. Forecast of Total Ustekinumab Sales Volumes – The forecast estimates total volume likely to be demanded in each individual province (separately), by private and public payers (separately), and by individual product format (separately). Those forecasts are then aggregated to a national level. The disaggregated forecast of sales volumes is observable in tab "Forecast Usteki Year 1" at cells A4 to AF19; those cells link to the "Sales per Province" tab, which contains actual 2023 sales data for ustekinumab sourced from IQVIA.

b. Penetration by Biosimilars – The forecast estimates the share of units that biosimilars are likely to capture of total ustekinumab sales, and how quickly biosimilars are likely to capture that share (i.e., presented as a month-by-month analysis). The rate that biosimilars are expected to capture share of ustekinumab is observable in tab "Forecast Usteki Year 1" at cells A21 to Z49. Those cells refer to

other tabs, which contain actual sales data for a different drug, adalimumab, sourced from IQVIA (tabs "Analog MA", "Analog per months" and "Analog ADA BC-NB-QC-ALB"). Using the rate of biosimilar penetration for adalimumab (whose brand name is Humira) is appropriate because there are a number of important commercial similarities between Humira / adalimumab and Stelara / ustekinumab, including that both are biologic drugs, both were sold in brand name versions by multinational innovative drug companies that aggressively defend their share of sales, both were high cost products used for the treatment of similar diseases (and so the set of prescribing physicians is similar), both were administered using prefilled syringes subcutaneously and both were subject to new competition from biosimilars. In my view, given those similarities, the most objective and reliable way of estimating the rate that biosimilars are likely to capture share of ustekinumab is by analyzing the rate that biosimilars captured share of adalimumab.

i. I understand that Johnson & Johnson's Chief Financial Officer made public comments to analysts and shareholders that the penetration by biosimilars for Stelara was expected to most resemble the penetration by biosimilars for Humira. In particular, he said that, "In relation to 2025, one question we often get is what the step down of STELARA sales will be due to the biosimilar entry in Europe of 2024 as well as the U.S. at the beginning of 2025. When modeling the impact, we see the Humira erosion curve as a relatively good proxy, with the assumption that STELARA's erosion could be slightly less steep in the first year post biosimilar launch. I will caveat, strongly caveat that there are many dynamics at play, which could result in

a slightly different curve." I attach as Exhibit "F7" a transcript of the remarks of Joseph Wolk, Johnson & Johnson's Executive Vice President and Chief Financial Officer of December 5, 2023. Mr. Wolk also explained in earlier comments to analysts and shareholders regarding the loss of exclusivity for Stelara, that: "In terms of our planning, we are expecting – despite learning a lot over the last few years with REMICADE, we're expecting a steeper erosion curve than what was experienced there because this is a self-administered subcutaneous product." I attach as Exhibit "F8" a transcript of the remarks of Joseph Wolk, Johnson & Johnson's Executive Vice President and Chief Financial Officer of April 18, 2023.

c. Taking Account of Biosimilar Competitors – The demand forecast takes account of the presence of other suppliers of ustekinumab biosimilars and likely future entry; see "Forecast Usteki Year 1" at cells A53 to N53. In particular, the demand forecasts that by the end of the first year of sales, there will be [redacted] suppliers of ustekinumab biosimilar drugs in Canada. This is one of the ways that the demand forecast is conservative; it assumes that BioJAMP's sales will be lower because BioJAMP's rivals will capture a significant portion of demand for ustekinumab biosimilars.

d. Forecast Sales Volumes and Revenues by BioJAMP – Using a series of inputs, including the total ustekinumab sales forecast and the anticipated penetration rate by biosimilars, among other things, the demand forecast estimates the volume of sales that BioJAMP can expect to generate in ustekinumab on a month-by-month basis in the first year; see "Forecast Usteki Year 1" at cells C74 to P77. The demand

forecast then requires that the user input assumed prices for different formats of Jamteki; see "Forecast Usteki Year 1" at cells A80 to C80, which presume that Jamteki will be sold at a [redacted]% discount to the price of Stelara [redacted] The forecast then multiplies JAMP's forecast sales volumes by its assumed price for Jamteki to generate estimates of monthly revenue; see "Forecast Usteki Year 1" at cells A81 to P97. As is observable in cells G93 to G97, in months two to four following its launch (i.e., the first quarter of commercial sales), JAMP estimated that Jamteki would generate sales of approximately $[redacted]. As is observable on tab "Forecast Usteki Year 2" at cells C92 to H97, in the second year after its launch JAMP estimated that Jamteki would generate sales of approximately $[redacted] per quarter.

e. [redacted]

22. Prior to the launch of Jamteki, BioJAMP also prepared a detailed profit and loss statement for Jamteki. I supervised the preparation of that statement, which is attached as Exhibit "F9". That statement's estimate of revenues was obtained from the demand forecast. The statement also sets out a forecast of direct costs for the sale of Jamteki, including different types of sales incentives, the cost of acquiring finished Jamteki, the cost of insurance and other costs (at cells C20 to D42). These estimates are detailed and match certain of the assumptions in the demand forecast (e.g., the percentage of sales likely to be made between different customer segments). The statement also sets out a forecast of the portion of SG&A costs of BioJAMP that are allocated to Jamteki (C47 to D72). As the statement explains at cells C75 and D75, [redacted]

23. These modest projected profit levels mean that if BioJAMP's demand forecast is inaccurate – for example, because a certain customer segment is not open to competition by BioJAMP due to Janssen's conduct – then BioJAMP's incentive to continue marketing Jamteki is diminished significantly (and may be eliminated).

V. BIOJAMP'S MARKETING OF JAMTEKI

24. Using its dedicated personnel, BioJAMP has made extensive marketing efforts to support adoption and sales of Jamteki.

25. For example, BioJAMP sales personnel have attempted to meet with physicians, to describe the safety and efficacy of Jamteki, to describe the effectiveness and ease of use of

JAMP Care, and to describe the benefits to public drug plans of the utilization of a lower cost biosimilar.

26. By further example, BioJAMP has commissioned an independent consultancy to study the financial impact for public drug plans and private insurers of treating different types of patients with Jamteki rather than Stelara. Attached to this affidavit as Exhibit "F10" is one such report, which concludes that adding Jamteki "to the private payer drug formularies for the treatment of patients with [psoriasis] leads to considerable savings, due to the list price of Jamteki™ being 37.5% less than the listed price of Stelara® in Ontario. As such, the [budget impact analysis model] predicts that the reimbursement of Jamteki™ [pre-filled syringe] by private drug plans would results in savings of approximately… $25.5M over the 3-year projection period." BioJAMP presented these types of reports to private insurers, in the hope of Jamteki being listed on their formularies. Attached to this affidavit as Exhibit "F11" is another such report, which concludes that adding Jamteki to the Ontario Drug Benefit Formulary "for the treatment of patients with [psoriasis] leads to substantial savings, due to the list price of Jamteki™ being 37.5% less than the listed price of Stelara® in ON. As such, the budget impact analysis predicts that the reimbursement of Jamteki™ [pre-filled syringe] by ODB Program would results in savings … $100,951,222 over the three-year projection period." BioJAMP presented these types of reports to public drug plans, in the hope of Jamteki being listed on their formularies.

VI. JANSSEN'S COMMUNICATIONS WITH PRESCRIBERS, INSURERS AND PATIENTS REGARDING STELARA AND USTEKINUMAB BIOSIMILARS, AND OTHER CONDUCT

a. Written and Unwritten Communications with Physicians

27. Attached to this affidavit as Exhibit "F12" is a copy of a letter sent by Janssen to certain physicians whose patients are enrolled in Janssen's BioAdvance patient support program ("**Targeted Physicians**"). This letter, sent May 1, 2024 (the day after the Ontario Ministry of Health ("**OMH**") issued a notice requiring that certain patients be prescribed a ustekinumab biosimilar rather than Stelara (which is described in the affidavit of Sukhad Juneja)), states that:

> *Janssen will be offering patients who are prescribed STELARA® and are impacted by the Ontario biosimilar initiative an opportunity to remain or be enrolled in BioAdvance®.*
> - *Newly prescribed STELARA® patients who do not have public or private STELARA® coverage will have the option to receive a ustekinumab biosimilar in the BioAdvance® program.*
> - *More information will be made available in the coming weeks.*
>
> *I will reach out to you…*

28. Attached to this affidavit as Exhibit "F13", is a forwarded email originally sent on May 7, 2024 by Andy Williams (Vice President, Immunology – Janssen Canada) to Targeted Physicians. After summarizing the changes to the OMH's reimbursement policy for Stelara, the email states that:

> *To preserve continuity of care and support physician choice, Janssen will be offering new patients who are prescribed STELARA® and do not have public or private STELARA® coverage an opportunity to be enrolled in BioAdvance® and receive a ustekinumab option.*
>
> *There is nothing you need to do at this time, your BioAdvance® Coordinator will reach out and notify you if there are any changes that need to be made for your patients.*

29. Neither the May 1 letter or the May 7 email identified the biosimilar that would be offered through BioAdvance. I am advised by prescribers who received the letter and email that representatives of Janssen called Targeted Physicians and advised verbally that the "ustekinumab biosimilar" and "ustekinumab option" described in the written communications would be Finlius (another Janssen ustekinumab drug that is described in the affidavit of Sukhad Juneja). Under the OMH's notice, Finlius is not eligible for reimbursement as a biosimilar. Moreover, as described in the affidavit of Sukhad Juneja, Finlius is not a biosimilar.

b. Creating Risks for Physicians to Meet with BioJAMP

30. As described in paragraph 11, I understand that Janssen engages extensively with prescribing physicians in different ways as part of its marketing of Stelara, and frequently requires that those physicians enter into non-disclosure agreements. As described in paragraph 24, as part of the launch of Jamteki, BioJAMP has made extensive marketing efforts, which include efforts by its sales personnel to meet with physicians. Many of those physicians have indicated their unwillingness to engage in any discussions with BioJAMP; in my experience, these types of refusals by physicians to engage with sales personnel about new drugs is very unusual. I have attached to this affidavit as Exhibits "F14", "F15" and "F16" copies of communications received by BioJAMP representatives from physicians cancelling meetings or otherwise refusing to meet with the BioJAMP representatives. All of these communications were received shortly after Janssen's communications described in paragraphs 27 to 29. One such email, found in Exhibit F16, provides one physician's reasoning for their refusal: "Bioadvance says we can hold off on making any switches until October. No switches need to make at this time."

c. Other Communications with Physicians

31. I attach as Exhibit "F17" an email among JAMP employees, reporting on discussions with a physician in [redacted]. The mail explains that "Janssen is telling the physicians NOT to switch their Ustekinumab patients and that worst case they'll provide free goods until they find a solution."

d. Communications with Private Insurers

32. Attached to this affidavit as Exhibit "F18" is Canada Life's prior-authorization form for ustekinumab prescriptions. On page 3, Finlius is listed as one of the ustekinumab drug options. Based on the document's file name, I believe that this form has been in use since approximately March 2024. As described in the affidavit of Sukhad Juneja, Janssen only commenced marketing of Finlius on July 2, 2024.

33. Attached as Exhibit "F19" is a March 2024 report by Alberta Blue Cross describing Finlius at page 11 thus: "if marketed, [Finlius] will be a first of a kind biosimilar launch as this biosimilar is manufactured by the same company that makes the innovator product, Stelara." As described in the affidavit of Sukhad Juneja, Finlius is not a biosimilar.

e. Direct Communications with Patients Through BioAdvance

34. Attached to this affidavit as Exhibit "F20" is an email dated June 25, 2024 from a representative of Janssen's patient support program, BioAdvance, to an enrolled patient. The email describes the patient's treatment history and then instructs the patient, "So you must continue your Stelara as prescribed by" your physician. The physician is not carbon copied on the email.

f. Supply and Pricing of Finlius

35. Attached to this affidavit as Exhibit "F21" is an email dated July 19, 2024 from a BioJAMP employee informing me that Finlius is available (that is, is in stock) [redacted] and is being offered for a wholesale price that is approximately the same as Jamteki.

VII. EFFECT OF JANSSEN'S CONDUCT ON BIOJAMP'S USTEKINUMAB AND OVERALL BUSINESS

36. As described above in paragraph 22, in the first quarter after the launch of Jamteki BioJAMP expected to have generated revenues of approximately $[redacted] from commercial sales. I have attached to this affidavit Exhibit "F22," which shows month-by-month sales of Jamteki since its launch at tab "JAMTEKI". Sales in March 2024 should be ignored; these sales represent wholesalers acquiring initial stock of Jamteki on a one-time basis to hold in inventory (and not demand from prescriptions), and were not included in the demand forecast. [redacted]

Commercial sales of Jamteki (that is, sales that result from actual prescribing by physicians) are observable in cells C12 to E12 and total less than [redacted]. In other words, Jamteki has underperformed its forecast by approximately [redacted] in the first quarter following its launch.

37. The sales of Jamteki in the first quarter following its launch can be contrasted with the sales of Simlandi (BioJAMP's adalimumab biosimilar) over a similar time period. When

BioJAMP launched Simlandi, it had no prior experience marketing biosimilars. In addition, BioJAMP's Simlandi was not the first adalimumab biosimilar to launch; at the launch of Simlandi, there were at least six other biosimilars that had been previously launched. Despite BioJAMP's lack of experience and the significant competition it faced, Simlandi was a success (see Exhibit 22 at tab "SIMLANDI"). In other words, although BioJAMP had less experience and faced more intense competition, Simlandi fared many times better upon its launch than did Jamteki.

38. As described in paragraph 22, above, BioJAMP forecasts that [redacted] [redacted] If Janssen's conduct continues and Jamteki's actual performance continues upon its current trajectory, then the sale of Jamteki will never become profitable and BioJAMP will re-evaluate whether it is viable to continue selling Jamteki.

39. As described in paragraph 17, above, BioJAMP only sells two products (one of which is Jamteki), and Jamteki was forecast to represent [redacted] of BioJAMP's total revenues. The relationship between revenues for each of Jamteki and Simlandi is observable by comparing Exhibit F6 at tab "Forecast Usteki Year 2" at cells C92 to H97 (for Jamteki) and Exhibit F22 at tab "SIMLANDI" at cells K13 to V13 (for Simlandi). If Janssen's conduct continues and Jamteki's actual performance continues upon its current trajectory, then the rationale for operating BioJAMP as a division of JAMP – that is, to participate in new biosimilar markets – will require re-evaluation by JAMP. Among other topics for re-evaluation is, if Janssen's conduct continues, whether BioJAMP should ever again launch a new drug that is biosimilar to a biologic drug offered by Janssen.

40. As described in paragraph 21(c), above, BioJAMP expects that additional competitors will begin selling ustekinumab biosimilars [redacted] If BioJAMP is not successful very soon at winning share (i.e., winning demand for biosimilars to Stelara that is created by the requirements of the provincial drug plans and winning demand from private insurers seeking lower cost options prior to the entry of additional competitors), then BioJAMP's capacity to win share of ustekinumab biosimilar sales will be significantly degraded and the "first mover advantage" that BioJAMP earned by entering on March 1, 2024 will be squandered. If Janssen's conduct continues, BioJAMP's sales of Jamteki are unlikely to ever recover from the loss of such a valuable first mover advantage.

41. I understand from data obtained from IQVIA that Amgen's sales of Wezlana are roughly comparable to JAMP's sales of Jamteki.

VIII. EFFECT OF JANSSEN'S CONDUCT ON PAYERS

42. I believe that Janssen's conduct has depressed sales of Jamteki (and potentially sales of Wezlana as well). As a result, I believe that since March 1 Janssen has sold more units of Stelara than it would have absent its conduct. Those sales of Stelara have occurred at prices that are significantly higher than Jamteki (or Wezlana).

SWORN remotely by Amélie Faubert, stated as being on the ship "Celebrity Ascent", in the Mediterranean Sea, before me at the City of Toronto, in the Province of Ontario, on July 25, 2024, in accordance with O. Reg. 431/20, Administering Oath or Declaration Remotely

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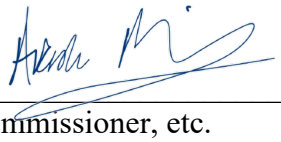

A Commissioner, etc.
Name: **Arash Rouhi**

Name: Amélie Faubert

Exhibit "F1"

This is Exhibit “F1” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

_____

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

The Advisory Board “Laboratory” for Key Message Development

Medical advisory boards are instrumental in helping companies develop key scientific messages that address unmet needs and best communicate new clinical trial findings. They have become an essential resource for pharmaceutical companies in providing thought leadership, subject matter expertise and scientific direction. By their very design, based on a conversational approach, advisory boards provide key opinion leaders a unique forum in which to express their views and provide recommendations on medical interpretation and scientific communication of new drug data.

The role of medical communications professionals in advisory boards

Careful selection of high-level advisors ensures that these boards are composed of key opinion leaders and influencers in their area of specialization.

Agencies can play an important role in the planning and execution of advisory boards:

1. As experienced professionals with a well-developed roster of physician contacts, they have long-term relationships with trusted key opinion leaders. This enables them to identify the most appropriate individuals in the sector or disease area for participation in the advisory board;
2. Expertise to assist the pharmaceutical company in developing an engaging and focused agenda that will ensure that their objectives are achieved and that they gain the best possible insights from the advisors;
3. Long-standing knowledge of the disease area and product to help create engaging advisory board content and workshop materials

designed to promote maximum participation and discussion;
4. Expert facilitation allowing the pharmaceutical company to concentrate on listening to advisor feedback, or to actively participate in a dialogue, rather than having to focus on facilitating;
5. Flawless meeting execution by event planning specialists in order to ensure that advisors have a positive experience, and that the pharmaceutical company obtains the input they are seeking from the meeting.

With each of the above elements, the medical communications agency acts as an extension of the pharmaceutical company’s medical affairs team to enhance their in-house capabilities. Members of medical advisory boards become, in effect, strategic partners with the medical communications agencies that organize – and sometimes facilitate – them, as well as with the pharmaceutical companies. In addition, the fact that boards are comprised of healthcare professionals with no vested interest in pharmaceutical manufacturers’ products ensures unbiased insights and objective messaging ideas.

Strategic, effective use of advisory boards

Advisory boards help drug makers identify ways to communicate key scientific information, such as product benefits or side effects that make a real difference to physicians and/or patients.

A variety of processes can be used for message development. One example is developing “a hierarchy of messaging” in which concepts and phrases are created along thematic lines and then ranked according to importance according to the target audience. Advisors then exchange feedback on these, continually honing them and shuffling their priority. In this scenario, the advisory board acts as a “laboratory” in which ingredients are defined and refined to produce an impactful result to be incorporated into the pharmaceutical company’s scientific communication strategy.

The members’ recommendations are incorporated consistently in publications, scientific communications, educational materials and company communications, even before the time of product launch and beyond. This often takes place over an extended period of time and throughout a product’s life cycle.

Fostering relationships between agencies and pharmaceutical companies

The importance of maintaining close communication and a feedback mechanism between drug companies and medical communications professionals cannot be over-stated. A consistent team of medical writers supporting strategic development of key messages at advisory boards helps provide traction for new products as they enter the marketplace. The agency’s challenge is to create key messaging that is at once scientifically sound and convincing. They act as a mediator between clients and global advisors, ensuring that both sides are heard.

The interface between the medical communications agency and the pharmaceutical company is ongoing. Agencies at the top of their game know their clients well and understand their communication strategies and style. They are proactive in continually seeking scientific updates and suggesting message refinements as new science emerges.

Well-thought-out advisory boards that are customized to client mandates have become foundational to establishing key messages and communication platforms. They help physicians make treatment decisions for their patients, utilize medications appropriately, and help patients understand the world of science.

About Us

The communications professionals at Six Degrees Medical Consulting have over a decade of experience working with top-tier pharmaceutical companies around the world. We provide our clients the services of a consistent team of medical writers who support medical advisory board execution, including key message development, helping them gain traction for new products.

Contact us today to learn more about how we can put our expertise to work for you in developing your key messages or check out our latest blog, “Six Factors to Consider When Designing Advisory Boards”.

SEARCH

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39

Exhibit "F2"

This is Exhibit “F2” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.

Arash Rouhi

Digestive and Liver Disease 56 (2024) 61–69

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Alimentary Tract

Real-world effectiveness and safety of ustekinumab in bio-naive patients with moderate-to-severe Crohn's disease: A Canadian multi-center study

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ABSTRACT

Background: Clinical practice guidelines recommend ustekinumab as a first-line biological treatment option for moderately-to-severely active Crohn's disease (CD). However, there is limited real-world effectiveness and safety data in bio-naïve patients.
Aims: To assess ustekinumab effectiveness and safety in bio-naïve CD patients.
Methods: Medical charts were reviewed retrospectively at seven Canadian centers. The primary outcome was the proportion of patients achieving clinical remission at Month 6 following ustekinumab initiation. Secondary outcomes included clinical, biochemical, and endoscopic response, and remission at Months 4, 6 and 12. Ustekinumab safety was assessed over the one-year follow-up period.
Results: 158 charts were reviewed. Clinical remission was achieved by 50.0% (36/72), 67.7% (105/155), and 73.7% (84/114) of patients at Months 4, 6, and 12, respectively. At these study timepoints, biochemical remission was observed in 65.2% (43/66), 71.6% (63/88), and 73.9% (68/92) of patients. At Months 6 and 12, endoscopic remission was observed in 40.5% (15/37) and 56.3% (27/48) of patients, respectively. Most participants (93.5%; 145/155) persisted on ustekinumab through Month 12. No serious adverse drug reactions were reported.
Conclusion: In this real-world study, ustekinumab presents as an effective first-line biologic for induction and maintenance of remission among bio-naïve Canadian patients with moderately-to-severely active CD.

1. Introduction

Inflammatory bowel disease (IBD) is a spectrum of inflammatory conditions affecting the gastrointestinal (GI) tract that includes Crohn's disease (CD) and ulcerative colitis (UC) [1]. CD is particularly prevalent in Canada where it affects as many as 319 per 100,000 persons [2,3]. As a chronic condition, CD requires lifelong treatment and results in frequent hospitalizations and substantial healthcare resource utilization [4–7].

Therapeutic management is supported by recommendations from the Selecting Therapeutic Targets in IBD initiative (STRIDE-II) [8,9]. Mucosal healing is the preferred long-term treatment goal for CD due to its association with reduced relapse and surgery risk [10]. Short- to mid-term treatment goals are to achieve clinical response and remission, as well as the normalization of relevant biomarker levels. Currently, biologics are recommended by clinical practice guidelines for induction and maintenance of remission in moderately-to-severely active CD [11,12]. Tumour necrosis factor-α (TNF-α) antagonists were the first available biologics and allowed patients resistant to conventional treatments to achieve and sustain clinical remission [13–15]. However, primary non-response and secondary loss of response to TNF-α antagonists have led to the need to identify alternative biologic targets [16–18]. Anti-integrin agents (including vedolizumab) [19], anti-interleukin 12/23p40 agents, and anti-interleukin 23p19 agents (e.g. risankizumab) [20,21] are more recent, alternative, biologics

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1590-8658/

approved or recommended for moderate-to-severely active CD patients [12].

Ustekinumab (Stelara®, Janssen Inc. North York, ON, Canada) is a fully human immunoglobulin G1κ (IgG1κ) monoclonal antibody that binds the p40 subunit of interleukin-12 (IL-12) and IL-23 [22]. Pivotal phase III trials demonstrated the safety and efficacy of ustekinumab in inducing and maintaining clinical remission in patients with CD after 44 weeks of treatment [23]. Recently, long-term extension studies from pivotal trials confirmed a favourable safety profile of ustekinumab for the treatment of moderately-to-severely active CD up to five years after treatment initiation [24,25].

Data obtained in controlled clinical trials may not translate to the real-world setting where there are more diverse patient populations, disease characteristics, and medical practices [26]. Real-world studies offer evidence of treatment effectiveness and safety in this diversity and may identify predictors of treatment response and persistence in routine clinical practice. Since medical practice has evolved towards earlier introduction of biologics in the treatment course, it is important to understand ustekinumab's value as a first-line biologic for CD in the real-world [27]. Most real-world studies have primarily considered ustekinumab therapy in biologic experienced patients [28–33]. The aim of the Joint Canadian Ustekinumab Real-world Effectiveness and Safety (JUSTify) study was to assess the real-world effectiveness and safety of ustekinumab for bio-naïve moderately-to-severely active CD in Canada.

2. Materials and methods

2.1. Study design

JUSTify was a retrospective, multicenter, cohort study of the real-world effectiveness and safety of ustekinumab in bio-naïve patients with moderately-to-severely active CD. Study data were collected from medical charts in seven gastroenterology clinics across Canada from December 11th, 2020, to September 30th, 2021.

Retrospective data collection was performed for ustekinumab initiation, Month 4, Month 6, and Month 12. The first follow-up assessment was performed at Month 4 to assess whether there would be a delayed clinical response in real-world ustekinumab treated patients. In the UNITI-1 and −2 trials, 50.5% of the patients who were not in clinical response after the intravenous (IV) ustekinumab induction dose achieved clinical response at week 8 after receiving the first subcutaneous maintenance dose (i.e., week 16 or month 4) [23]. To account for the variability of real-world clinic visits and optimize data completeness, data were collected with defined windows around each timepoint. Baseline data were collected within a window of 183 days (six months) prior to ustekinumab initiation date (Day 0). Data collection windows after ustekinumab initiation were: ±30 days, −30/+61 days, and −121/+61 days for the Months 4, 6 and 12 timepoints, respectively. If more than one visit occurred within a timepoint window, data from the visit closest to the defined evaluation timepoint was used; whereas if two visits were equidistant from the timepoint within a visit window, the latest visit was used. Medical history including diagnosis, comorbidities, and prior treatment were collected from the time of CD diagnosis up to the time of treatment initiation with ustekinumab, as available. Ustekinumab treatment information and adverse drug reactions (ADRs) were collected from ustekinumab initiation up to discontinuation or Month 12, whichever occurred first.

2.2. Study outcomes

The primary outcome was the rate of clinical remission at Month 6 following initiation of ustekinumab. Secondary outcomes included the rate of clinical remission at Months 4 and 12, clinical response, corticosteroid-free remission, and biochemical and endoscopic response and remission at all study-defined timepoints after initiation. Additional descriptive outcomes included concomitant medication use, ustekinumab dosing, ADRs/serious ADRs (sADRs), and stratification of clinical remission and response results by dose optimization status. A patient was considered dose optimized if they had a dose escalation (i.e., maintenance dose >90 mg or maintenance frequency less than eight weeks) or ustekinumab re-induction (i.e., occurrence of at least one IV infusion of ustekinumab following subcutaneous administration of maintenance dose). However, no JUSTify participant had a dose de-escalation during the study period. Exploratory aims were to identify baseline variables associated with clinical remission, clinical response, and ustekinumab persistence.

2.3. Study participants

Patients aged ≥18 years with a confirmed diagnosis of CD at the time of ustekinumab initiation were eligible. Patients were included if they *1.* received at least one IV induction dose of ustekinumab, *2.* had a minimum of six months of follow-up data available from ustekinumab initiation, regardless of ustekinumab discontinuation status, *3.* had a Harvey Bradshaw Index (HBI) [34] score ≥8, or a CD activity index (CDAI) [35] score ≥150, or a physician assessment rating of moderately-to-severely active disease prior to initiating ustekinumab, and *4.* had at least one clinical or endoscopic follow-up between five and seven months after initiating ustekinumab. Patients were excluded if they received ustekinumab for any indication outside of CD or received any other biologic therapy (TNF-α antagonists, IL-17/IL-23 inhibitors, mucosal addressing cell adhesion molecule 1 [MadCAM-1] inhibitors, and integrin inhibitors) before the initiation of ustekinumab. Additionally, patients were excluded if they received ustekinumab outside of routine medical care (e.g., prior to the drug's marketing authorization). Sites were asked to screen all patients who initiated ustekinumab during the selection period for eligibility. During study monitoring, physicians confirmed eligibility of any patients with HBI <8. Invariably, physician assessment was relied upon to determine eligibility.

Prior to data collection, a waiver of consent was obtained from the research ethics boards at each participating site for the use of routinely collected, anonymized, medical record data in accordance with local requirements. All research procedures complied with the ethical principles of the Declaration of Helsinki.

2.4. Definitions

Clinical remission was defined, in order of evaluation, as CDAI <150, HBI <5, or a physician assessment of "normal or inactive disease" depending on availability. If remission was achieved and the patient was not reported to be using corticosteroids at the time of the disease activity evaluation, the remission was deemed to be 'corticosteroid-free'. Clinical response occurred if a patient experienced *1.* a 70-point decrease in CDAI that also accounted for ≥25% reduction from baseline CDAI or, *2.* an HBI reduction of ≥3 points from baseline or, if both CDAI and HBI were missing, *3.* an improvement from the baseline physician assessment of disease activity. CDAI scores were available in the charts for less than 5 patients. For the majority of patients, disease activity was assessed using HBI scores and physician assessments. Please refer to Supplementary Table 1 for the number of patients that received each assessment. Biochemical remission was achieved if a patient had C-reactive protein (CRP) serum levels <5 mg/L or fecal calprotectin (Fcal) levels <250 µg/g.

Endoscopic remission was defined as a simple endoscopic score for CD (SES-CD) ≤2 or a physician assessment of endoscopic findings of "normal or inactive disease". Endoscopic response was defined as a SES-CD score of 0–2, a decrease of ≥50% from SES-CD score at baseline, or improvement based on the physician rating of endoscopic findings as compared to baseline evaluation.

For the analyses of ustekinumab persistence, discontinuation at any time prior to the study end was considered an 'event'. The date of discontinuation was used to calculate time-to-event. Patients with no record of ustekinumab discontinuation were censored. The date of last ustekinumab administration or date of last physician assessment of disease activity, whichever occurred last, served as the time of censoring.

2.5. Statistical analysis

The statistical analysis was primarily descriptive in nature. All the endpoints analysed via proportions were calculated by a division between participants satisfying the endpoint criteria and the denominator consisting of the participants with available data for the endpoint (i.e., as observed analyses). For effectiveness outcomes, sensitivity analyses were performed for clinical remission at Month 6 and Month 12 following ustekinumab initiation using non-responder imputation (i.e., patients with missing observations were considered as non-responders) and last observation carried forward (i.e., the last observed value was assumed to be maintained at the following timepoint if the patient had a missing evaluation; LOCF). LOCF analyses excluded patients missing all follow-up assessments or with a baseline assessment only.

Where the 95% confidence interval (CI) associated with an endpoint is reported, the CI was derived based on a binomial exact method by Clopper and Pearson [36]. For the endpoints that were based on change from baseline, the calculation was performed only for those participants with both data points available. Descriptive statistics include mean and standard deviation (SD) or median and interquartile range (IQR), where appropriate, for continuous variables or number and percentage in each category for categorical variables.

Regression analysis identified variables correlated with each outcome of interest – persistence, clinical remission or clinical response at Month 6. Please refer to the Supplementary Methods for modeling details.

All statistical tests were two-sided and no adjustment for multiple testing was performed. A p value ≤0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

2.6. Data availability statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access [YODA] Project site at http://yoda.yale.edu.

3. Results

3.1. Patient demographic and clinical characteristics

Baseline demographic and clinical characteristics are summarized in Table 1. In total,158 eligible patient charts were reviewed at seven Canadian sites. Study participants were on average 42.3 years old (SD 16.6) at ustekinumab initiation and more frequently female (53.8%). Mean age at CD diagnosis was 33.7 years (SD 17.0), and mean disease duration was 8.6 years (SD 12.1). However, some patients had an unusually long disease duration prior to initiating their first biologic (range 0–55 years) which skewed this observation.

Table 1
Baseline demographic and clinical characteristics.

Characteristics	Study Population (N = 158)
Weight (kg), mean (SD)[1]	76.2 (19.3)
Smoking status (n = 150)	
Current, n (%)	31 (20.7)
Former, n (%)	16 (10.7)
Never, n (%)	103 (68.7)
CD duration (years), median (IQR)	2 (1,12)
HBI score, mean (SD)[2]	6.9 (3.9)
Disease location (n = 157)	
L1 Terminal ileum, n (%)	56 (35.7)
L2 Colon, n (%)	30 (19.1)
L3 Ileocolon, n (%)	54 (34.4)
L4 Upper GI, n (%)	9 (5.7)
Other, n (%)[3]	8 (5.1)
Disease behavior (n = 156)	
Non-stricturing, non-penetrating, n (%)	97 (62.2)
Stricturing, n (%)	39 (25.0)
Penetrating, n (%)	9 (5.8)
Both stricturing and penetrating, n (%)	11 (7.1)
Active perianal involvement (n = 157), n (%)	10 (6.4)
Biochemical Markers[4]	
CRP (mg/L), mean (SD)	14.0 (22.3)
Fcal (µg/g), mean (SD)	691.0 (953.8)
Albumin (g/L), mean (SD)	40.0 (5.5)
Any extraintestinal manifestations	
No, n (%)	143 (90.5)
Yes, n (%)	15 (9.5)

CRP: C reactive protein; Fcal: Faecal calprotectin; SD: Standard Deviation; GI: Gastrointestinal.
[1] 148 patients had baseline weight information.
[2] 103 patients had baseline HBI score information.
[3] Includes L1 + L4 terminal ileum + Upper GI, L2 + L4 Colon + Upper GI, L3 + L4 Ileocolon + Upper GI and Ileal pouch.
[4] 125 patients had baseline CRP information, 37 had baseline Fcal information, and 73 had baseline albumin information.

At ustekinumab initiation, all patients had a confirmed diagnosis of moderately-to-severely active CD based on CDAI, HBI, or physician assessment. Based on physician assessment 28.2% (44/156) of patients had severe disease and 71.8% (112/156) had moderate disease.

3.2. CD therapy before ustekinumab initiation

At baseline, 16.5% (26/158) of patients had no documented use of a prior CD medication. The most common prior medications were corticosteroids (62.7%; 99/158), aminosalicylic acids (5-ASA; 25.3%; 40/158), azathioprine (22.8%; 36/158), and methotrexate (17.7%; 28/158).

3.3. CD therapy at and after ustekinumab initiation

Concomitant medications at ustekinumab initiation are described in Table 2.

3.4. Primary outcome

The proportion of patients achieving clinical remission are provided in Fig. 1**A**.

3.5. Secondary outcomes

3.5.1. Corticosteroid-free remission, biochemical remission, endoscopic remission, and clinical and endoscopic response

The proportion of patients achieving corticosteroid-free remission, biochemical remission, and endoscopic remission among those with corresponding assessments are provided in Fig. 1**B,C,D**. Evaluation of endoscopic remission and response was not feasible

Table 2
Concomitant Crohn's disease medications.

	Baseline (N = 158)	Month 4 (N = 158)	Month 6 (N = 158)	Month 12 (N = 155)
Concomitant Medication Categories				
No concomitant medications, n (%)[1]	106 (67.1)	118 (74.7)	122 (77.2)	125 (80.6)
Steroid use, n (%)[2]	30 (19.0)	21 (13.2)	16 (10.1)	13 (8.4)
Immunomodulator use, n (%)[3]	20 (12.7)	18 (11.4)	18 (11.4)	16 (10.3)
Other[4]	6 (3.8)	6 (3.8)	7 (4.4)	6 (3.9)

CI: Confidence Interval; SD: Standard Deviation.
[1] Less than six patients reported concomitant use of 5-ASA, CD-specific antibiotics, or narcotic pain medication at any given timepoint.
[2] Includes budesonide (entocort), budesonide MMX (e.g., cortiment), and oral corticosteroids.
[3] Includes azathioprine, methotrexate, and 6-mercaptopurine.
[4] Includes 5-ASA, CD-specific antibiotics, and narcotic pain medication.

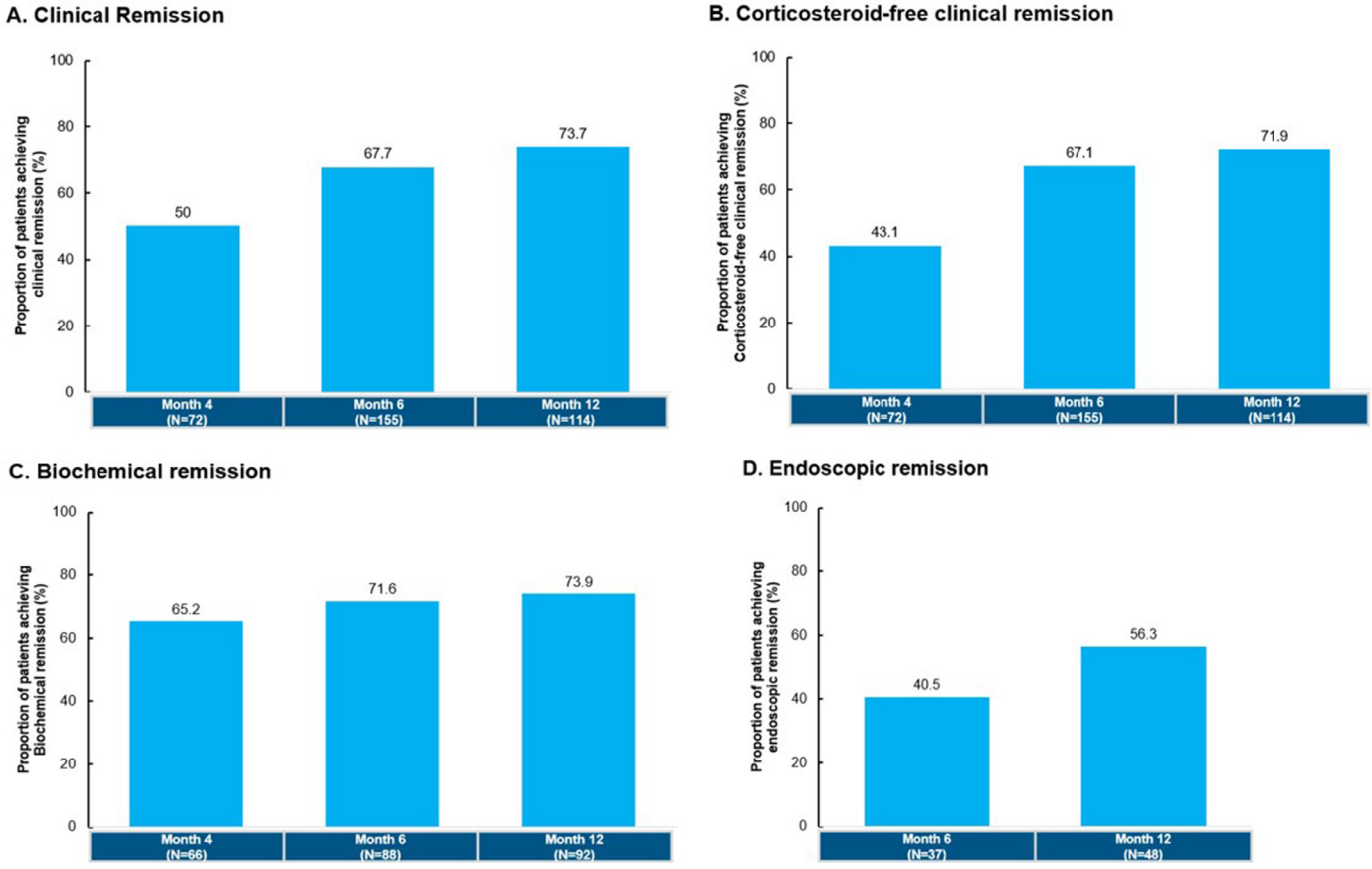

Fig. 1. Clinical remission, corticosteroid-free remission, Biochemical Remission and endoscopic remission following ustekinumab initiation
Clinical remission was achieved if a patient had a reported CDAI <150, HBI <5 (if CDAI not available), or a physician assessment of "normal or inactive disease". If the patient did not use corticosteroids, the remission was deemed to be 'corticosteroid-free'. Endoscopic remission was achieved if a patient had a simple endoscopic score for CD (SES-CD) of 0–2 or had a physician assessment of endoscopic findings of "normal or inactive disease". Biochemical remission was achieved if a patient had C-reactive protein (CRP) <5 mg/L or fecal calprotectin (Fcal) <250 µg/g.
Note: Denominators vary at each study timepoint because analyses were performed as observed.

at Month 4 due to the small proportion of patients undergoing assessment at this timepoint.

Among patients with clinical assessments, 62.9% (44/70; 95% CI [50.5,74.1]), 69.9% (107/153; 95% CI [62.0,77.1]), and 72.1% (80/111; 95% CI [62.8,80.2]) of patients achieved clinical response at Months 4, 6, and 12 post-ustekinumab initiation, respectively. Endoscopic response was achieved by 72.7% (16/22; 95% CI [49.8, 89.3]) and 70.0% (21/30; 95% CI [50.6, 85.3]) of patients at Months 6 and 12, respectively.

3.5.2. Clinical remission and dose optimization

Stratification of clinical remission by ustekinumab dose optimization was not feasible at Month 4 due to the small proportion of patients undergoing dose optimization at this timepoint. Patients who remained on ustekinumab maintenance doses of 90 mg Q8W generally had higher clinical remission rates and corticosteroid-free clinical remission rates than those who underwent dose optimization at Month 6 and at Month 12 (Fig. 2).

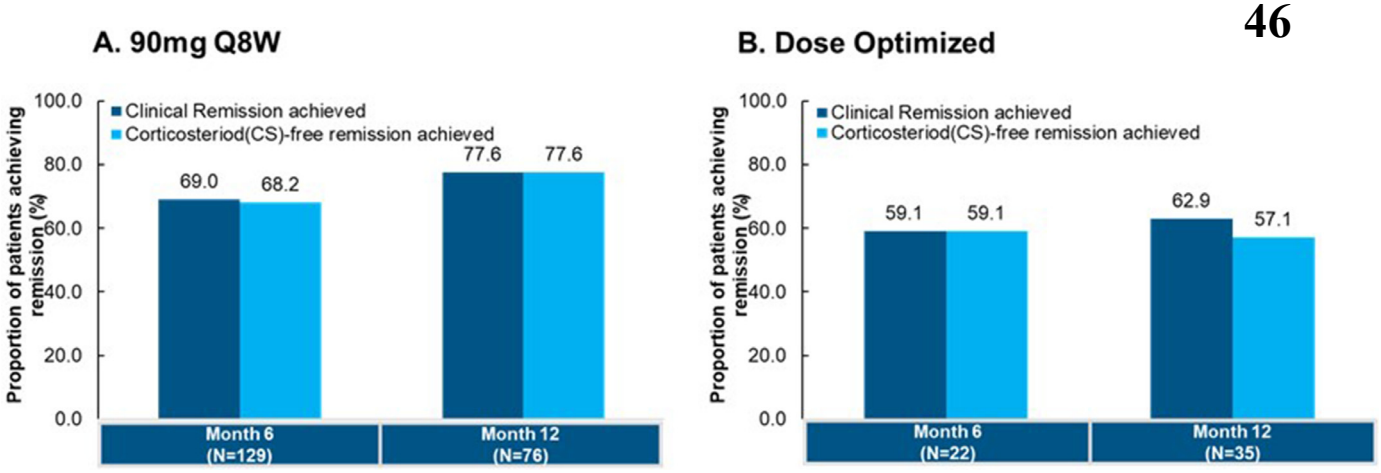

Fig. 2. Clinical remission and corticosteroid-free remission among patients on ustekinumab 90 mg Q8W or who were dose optimized following ustekinumab initiation
Clinical remission was achieved if a patient had a reported CDAI <150, HBI <5 (if CDAI not available), or a physician assessment of "normal or inactive disease". If the patient did not use corticosteroids, the remission was deemed to be 'corticosteroid-free'. A patient was dose optimized if they had a dose escalation (i.e., maintenance dose >90 mg or maintenance frequency less than eight weeks), dose de-escalation, or ustekinumab re-induction (i.e., occurrence of at least one IV of ustekinumab following subcutaneous administration of maintenance dose).
Note: Denominators vary at each study timepoint because analyses were performed as observed.

3.6. Sensitivity analyses of ustekinumab effectiveness

3.6.1. Non-responder imputation analyses

Ustekinumab effectiveness endpoints could not be assessed for all patients at each timepoint because of missing measures within the pre-specified data collection windows. When assuming patients missing an evaluation were non-responders to ustekinumab, 66.5% (105/158; 95% CI [58.5 73.8]) of patients achieved clinical remission at Month 6, and 53.2% (84/158; 95% CI [45.1 61.1]) at Month 12. Similarly, 65.8% (104/158; 95% CI [57.9, 73.2]) of patients achieved corticosteroid-free remission at Month 6 and 51.9% (82/158; 95% CI [43.8, 59.9]) at Month 12.

3.6.2. Last observation carried forward analyses

When assuming patients with missing evaluations maintained the status observed at their previous visit, 68.2% (107/157; 95% CI [60.3, 75.4]) of patients achieved clinical remission at Month 6 and 75.2% (118/157; 95% CI [28.2, 43.7]) at Month 12. Corticosteroid-free remission was achieved by 67.5% (106/157; 95% CI [596.6, 74.8]) of patients at Month 6 and 73.9% (116/157; 95% CI [66.3, 80.6]) at Month 12.

3.7. Ustekinumab persistence

In the study population, 96.2% (152/158) of patients persisted on ustekinumab at Month 6 and 93.5% (145/155) at Month 12 (Fig. 3).

3.8. Safety outcomes

In the first year following treatment initiation, eight ADRs including pyrexia, dizziness, headache, dyspnea, acne, alopecia, and pruritus were observed. Most ADRs (87.5%; 7/8) did not result in any action being taken with ustekinumab and 87.5% (7/8) were resolved by the end of the first year post-initiation. No sADRs were observed.

3.9. Associations of baseline variables with clinical remission, response, and persistence

Univariable models assessed the association of baseline variables with clinical remission and response at Month 6 following ustekinumab initiation. Sex, CD duration, and HBI score met criteria for inclusion in multivariable models, but none were significantly associated with clinical remission at Month 6 (Supplementary Table 2). In univariable models, higher baseline HBI scores were associated with higher likelihood of achieving clinical response at Month 6 (odds ratio [OR] = 2.40; 95% CI = [1.60, 3.59]; *p*-value <0.01 Supplementary Table 3). To ensure that the largest available sample was used for multivariable modeling, baseline HBI score was not used as one of the predictors. In the multivariable logistic regression models, female patients tended to have 45% lower chance than males of achieving clinical remission at Month 6 (OR = 0.55; 95% CI = [0.27, 1.09]; *p*-value = 0.09; Supplementary Table 4).

Given the high degree of persistence in the study cohort, only univariable Cox regression models assessed the association of baseline variables with ustekinumab discontinuation. Older age at CD diagnosis, female sex, longer CD duration, a physician assessment of severe disease at ustekinumab initiation, and higher baseline CRP levels were associated with increased risk of ustekinumab discontinuation within one year of treatment initiation (Table 3).

4. Discussion

JUSTify assessed the real-world effectiveness and safety of ustekinumab in bio-naïve moderately-to-severely active CD patients in Canada. Two-thirds (67.7%) of patients achieved the primary outcome of clinical remission by Month 6 following ustekinumab initiation. By Month 12, 73.7% of patients were in clinical remission and 93.5% of patients persisted on ustekinumab therapy. Ustekinumab had an excellent safety profile with no reported sADRs over the 12-month observation period.

STRIDE-II refined the clinically relevant treatment targets originally set by the STRIDE initiative and identified endoscopic healing as an important long-term goal of CD management [8]. Clinical response and remission, along with normalization of CRP and Fcal levels, are short- to mid-term goals which, if not met, may lead to a reconsideration of the treatment used [9]. The JUSTify study assessed effectiveness in the context of current treatment goals for CD.

Endoscopic healing is viewed as the preferred treatment target for CD due to its association with reduced relapse and CD-related surgery risk [10,37,38]. Among JUSTify patients with endo-

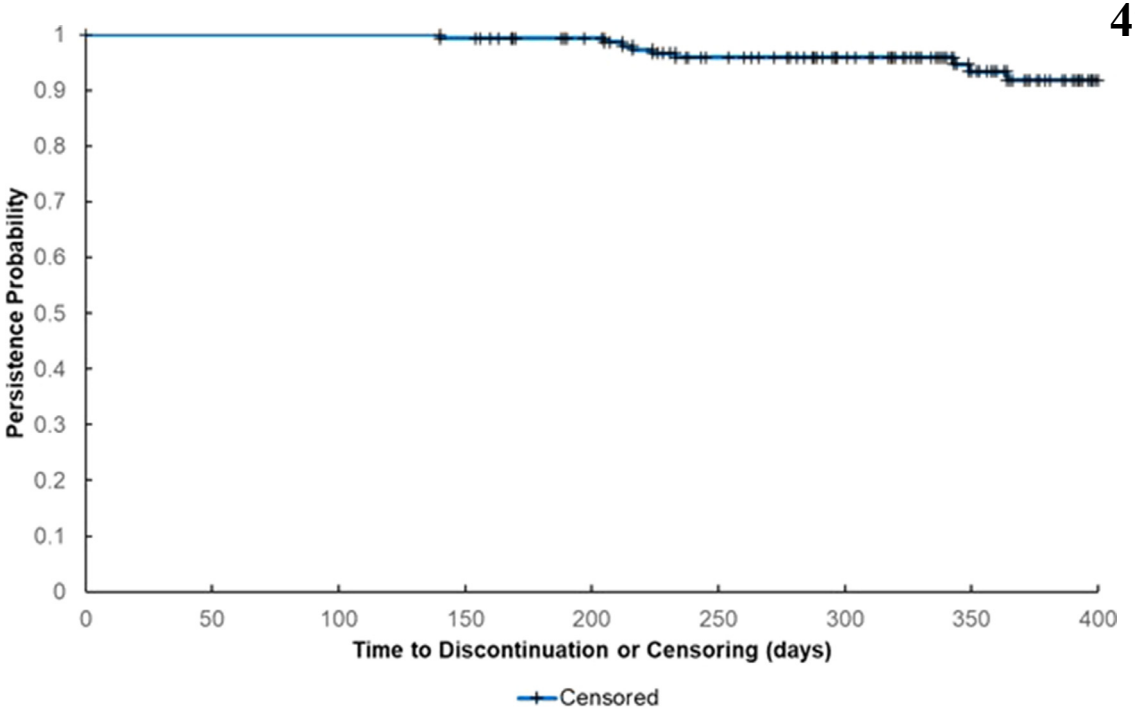

Fig. 3. Kaplan–Meier analysis of real-world ustekinumab persistence.

Table 3
Univariable Cox regression models of association with ustekinumab discontinuation by month 12.

Predictors	HR [95%, CI]	P-value
Age at diagnosis of Crohn's disease (years)	1.25 [0.92, 2.28]**	0.01
Sex, Female vs. Male	3.57 [0.98, 18.96]	0.03
Crohn's disease duration at baseline (years)	1.01 [0.95, 1.05]**	0.01
Physician assessment at baseline (DA),[1] Severe vs. Moderate disease	3.01 [0.88, 10.26]	0.05
CRP at baseline (mg/L)[2]	1.02 [1.00, 1.03]	<0.01

CI: Confidence Interval; CRP: C reactive protein; HR: Hazard Ratio; DA: Disease Activity.
[1] Five patients with missing or unknown physician assessment were omitted from the model.
[2] 33 patients with missing CRP were omitted from the model.
** Hazard ratio presented for each year increase.

scopic assessments, endoscopic remission was achieved by 40.5% and 56.3% of patients at Months 6 and 12 following ustekinumab initiation. This was generally greater than endoscopic remission rates observed in a sub-analysis of the UNITI trials [39]. In previous real-world reports, one-year endoscopic remission rates varied from 15.0 to 39.0% [28,31,40-44]. These differences may be partly explained by the inclusion of biologic-experienced patients. Therefore, JUSTify results may suggest ustekinumab is more likely to achieve endoscopic remission among real-world, bio-naïve patients than those with prior biologic treatment experience.

Common symptoms of CD include abdominal pain, weight loss, and fatigue, which impact patients' quality of life. Thus, short-term resolution of symptoms is critical to alleviate the impact of the disease with daily activities. Ustekinumab is recommended for patients with moderate-to-severe luminal CD who have failed or who are intolerant to conventional therapies (e.g. immunosuppressors) or anti-TNF [12]. However, findings from other studies show that the efficacy of ustekinumab may be the same or higher in bio-naive patients than in bio-experienced CD patients [23,45,46]. In JUSTify, approximately 69.9% and 67.7% of bio-naïve patients achieved clinical response or remission, respectively, at Month 6. This level of clinical effectiveness was higher than those observed in European studies where six-month effectiveness varied from 32% [40] to the mid-50% range [29,31,47]. However, these studies primarily included biologic-experienced patients. A subgroup analysis of the ENEIDA registry suggested ustekinumab remission rates decreased with increasing experience to TNF-α and integrin antagonists. Among bio-naïve subgroups, the proportion of patients achieving clinical remission were similar to or higher than those observed in JUSTify [31]. Notably, ustekinumab response and remission rates in JUSTify were sustained through the end of the first year of treatment as similarly reported in other studies [48,49].

Although anti-TNF agents are recommended as the first-line therapy for moderate-to-severe CD, primary nonresponse has been observed in 10–40% of patients and secondary loss of response in 23–46% of patients at 12 months [1,50]. A recent meta-analysis of observational studies suggests medium- (6 months) and long-term (12 months) loss of response of ustekinumab may be more favorable than that observed for anti-TNFs at 18% [51]. In JUSTify, clinical and corticosteroid-free remission were also observed in larger proportions of patients who did not have dose optimization than among those who did. This may result from patients requiring dose optimization experiencing either loss of or inadequate response. Nonetheless, remission rates among dose optimized patients in JUSTify were consistent with other real-world reports [48,52].

Short-term resolution of CD symptoms is important to patients but may occur despite persisting inflammation. To better evaluate

treatment effectiveness, it is important to assess symptomatic relief concomitantly with relevant inflammatory biomarkers such as CRP or FCal. In JUSTify, 71.6% of patients with biochemical marker assessments had normalized CRP *or* FCal levels at Month 6. This was higher than in a previous real-world report where 24.6% of patients achieved normalization of CRP *and* FCal six months following ustekinumab initiation [29]. Although biochemical remission definitions vary across studies, several real-world investigations confirm CRP and FCal levels decrease within one year of ustekinumab initiation [31,40,47]. These declines may reflect immediate effects of ustekinumab on inflammatory activity but may also have predictive value for risk of future relapse. Overall, real-world evidence from JUSTify and other studies suggests ustekinumab treatment results in a time-dependent normalization of biochemical markers, in bio-naïve CD patients.

Persistence on therapy is recognized as a surrogate of real-world patient outcomes. In JUSTify, 93.5% of enrolled patients remained on treatment by Month 12 compared to previous real-world studies which report persistence to be at or around 80% [29,30]. However, these studies considered large proportions of patients with prior exposure to biologics. Reports from the ICC registry and the PANIC cohort suggest ustekinumab persistence is highest among patients with little or no prior exposure to biologic therapies. Importantly, data from the PANIC cohort indicates ustekinumab persistence over two years is higher than that observed with TNF-α antagonists. The TNF-α antagonist persistence rates observed in PANIC are similar to those from a recent real-world investigation including Canadian bio-naïve moderately-to-severely active CD patients [53]. Therefore, JUSTify provides additional evidence that persistence on ustekinumab may be highest among bio-naïve patients. Consequently, ustekinumab persistence may surpass what is typically observed within the first year of TNF-α antagonist treatment for bio-naïve CD patients.

In real-world studies, ADRs are generally rare, with the ADR rate in JUSTify lower than similar studies [29,31,40,48]. Furthermore, evidence suggests that ustekinumab treatment may be associated with a relatively lower risk of infection than that observed with anti-TNF agents [54,55]. Overall, real-world evidence studies support ustekinumab as having an excellent safety profile among bio-naïve and bio-experienced CD patients.

Strengths of this study include the first real-world evaluation of ustekinumab effectiveness and safety among a large cohort of bio-naïve moderately-to-severely active CD patients across Canada. The retrospective chart review allowed for data collection of up to one-year following treatment initiation. The limitations inherent to retrospective designs apply to this study, including potential selection bias, accuracy, and availability of data from patient charts, non-standardized follow-up intervals, and generalizability to the larger Canadian moderately-to-severely active CD patient population.

Overall, JUSTify demonstrates the value and supports clinical guidelines that recommend the use of ustekinumab as the first-line biologic for the treatment of patients with moderately-to-severely active CD. The results of this study provide further real-world evidence of ustekinumab effectiveness at inducing and maintaining remission in Canadian bio-naïve CD patients.

Authors' contributions

Talat Bessissow, Tracy S.H. In, Maria Eberg and Kinda Karra contributed to the conception and design of the study. Talat Bessissow, Vipul Jairath, Neeraj Narula and Christopher Ma contributed to the acquisition of the data. Maria Eberg contributed to the analysis of the data. All authors contributed to the interpretation of data for the study. All authors provided critical revision for important intellectual content of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

This study was funded by Janssen Inc. The sponsor was involved in the design, interpretation, and reporting of study results. TB acted as a speaker or advisor for AbbVie, Alimentiv (formerly Robarts Inc.), Amgen, Bristol-Myers-Squibb, Ferring, Gilead, Janssen, Merck, Pentax, Pfizer, Roche, Sandoz, Takeda, Viatris. NN has received honoraria from Janssen, AbbVie, Takeda, Pfizer, Merck, Sandoz, Novartis, and Ferring. CM has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Ferring, Janssen, Takeda, and Pfizer; research support from Ferring, Pfizer. VJ served on advisory boards, consulted or was an investigator for AbbVie, Alimentiv Inc. (formerly Robarts Clinical Trials Inc.), Amgen, Applied Strategic, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, BioJamp. Celgene/BMS, Celltrion, Eli Lilly, Ferring, F. Hoffman-La Roche Ltd., Flagship Pioneering, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Organon (Merck), Landos BioPharma, Mylan, Pandion, Pendopharm, Pfizer, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Topivert, Ventyx Biosciences, and Vividion Therapeutics. VJ acted as a speaker for AbbVie, Ferring, Galapagos, Janssen, Pfizer, and Takeda and is an employee of Western University. KK was full time employees of Janssen Inc. at the time of the study. TI is a full-time employee of Janssen Inc. ME is a full-time employee of IQVIA Solutions Canada Inc. (IQVIA). Janssen Inc. contracted with IQVIA to manage the study.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dld.2023.08.042.

References

[1] Roda G, Chien Ng S, Kotze PG, et al. Crohn's disease. Nat Rev Dis Primers 2020;6(1):22 (In eng). doi:10.1038/s41572-020-0156-2.
[2] Alatab S, Sepanlou SG, Ikuta K, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 2020;5(1):17–30. doi:10.1016/S2468-1253(19)30333-4.
[3] Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet 2017;390(10114):2769–78 (In eng). doi:10.1016/s0140-6736(17)32448-0.
[4] Golovics PA, Lakatos L, Mandel MD, et al. Prevalence and predictors of hospitalization in Crohn's disease in a prospective population-based inception cohort from 2000 to 2012. World J Gastroenterol 2015;21(23):7272–80 (In eng). doi:10.3748/wjg.v21.i23.7272.
[5] Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. Gastroenterology 2008;135(6):1907–13 (In eng). doi:10.1053/j.gastro.2008.09.012.

[6] Kappelman MD, Porter CQ, Galanko JA, et al. Utilization of healthcare resources by U.S. children and adults with inflammatory bowel disease. Inflamm Bowel Dis 2011;17(1):62–8 (In eng). doi:10.1002/ibd.21371.
[7] Kuenzig ME, Benchimol EI, Lee L, et al. The impact of inflammatory bowel disease in Canada 2018: direct costs and health services utilization. J Can Assoc Gastroenterol 2019;2(Suppl 1):S17–33 (In eng). doi:10.1093/jcag/gwy055.
[8] Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting therapeutic targets in inflammatory bowel disease (STRIDE): determining therapeutic goals for treat-to-target. Am J Gastroenterol 2015;110(9):1324–38 (In eng). doi:10.1038/ajg.2015.233.
[9] Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an Update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the international organization for the study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterology 2021;160(5):1570–83. doi:10.1053/j.gastro.2020.12.031.
[10] Neurath MF, Travis SP. Mucosal healing in inflammatory bowel diseases: a systematic review. GutGut 2012;61(11):1619–35. doi:10.1136/gutjnl-2012-302830.
[11] Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing crohn's disease. Gastroenterology 2021;160(7):2496–508 (In eng). doi:10.1053/j.gastro.2021.04.022.
[12] Panaccione R, Steinhart AH, Bressler B, et al. Canadian association of gastroenterology clinical practice guideline for the management of luminal Crohn's disease. Clin Gastroenterol Hepatol 2019;17(9):1680–713 (In eng).. doi:10.1016/j.cgh.2019.02.043.
[13] Stidham RW, Lee TC, Higgins PD, et al. Systematic review with network meta-analysis: the efficacy of anti-TNF agents for the treatment of Crohn's disease. Aliment Pharmacol Ther 2014;39(12):1349–62 (In eng).. doi:10.1111/apt.12749.
[14] Ford AC, Sandborn WJ, Khan KJ, Hanauer SB, Talley NJ, Moayyedi P. Efficacy of biological therapies in inflammatory bowel disease: systematic review and meta-analysis. Am J Gastroenterol 2011;106(4):644–59 quiz 660. (In eng). doi:10.1038/ajg.2011.73.
[15] Cholapranee A, Hazlewood GS, Kaplan GG, Peyrin-Biroulet L, Ananthakrishnan AN. Systematic review with meta-analysis: comparative efficacy of biologics for induction and maintenance of mucosal healing in Crohn's disease and ulcerative colitis controlled trials. Aliment Pharmacol Ther 2017;45(10):1291–302 (In eng). doi:10.1111/apt.14030.
[16] Adegbola SO, Sahnan K, Warusavitarne J, Hart A, Tozer P. Anti-TNF therapy in Crohn's disease. Int J Mol Sci 2018;19(8) (In eng). doi:10.3390/ijms19082244.
[17] Billioud V, Sandborn WJ, Peyrin-Biroulet L. Loss of response and need for adalimumab dose intensification in Crohn's disease: a systematic review. Am J Gastroenterol 2011;106(4):674–84 (In eng). doi:10.1038/ajg.2011.60.
[18] Papamichael K, Gils A, Rutgeerts P, et al. Role for therapeutic drug monitoring during induction therapy with TNF antagonists in IBD: evolution in the definition and management of primary nonresponse. Inflamm Bowel Dis 2015;21(1):182–97 (In eng). doi:10.1097/mib.0000000000000202.
[19] Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2013;369(8):711–21. doi:10.1056/NEJMoa1215739.
[20] D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. Lancet 2022;399(10340):2015–30. doi:10.1016/S0140-6736(22)00467-6.
[21] Ferrante M, Panaccione R, Baert F, et al. Risankizumab as maintenance therapy for moderately to severely active Crohn's disease: results from the multicentre, randomised, double-blind, placebo-controlled, withdrawal phase 3 FORTIFY maintenance trial. Lancet 2022;399(10340):2031–46. doi:10.1016/S0140-6736(22)00466-4.
[22] USFDA. Janssen Biotech Stelara®(ustekinumab) injection; Prescribing injection. 2016.
[23] Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2016;375(20):1946–60. doi:10.1056/NEJMoa1602773.
[24] Sandborn W, Rebuck R, Wang Y, et al. Five-year efficacy and safety of ustekinumab treatment in Crohn's disease: the IM-UNITI trial. Clin Gastroenterol Hepatol 2021;20. doi:10.1016/j.cgh.2021.02.025.
[25] Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: three-year efficacy, safety, and immunogenicity of ustekinumab treatment of Crohn's disease. J Crohns Colitis 2020;14(1):23–32 (In eng). doi:10.1093/ecco-jcc/jjz110.
[26] Meserve J, Barsky M, Dulai PS. In the absence of head-to-head trials, what do real world studies tell us about the comparative effectiveness of biologics in Crohn's disease. Best Pract Res Clin Gastroenterol 2019;38-39:101619 (In eng). doi:10.1016/j.bpg.2019.05.006.
[27] Sandborn WJ. Current directions in IBD therapy: what goals are feasible with biological modifiers? Gastroenterology 2008;135(5):1442–7 (In eng). doi:10.1053/j.gastro.2008.09.053.
[28] Battat R, Kopylov U, Bessissow T, et al. Association between Ustekinumab trough concentrations and clinical, biomarker, and endoscopic outcomes in patients with Crohn's disease. Clin Gastroenterol Hepatol 2017;15(9):1427–34 e2. (In eng). doi:10.1016/j.cgh.2017.03.032.
[29] Biemans VBC, van der Meulen-de Jong AE, van der Woude CJ, et al. Ustekinumab for Crohn's disease: results of the ICC registry, a nationwide prospective observational cohort study. J Crohns Colitis 2020;14(1):33–45 (In eng). doi:10.1093/ecco-jcc/jjz119.
[30] Kubesch A, Rueter L, Farrag K, et al. Short and long-term effectiveness of ustekinumab in patients with Crohn's disease: real-world data from a German IBD cohort. J Clin Med 2019;8(12) (In eng). doi:10.3390/jcm8122140.
[31] Iborra M, Beltrán B, Fernández-Clotet A, et al. Real-world long-term effectiveness of ustekinumab in Crohn's disease: results from the ENEIDA registry. Aliment Pharmacol Ther 2020;52(6):1017–30 (In eng).. doi:10.1111/apt.15958.
[32] Engel T, Yung DE, Ma C, et al. Effectiveness and safety of Ustekinumab for Crohn's disease; systematic review and pooled analysis of real-world evidence. Dig Liver Dis 2019;51(9):1232–40 (In eng). doi:10.1016/j.dld.2019.05.002.
[33] Parrot L, Dong C, Carbonnel F, Meyer A. Systematic review with meta-analysis: the effectiveness of either ustekinumab or vedolizumab in patients with Crohn's disease refractory to anti-tumour necrosis factor. Aliment Pharmacol Ther 2022;55(4):380–8 (In eng). doi:10.1111/apt.16714.
[34] Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980;1(8167):514 (In eng). doi:10.1016/s0140-6736(80)92767-1.
[35] Vermeire S, Schreiber S, Sandborn WJ, Dubois C, Rutgeerts P. Correlation between the Crohn's disease activity and Harvey-Bradshaw indices in assessing Crohn's disease severity. Clin Gastroenterol Hepatol 2010;8(4):357–63 (In eng). doi:10.1016/j.cgh.2010.01.001.
[36] Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. BiometrikaBiometrika 1934;26(4):404–13. doi:10.2307/2331986.
[37] Thia KT, Sandborn WJ, Harmsen WS, Zinsmeister AR, Loftus EV Jr. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. Gastroenterology 2010;139(4):1147–55 (In eng).. doi:10.1053/j.gastro.2010.06.070.
[38] Frøslie KF, Jahnsen J, Moum BA, Vatn MH. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. Gastroenterology 2007;133(2):412–22 (In eng).. doi:10.1053/j.gastro.2007.05.051.
[39] Rutgeerts P, Gasink C, Chan D, et al. Efficacy of ustekinumab for inducing endoscopic healing in patients with Crohn's disease. Gastroenterology 2018;155(4):1045–58 (In eng).. doi:10.1053/j.gastro.2018.06.035.
[40] Plevris N, Fulforth J, Siakavellas S, et al. Real-world effectiveness and safety of ustekinumab for the treatment of Crohn's disease: the Scottish ustekinumab cohort. J Gastroenterol Hepatol 2021;36(8):2067–75 (In eng).. doi:10.1111/jgh.15390.
[41] Kopylov U, Afif W, Cohen A, et al. Subcutaneous ustekinumab for the treatment of anti-TNF resistant Crohn's disease–the McGill experience. J Crohns Colitis 2014;8(11):1516–22 (In eng).. doi:10.1016/j.crohns.2014.06.005.
[42] Ma C, Fedorak RN, Kaplan GG, et al. Long-term maintenance of clinical, endoscopic, and radiographic response to ustekinumab in moderate-to-severe Crohn's disease: real-world experience from a multicenter cohort study. Inflamm Bowel Dis 2017;23(5):833–9 (In eng). doi:10.1097/mib.0000000000001074.
[43] Khorrami S, Ginard D, Marín-Jiménez I, et al. Ustekinumab for the treatment of refractory Crohn's disease: the spanish experience in a large multicentre open-label cohort. Inflamm. Bowel Dis. 2016;22:1662–9. doi:10.1097/MIB.0000000000000842.
[44] Wils P, Bouhnik Y, Michetti P, et al. Long-term efficacy and safety of ustekinumab in 122 refractory Crohn's disease patients: a multicentre experience. Aliment Pharmacol Ther 2018;47(5):588–95 (In eng).. doi:10.1111/apt.14487.
[45] Monin L, Dubois S, Reenaers C, et al. Ustekinumab in bio-naïve and bio-failure Crohn's disease patients: results from a « real-life » monocentric cohort. Dig Liver Dis 2021;53(1):72–8 (In eng). doi:10.1016/j.dld.2020.10.040.
[46] Bokemeyer B, Plachta-Danielzik S, di Giuseppe R, et al. Real-world comparative effectiveness of ustekinumab vs anti-TNF in Crohn's disease with propensity score adjustment: induction phase results from the prospective, observational RUN-CD study. Inflamm Bowel Dis 2023 (In eng). doi:10.1093/ibd/izac271.
[47] Lorenzo González L, Valdés Delgado T, Vázquez Morón JM, et al. Ustekinumab in Crohn's disease: real-world outcomes and predictors of response. Rev Esp Enferm Dig 2022;114(5):272–9 (In eng). doi:10.17235/reed.2020.7352/2020.
[48] Chaparro M, Baston-Rey I, Fernández-Salgado E, et al. Long-term real-world effectiveness and safety of ustekinumab in Crohn's disease patients: the SUSTAIN study. Inflamm Bowel Dis 2022;28(11):1725–36 (In eng). doi:10.1093/ibd/izab357.
[49] Irving PM, Sands BE, Hoops T, et al. OP02 Ustekinumab versus adalimumab for induction and maintenance therapy in Moderate-to-Severe Crohn's Disease: the SEAVUE study. J Crohn's Colitis 2021;15(Suppl 1):S001–2. doi:10.1093/ecco-jcc/jjab075.001.
[50] Ben-Horin S, Kopylov U, Chowers Y. Optimizing anti-TNF treatments in inflammatory bowel disease. Autoimmun Rev 2014;13(1):24–30 (In eng).. doi:10.1016/j.autrev.2013.06.002.
[51] Rubín de Célix C, Chaparro M, Gisbert JP. Real-world evidence of the effectiveness and safety of ustekinumab for the treatment of Crohn's disease: systematic review and meta-analysis of observational studies. J Clin Med 2022;11(14) (In eng). doi:10.3390/jcm11144202.
[52] Dalal RS, Njie C, Marcus J, Gupta S, Allegretti JR. Predictors of ustekinumab failure in Crohn's disease after dose intensification. Inflamm Bowel Dis 2021;27(8):1294–301 (In eng). doi:10.1093/ibd/izaa282.
[53] Bressler B, Yarur A, Silverberg MS, et al. Vedolizumab and anti-tumour necrosis factor α real-world outcomes in biologic-naïve inflammatory bowel disease patients: results from the EVOLVE study. J Crohns Colitis 2021;15(10):1694–706 (In eng). doi:10.1093/ecco-jcc/jjab058.

[54] Vulliemoz M, Brand S, Juillerat P, Mottet C, Ben-Horin S, Michetti P. TNF-alpha blockers in inflammatory bowel diseases: practical recommendations and a user's guide: an update. DigestionDigestion 2020;101(Suppl 1):16–26 (In eng). doi:10.1159/000506898.

[55] Cheng D, Kochar BD, Cai T, Ananthakrishnan AN. Risk of infections with ustekinumab and tofacitinib compared to tumor necrosis factor α antagonists in inflammatory bowel diseases. Clin Gastroenterol Hepatol 2022;20(10):2366–72 e6. (In eng). doi:10.1016/j.cgh.2022.01.013.

Exhibit "F3"

This is Exhibit “F3” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.

Arash Rouhi

Digestive and Liver Disease xxx (xxxx) xxx

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Alimentary Tract

Healthcare resource utilization following ustekinumab initiation among bio-naïve Canadian patients with moderately-to-severely active Crohn's disease

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ABSTRACT

Background/aims: Real-world healthcare resource utilization (HCRU) of bio-naïve patients with Crohn's disease (CD) receiving ustekinumab was assessed.

Methods: A multicentre, retrospective chart review study of bio-naïve Canadian adult patients with moderately-to-severely active CD treated with ustekinumab was conducted. CD-related HCRU (i.e., surgery, hospitalization, or emergency room [ER] visits) was evaluated at Months 4, 6, and 12 post-ustekinumab initiation, and associated costs were sourced from a provincial database. Proportion of patients with HCRU events and ustekinumab persistence were summarized at each timepoint. Paired analysis compared HCRU events and associated costs incurred by the same patient whilst in remission vs. when not in remission.

Results: By Month 12, 11.1 % (17/153) of patients had record(s) of any CD-related HCRU event, with ER visits being the most common (7.7 %; 12/155). Hospitalization had the highest average cost (CAD $436.10; SD $2,089.25) across all patients, accounting for 82.2 % of the mean total annual cost/patient (CAD $530.47; SD $2,229.92). While in remission, ≤5 % of patients experienced some healthcare encounter, compared with 7 % when not in remission ($P = 0.289$). Finally, 93.5 % of patients persisted on ustekinumab at Month 12.

Conclusions: HCRU rates and associated total annual costs were lower for bio-naïve CD patients receiving ustekinumab, and when patients were in remission. Most patients continued with ustekinumab at Month 12.

1. Introduction

Crohn's disease (CD) is a chronic, idiopathic, relapsing-remitting condition of the gastrointestinal tract and one of the two main forms of inflammatory bowel disease (IBD) [1,2]. Canada reports one of the highest rates of prevalence and incidence of IBD in the world, approximately half of which are related to a confirmed diagnosis of CD [3–5].

While achieving and maintaining remission is the long-term goal of therapy, managing unexpected disease flares and relapses in patients with CD can result in considerable direct medical costs, which are driven by healthcare resource utilization (HCRU), including visits to clinicians' offices, emergency departments, and hospitalizations [6–14].

A growing body of evidence has highlighted benefits of early use of biologics for controlling disease and reducing the risk of relapse in moderately-to-severely active CD [15–18]. In some instances, biologics are recommended as first-line therapy to achieve clinical and endoscopic remission, ultimately aiming to prevent relapse and thereby reduce HCRU [17–19]. Over the past two decades in Canada, rates of HCRU for CD-related surgeries and hospitalizations have steadily declined – a trend that is primarily attributed to the availability of better pharmacological treatment options, such as biologics [10,20].

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1590-8658/

Ustekinumab, a subcutaneously administered monoclonal antibody, is the only approved anti-IL-12/23 biologic for induction and maintenance therapy for moderately-to-severely active CD [21–23]. Real-world data on HCRU following ustekinumab use in bio-naïve patients are currently lacking. Previous real-word studies assessing HCRU among ustekinumab recipients have primarily involved bio-experienced patients [24–26]. Thus, we present findings from the Joint Canadian Ustekinumab Real-World Effectiveness and Safety (JUSTify) study to provide insights into HCRU and associated costs in bio-naïve patients with moderately-to-severely active CD starting ustekinumab as their first advanced therapy.

2. Materials and methods

2.1. Study design and timepoints for data collection

JUSTify was a retrospective, multicentre, chart review study designed to obtain real-world data on ustekinumab in bio-naïve patients with moderately-to-severely active CD. Data were collected from medical charts of CD patients treated at seven gastroenterology clinics across Canada from December 11th, 2020, to September 30th, 2021. Retrospective data collection was performed at four different timepoints: baseline, Month 4, Month 6, and Month 12 (Fig. 1). To accommodate variability in routine care visit schedules, baseline data were collected within a window of 183 days (six months) prior to the date of ustekinumab initiation (Day 0). After ustekinumab initiation, windows for the data collection timepoints were as follows: ±30 days for the Month 4 timepoint, −30/+61 days for the Month 6 timepoint, and −121/+61 days for the Month 12 timepoint. For any given timepoint, if more than one visit occurred within the data collection window, data available from the visit closest to the defined timepoint was used. In instances when two visits were equidistant from the evaluation timepoint within a visit window, the more recent visit was used. Medical history variables including diagnosis, comorbidities, and prior treatment were collected from the time of CD diagnosis up to the time of treatment initiation with ustekinumab, as available. Ustekinumab treatment information was collected continuously from ustekinumab initiation up to discontinuation or Month 12, whichever occurred first.

2.2. Inclusion and exclusion criteria

Patients ≥18 years old with a confirmed diagnosis of CD at the time of ustekinumab initiation were included in JUSTify if they 1. received at least one intravenous (IV) induction dose of ustekinumab, 2. had a minimum of six months of follow-up data available from the time of ustekinumab initiation, regardless of ustekinumab discontinuation status, 3. had a Harvey Bradshaw Index (HBI) [27] score ≥8, or a CD activity index (CDAI) [28] score ≥150, or a physician assessment rating of moderately-to-severely active disease prior to initiating ustekinumab, and 4. had at least one clinical or endoscopic follow-up between five and seven months after initiating ustekinumab. Patients were excluded if they received ustekinumab for any indication outside of CD or received any other biologic therapy (TNF-α antagonists, IL-17/IL-23 inhibitors, mucosal addressing cell adhesion molecule 1 [MadCAM-1] inhibitors, and integrin inhibitors) before ustekinumab initiation. Patients were also excluded if they had received ustekinumab outside of routine medical care (e.g., compassionate use programs prior to the drug's marketing authorization).

A waiver of consent was obtained from the research ethics boards at each participating site prior to the extraction and secondary use of routinely collected, anonymized, medical record data in accordance with local requirements. All research procedures complied with the ethical principles of the Declaration of Helsinki.

2.3. Study outcomes

Clinical data (including rates of remission and response) were assessed as primary and secondary outcomes. JUSTify's primary and secondary outcomes as well as additional descriptive outcomes (such as concomitant medication use, ustekinumab dosing, adverse drug reactions, and stratification of clinical remission and response results by dose optimization status) have been presented in a separate publication [29]. Assessment of HCRU and ustekinumab persistence were exploratory objectives of JUSTify. HCRU-related objectives included describing (a) rate of HCRU at Month 4, Month 6, and Month 12 from ustekinumab initiation, (b) costs of CD-related HCRU at Month 4, Month 6, and Month 12 from ustekinumab initiation, (c) association between CD-related HCRU and

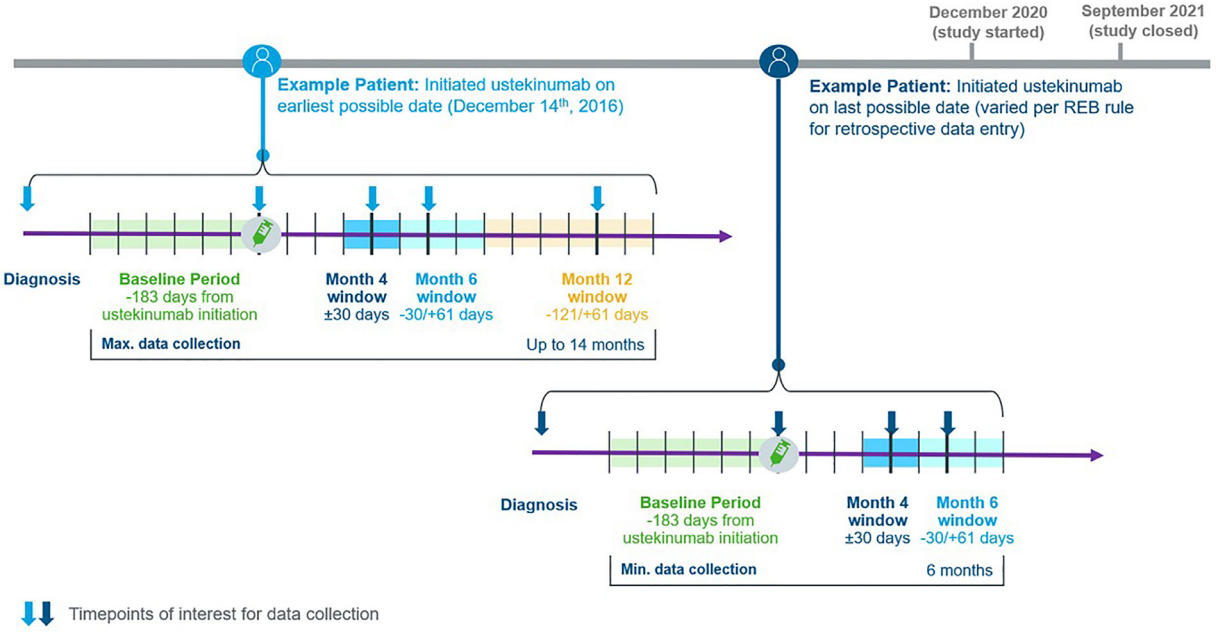

Fig. 1. Data collection schedule.

clinical remission, (d) costs of CD-related HCRU by clinical remission subgroups at Month 4, Month 6, and Month 12 from ustekinumab initiation, and (e) association between CD-related HCRU and ustekinumab persistence.

2.4. Definitions

Data collection for HCRU occurring at study sites was limited to available records and included pre-defined CD-related events: surgery, hospitalization, and emergency room (ER) visits. CD-related surgery included but was not limited to bowel resection surgery (ileal resection, ileocecal resection, proctocolectomy, colectomy, enterectomy, ostomy formation and repair, anastomosis/reanastomosis, strictureplasty) and fistula repair (incision and drainage of abscess, seton placement, fistulotomy, fistulectomy). For each patient, CD-related surgery status was a binary variable defined as “yes”, if the patient had a surgical procedure for the treatment of CD any time between ustekinumab initiation and the respective timepoint, and “no” otherwise. Likewise, CD-related hospitalization status was a binary variable defined as “yes” or “no” depending on the patient’s history of undergoing a CD-related inpatient admission any time between ustekinumab initiation and the respective timepoint. CD-related ER visit status was a binary variable defined as “yes” or “no” depending on the patient’s history of an ER visit related to CD any time between ustekinumab initiation and the respective timepoint.

Number of CD-related ER visits, CD-related surgeries, and CD-related hospitalizations and the corresponding lengths of stay were recorded to estimate rates of CD-related HCRU (along with confidence intervals (CI)) and to estimate costs associated with CD.

For CD-related surgeries, dates of CD-related surgeries and CD-related hospital admissions were assessed to determine the number of CD-related surgeries and CD-related surgeries associated with hospitalization as well as the length of in-hospital stay. The average expenditures for HCRU events were calculated using cost inputs available from the Ontario Case Costing Initiative (OCCI) for each type of surgery (bowel surgery, strictureplasty, fistula repair) [30]. The cost per inpatient surgical case, cost per surgical case for same day surgery, and cost of CD-related hospitalization without surgery were collected for cost estimation.

Clinical remission was defined as a CDAI <150, HBI <5, or a physician assessment of “normal or inactive disease”. If both CDAI and HBI were available, the CDAI score was used to assess clinical remission.

Ustekinumab discontinuation at any time prior to the study end was considered an ‘event’ and was used to determine ustekinumab persistence. The date of discontinuation was used to calculate the time-to-event.

Patients with no record of ustekinumab discontinuation were censored. The time of censoring was determined from the date of last ustekinumab administration or date of last physician assessment of disease activity, whichever occurred last.

2.5. Statistical analysis

The statistical analysis was primarily descriptive. Patient characteristics and endpoints were described with mean, standard deviation (SD), median, and interquartile range (IQR) for continuous variables, and number and percentage in each category for categorical variables.

All proportions were calculated by dividing the number of patients satisfying a given endpoint criterion by the number of patients with available data for that endpoint (i.e., as observed analyses). Patients with missing values were omitted from the total number prior to calculation of percentages; 95 % CI were derived based on a binomial exact method by Clopper and Pearson [31]. For endpoints that were based on change from baseline, calculation was performed only for those patients for whom both data points were available. At each timepoint, proportion of patients continuing ustekinumab (i.e., persistence) was summarized. Time-dependent Cox proportional hazard regression was used to estimate hazard ratio (HR) of ustekinumab discontinuation associated with having any CD-related HCRU. Costs for medical services were obtained from the OCCI and used to estimate HCRU costs in 2021 Canadian dollars (CAD) [25]. Paired analysis compared HCRU events and associated costs incurred by the same patient whilst in remission vs. when not in remission. Patients who never went "in remission" were excluded from the paired analysis. Paired analysis was performed using the McNemar test for normally distributed data, and using the Wilcoxon signed rank test for not normally distributed data.

When applicable, statistical tests were two-sided and no adjustment for multiple testing was performed. Statistical significance was defined by $P \leq 0.05$. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Finally, to reduce the risk of patient identification, all outcomes involving <6 patients were suppressed.

3. Results

3.1. Baseline demographics and patient characteristics

A total of 158 eligible patients were included in the study. Baseline demographics and patients’ clinical characteristics are summarized in Table 1. The patients’ female-to-male ratio was 1.16, and

Table 1
Baseline demographics and clinical characteristics.

Characteristics	Study Population
Age at baseline (years), (*n* = 158)	
Mean (SD)	42.3 (16.6)
Female sex, n (%), (*n* = 158)	85 (53.8)
Age at diagnosis of CD (years), (*n* = 158)	
Mean (SD)	33.7 (17.0)
Weight (kg), (*n* = 148)	
Mean (SD)	76.2 (19.3)
Smoking status (*n* = 150)	
Current, n (%)	31 (20.7)
Former, n (%)	16 (10.7)
Never, n (%)	103 (68.7)
CD duration (years), (*n* = 158)	
Mean (SD)	8.6 (12.1)
HBI score, (*n* = 103)	
Mean (SD)	6.9 (3.9)
Physician assessment of disease severity (*n* = 156)	
Severe disease, n (%)	44 (28.2)
Moderate disease, n (%)	112 (71.8)
Disease location (*n* = 157)	
L1 Terminal ileum, n (%)	56 (35.7)
L2 Colon, n (%)	30 (19.1)
L3 Ileocolonic, n (%)	54 (34.4)
L4 Upper GI, n (%)	9 (5.7)
Other, n (%)1	8 (5.1)
Disease behavior (*n* = 156)	
Non-stricturing, non-penetrating, n (%)	97 (62.2)
Stricturing, n (%)	39 (25.0)
Penetrating, n (%)	9 (5.8)
Both Stricturing and penetrating, n (%)	11 (7.1)
Active perianal involvement (*n* = 157), n (%)	10 (6.4)
Any prior CD-related surgery (*n* = 157), n (%)	32 (20.4)
Presence of ulcerations at endoscopic assessment (*n* = 74), n (%)	60 (81.1)

CD: Crohn’s disease; GI: Gastrointestinal; HBI: Harvey-Bradshaw Index; IQR: interquartile range; SD: standard deviation.
CD-related surgeries included resective bowel surgery, strictureplasty, or fistula repair.
[1]Includes L1 + L4 terminal ileum + Upper GI, L2 + L4 Colon + Upper GI, L3 + L4 Ileocolon + Upper GI and Ileal pouch.

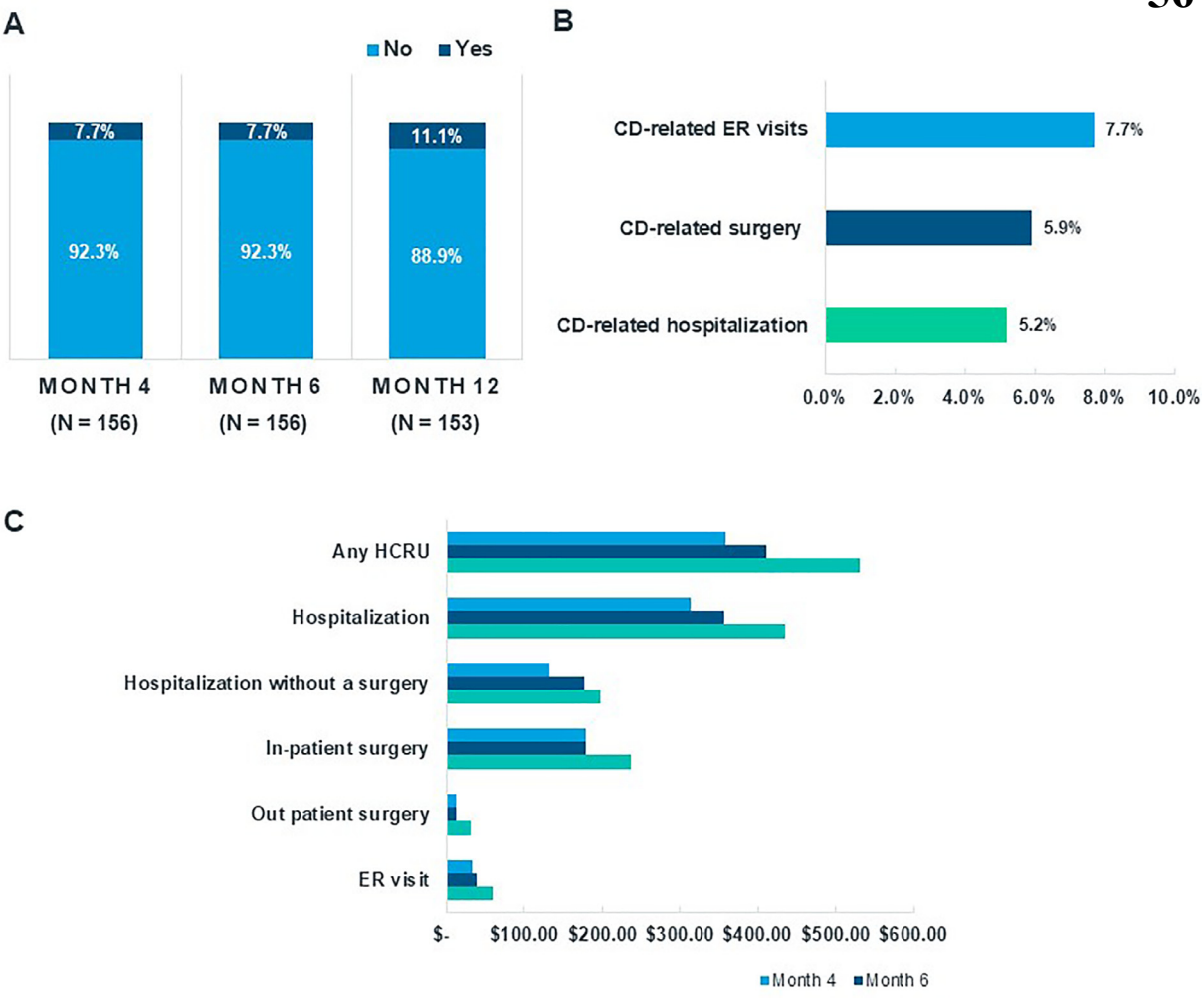

Fig. 2. CD-related HCRU Events following ustekinumab initiation, and costs (in CAD) estimated from OCCI costs.
CAD: Canadian dollars; CD: Crohn's disease; ER: emergency room; HCRU: healthcare resource utilization; OCCI: Ontario Case Costing Initiative.
CD-related surgeries included resective bowel surgery, strictureplasty, or fistula repair
2 patients had a missing date of surgery and no other CD-related HCRU and could not be assigned to a study timepoint. 1 patient had a missing date of hospitalization and could not be assigned to a study timepoint. $N = 154$ for CD-related hospitalization, $N = 155$ for CD-related ER visits, $N = 153$ for CD-related surgery.

average age at ustekinumab initiation was 42.3 years (SD 16.6). Based on physician assessment at baseline, 71.8 % (112/156) had moderate disease and 28.2 % (44/156) of patients had severe disease. Active perianal involvement was present in 6.4 % (10/157) of patients.

3.2. Rate of CD-related HCRU

By Month 6, 7.7 % (12/156; 95 % CI [4.0, 13.1]) of patients had records for any CD-related HCRU events. By Month 12 (Fig. 2A and 2B), the rate of CD-related HCRU was 11.1 % (17/153; 95 % CI [6.6,17.2]) with CD-related ER visits (7.7 %; 12/155; 95 % CI [4.1,13.1]) being the most common type followed by CD-related surgeries (5.9 %; 9/153; 95 % [CI 2.7,10.9]), and CD-related hospitalization (5.2 %; 8/154; 95 % CI [2.3,10.0]).

3.3. Cost analysis of CD-related HCRU events

Mean total annual cost for the study population for CD-related HCRU was CAD $530.47/patient (SD $2229.92; Fig. 2C). The total costs for CD-related HCRU ranged from $0.0 to $13,859.0. Mean annual costs were the highest for CD-related hospitalizations (CAD $436.10, SD $2089.25), which accounted for 82.2 % of the total annual cost/patient. Mean annual costs of ER visits and outpatient surgeries for the study population were CAD $59.57 (SD $226.08) and CAD $31.04 (SD $169.44) per patient, respectively.

HCRU costs were also assessed by restricting cost analysis to only the patients who incurred any cost during study follow-up (Table 2). The mean total annual cost for CD-related HCRU was $5039.51/patient (SD $5081.23), and the range was $513.0 to $13,859.0. Mean annual costs for CD-related hospitalizations, ER visits, and outpatient surgeries were $4197.60 (SD $5261.28), $545.06 ($476.43), and $296.84 ($454.73) per patient, respectively.

3.4. Association between CD-related HCRU costs and clinical remission

Clinical remission was achieved by 50.0 % (36/72), 67.7 % (105/155), and 73.7 % (84/114) of patients at Month 4, 6, and 12, respectively. Overall, 81.6 % (129/158) of patients experienced clinical remission at one or more time points during the study follow-up. There was a trend towards lower CD-related HCRU for patients who achieved remission at Month 6 vs. those not in remission (odds ratio [OR], 0.385 [CI 0.130, 1.117]; $P = 0.076$; Table 3).

Paired analysis in patients experiencing remission revealed that ≤5 % of patients had some healthcare encounter whilst in clin-

Table 2
Costs incurred for patients with Any CD-related HCRU (in CAD).*

	Month 4 ($N = 11$)	Month 6 ($N = 11$)	Month 12 ($N = 16$)
Total costs of CD-related HCRU			
Mean (SD)	5058.42 (4987.13)	5781.65 (5563.57)	5039.51 (5081.23)
Median (IQR)	3284.8 (513.0, 11,087.2)	3284.8 (513.0, 12,181.3)	2630.4 (949.9, 10,185.8)
Costs of CD-related hospitalizations			
Mean (SD)	4465.98 (5064.95)	5095.94 (5782.14)	4197.60 (5261.28)
Median (IQR)	2771.8 (0.0, 11,087.2)	2771.8 (0.0, 11,668.3)	1385.9 (0.0, 9710.9)
Costs of CD-related hospitalizations associated with CD-related surgeries			
Mean (SD)	2576.12 (4736.09)	2576.12 (4736.09)	2291.99 (4341.41)
Median (IQR)	0.0 (0.0, 5000.7)	0.0 (0.0, 5000.7)	0.0 (0.0, 2500.4)
Costs of CD-related hospitalizations not associated with CD-related surgeries			
Mean (SD)	1889.86 (3732.82)	2519.82 (5028.28)	1905.61 (4260.37)
Median (IQR)	0.0 (0.0, 2771.8)	0.0 (0.0, 2771.8)	0.0 (0.0, 1385.9)
Costs of CD-related surgeries not associated with hospitalizations			
Mean (SD)	172.71 (384.25)	172.71 (384.25)	296.84 (454.73)
Median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 949.9)
Costs of CD-related ER visits			
Mean (SD)	419.73 (385.14)	513.00 (397.37)	545.06 (476.43)
Median (IQR)	513.0 (0.0, 513.0)	513.0 (0.0, 1026.0)	513.0 (0.0, 1026.0)

CD: Crohn's disease; CI: confidence interval; ER: emergency room; IQR: interquartile range; HCRU: healthcare resource utilization; SD: standard deviation.

* For each timepoint, the cost summaries were restricted to patients who incurred any costs for the respective category. Data from Ontario Case Costing Initiative (OCCI) were used to estimate the costs of CD-related HCRU.[30]

Table 3
Association between clinical remission and CD-related HCRU.

Variable	OR [95 % CI]	*P*-value
Clinical remission at 6 months, Yes vs. No	0.385 [0.130, 1.117]	0.076
Age at diagnosis of CD (years)	1.009 [0.977, 1.039]	0.560
Sex, Female vs. Male	1.236 [0.425, 3.766]	0.697
Physician assessment (DA), Severe vs. Moderate disease	1.987 [0.648, 5.819]	0.213

CD: Crohn's disease; CI: confidence Interval; HCRU: healthcare resource utilization; OR: odds ratio. The model is based on 145 patients with non-missing variable or outcome data.

ical remission compared with almost double (7 %) when not in remission (Fig. 3). Finally, patients in clinical remission showed a trend toward lower total costs for any HCRU (CAD $102.50 vs. CAD $413.20, $P = 0.080$).

3.5. Association between CD-related HCRU and ustekinumab persistence

At Month 12, most patients (93.5 %; 145/155) persisted with ustekinumab treatment. Overall, the frequency of any CD-related HCRU was higher for patients who discontinued ustekinumab by Month 12 when compared with patients who persisted. Likewise, rates of CD-related surgery, CD-related hospitalization, and CD-related ER visits were higher among patients who discontinued ustekinumab by Month 12 vs. those who persisted. Patients who had a CD-related healthcare encounter were 6.66 (95 % CI: 1.53, 25.17) times more likely to discontinue ustekinumab ($P = 0.018$).

4. Discussion

This is the first analysis in Canada that presents insights into real-world HCRU following ustekinumab initiation in adult, bio-naïve patients with moderately-to-severely active CD. Using retrospective chart review data, JUSTify showed that >90 % of patients had no record of any CD-related HCRU following ustekinumab initiation and that HCRU and associated costs tended to be lower when patients were in remission vs. not in remission.

Most real-world studies reporting CD-related HCRU post-ustekinumab initiation have, until now, involved bio-experienced patients. In an Israel-based retrospective study involving bio-experienced patients treated with ustekinumab, cumulative rates of CD-related surgery and CD-related hospitalization were estimated to be 4.7 % and 9.8 %, respectively [26]. A U.S. study leveraging real-world claims data from three commercial databases reported a 29 % annual hospitalization rate in patients initiated with ustekinumab, and identified a significant downward trend in the number and costs associated with annual CD-related ER visits, CD-related surgeries, and CD-related inpatient stays following ustekinumab initiation [24]. By exclusively including bio-naïve patients, JUSTify explored trends in HCRU with ustekinumab as first-line biological therapy. Low rates of HCRU were observed among bio-naïve patients in JUSTify and approximately 11 % of patients had any record of CD-related HCRU by Month 12. Most patients did not incur any costs after ustekinumab initiation, leading to low total annual costs. A study conducted in Manitoba, Canada found that CD patients had lower mean inpatient costs ($5628 vs $6419) and median outpatient costs ($3504 vs $3788) after receiving anti-TNF therapy compared to before [40]. Further research is needed to assess ustekinumab's impact on HCRU in comparison to other treatment options.

Ustekinumab effectiveness in JUSTify was generally greater than reported in previous real-world studies, which predominantly included bio-experienced patients and reported 12-month clinical remission rates ranging from ~30 % to ~40 % [29,32-37]. However, no prior studies have assessed HCRU associated with ustekinumab-induced clinical remission. In JUSTify, bio-naïve patients receiving ustekinumab had clinical remission rates of 73.7 % by Month 12 [29]. There are various potential predictors of ustekinumab efficacy, such as patient demographics (e.g. sex, age), disease severity and location, patient demographics, prior CD-related surgery, and con-

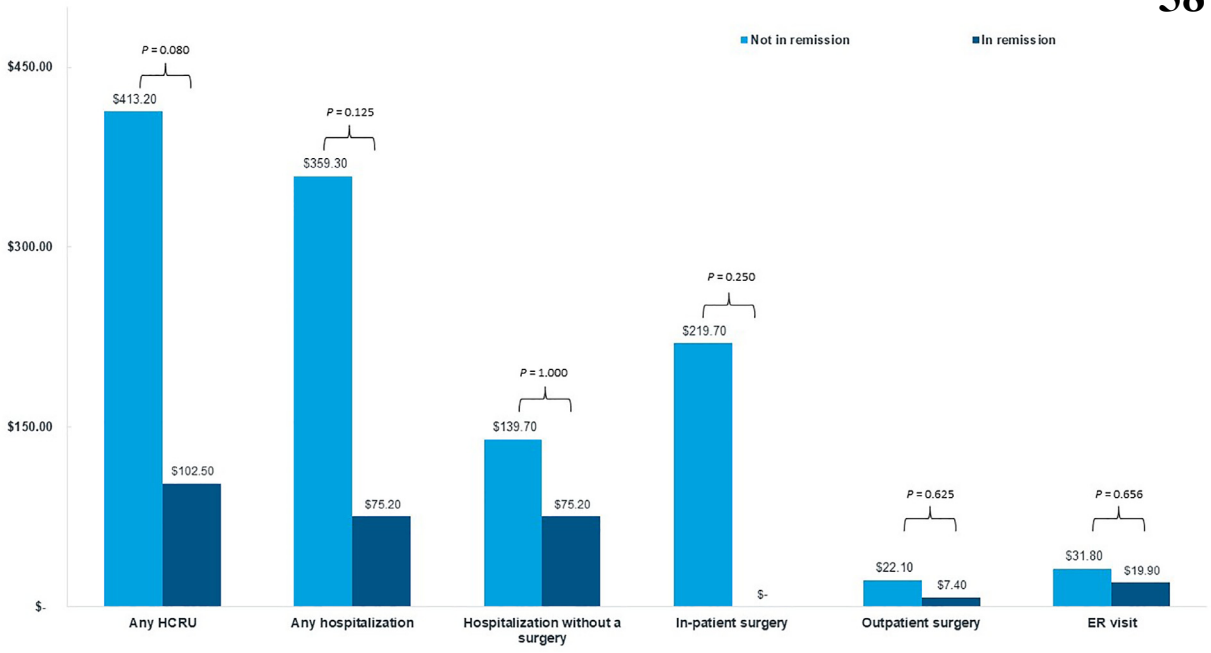

Fig. 3. Paired analysis of average HCRU costs/patient (in CAD) by remission status.
ER: emergency room; HCRU: healthcare resource utilization.

comitant immunomodulator use [38,39]. In a previous publication based on the same group of patients, it was found that sex, CD duration and HBI score were not significantly associated with clinical remission at Month 6 [29]. When JUSTify patients were in clinical remission, they showed a trend towards lower HCRU and lower total costs per HCRU. Patients who never went in remission were excluded from the analysis. As a result, the higher HCRU events and associated costs when not in remission only pertain to patients who experienced clinical remission at one or more time points during the study follow-up, and not to those that never went in remission.

The clinical guidelines for the management of CD in adults recommend that ustekinumab be used as a first-line biologic for moderately-to-severely active CD, and to maintain remission in patients who have responded to ustekinumab [18,19]. The findings that HCRU rates and associated total annual costs were generally low for ustekinumab-treated patients and when patients were in remission further support the use of ustekinumab as first-line therapy.

This analysis might not be applicable to other healthcare systems outside of Canada in regard to the costs associated with healthcare encounters and events, but the number of events could be relative. Variations in access to general physicians, specialists, and medications, and differences in standard of care recommendations can influence healthcare resource utilization across different countries [41,42].

In JUSTify, 93.5 % of patients persisted with ustekinumab treatment. High rates of 12-month persistence with ustekinumab have been consistently reported by other studies, for both bio-naïve and bio-experienced populations [24,32,35,37,43-46]. In JUSTify, rates of CD-related surgery, CD-related hospitalization, and CD-related ER visits were higher among bio-naïve patients who discontinued ustekinumab by Month 12 vs. bio-naïve patients who persisted. Real-world studies reporting high persistence have also reported reduced use of corticosteroids and other drugs among ustekinumab-treated patients [24,35,37,46-48]. By Month 12, 93.5 % of patients persisted with ustekinumab [29].

The limitations of retrospective data collection and descriptive analyses apply to this study, including potential selection bias, non-standardized follow-up intervals, and dependence on the accuracy and availability of patient chart data [29]. Also, non-random sampling used in patient selection may limit generalizability of the results. Other limitations include missing data on the recorded HCRU and absence of data on HCRU beyond the predefined list of CD-related services or on HCRU that may occur outside of the study sites – all of which may result in estimated costs that do not accurately reflect the actual costs incurred. To further understand ustekinumab's impact on HCRU and address the limitations of the study, prospective studies and linkage with administrative health services records can be done. Linkage with administrative health services records would enable the validation of data collected at standardized follow-up intervals, thereby minimizing the risk of missing data.

5. Conclusion

Most patients continued with ustekinumab therapy over the study follow-up period. Rates of HCRU and associated total annual costs were generally low for bio-naïve CD patients treated with ustekinumab and lower when patients were in remission.

Authors' contributions

Talat Bessissow, Tracy S.H. In, Eneda Pone, and Maria Eberg contributed to the conception and design of the study. Talat Bessissow, Vipul Jairath, Neeraj Narula, and Christopher Ma contributed to the acquisition of the data. Maria Eberg contributed to the analysis of the data. All authors contributed to the interpretation of data for the study. All authors provided critical revision for important intellectual content of the manuscript. All authors read and approved the final manuscript.

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Conflicts of interest

This study was funded by Janssen Inc. The sponsor was involved in the design, interpretation, and reporting of study results.

Talat Bessissow acted as a speaker or advisor for AbbVie, Alimentiv (formerly Robarts Inc.), Amgen, Bristol-Myers-Squibb, Ferring, Gilead, Janssen, Merck, Pentax, Pfizer, Roche, Sandoz, Takeda, Viatris. Neeraj Narula has received honoraria from Janssen, AbbVie, Takeda, Pfizer, Merck, Sandoz, Novartis, and Ferring.

Christopher Ma has received consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche; speaker's fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Ferring, Janssen, Takeda, and Pfizer; research support from Ferring, Pfizer.

Vipul Jairath served on advisory boards, consulted or was an investigator for AbbVie, Alimentiv Inc. (formerly Robarts Clinical Trials Inc.), Amgen, Applied Strategic, Arena Pharmaceuticals, Asahi Kasei Pharma, Asieris, Astra Zeneca, BioJamp. Celgene/BMS, Celltrion, Eli Lilly, Ferring, F. Hoffman-La Roche Ltd., Flagship Pioneering, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Organon (Merck), Landos BioPharma, Mylan, Pandion, Pendopharm, Pfizer, Protagonist Therapeutics, Reistone Biopharma, Roche, Sandoz, Second Genome, Takeda, Teva, Topivert, Ventyx Biosciences, and Vividion Therapeutics. Vipul Jairath acted as a speaker for AbbVie, Ferring, Galapagos, Janssen, Pfizer, and Takeda and is an employee of Western University.

Tracy S.H. In and Eneda Pone are full-time employees of Janssen Inc. Maria Eberg is a full-time employee of IQVIA Solutions Canada Inc. (IQVIA). Janssen Inc. contracted IQVIA to manage the study.

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References

[1] Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC). 2018 Impact of Inflammatory Bowel Disease in Canada. Toronto, ON; 2018.
[2] Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG clinical guideline: management of Crohn's disease in adults. Am J Gastroenterol 2018;113(4):481–517. doi:10.1038/ajg.2018.27.
[3] Kaplan GG, Bernstein CN, Coward S, et al. The impact of inflammatory bowel disease in Canada 2018: epidemiology. J Can Assoc Gastroenterol 2019;2(Suppl 1):S6–S16. doi:10.1093/jcag/gwy054.
[4] Coward S.C.F,. Benchimol E.I., Bernstein C.N., Bitton A., Carroll M.W., et al. A29 the rising prevalence of inflammatory bowel disease in Canada: analyzing the past to predict the future. J Can Assoc Gastroenterol;Feb 2018:1(suppl_2):47–8. DOI: 10.1093/jcag/gwy009.029.
[5] Coward S, Benchimol EI, Kuenzig ME, et al. The 2023 impact of inflammatory bowel disease in canada: epidemiology of IBD. J Can Assoc Gastroenterol 2023;6(Suppl 2):S9–S15. doi:10.1093/jcag/gwad004.
[6] Rocchi A, Benchimol EI, Bernstein CN, et al. Inflammatory bowel disease: a Canadian burden of illness review. Can J Gastroenterol 2012;26(11):811–17. doi:10.1155/2012/984575.
[7] Rubin DT, Mody R, Davis KL, Wang CC. Real-world assessment of therapy changes, suboptimal treatment and associated costs in patients with ulcerative colitis or Crohn's disease. Aliment Pharmacol Ther 2014;39(10):1143–55. doi:10.1111/apt.12727.
[8] Long GH, Tatro AR, Oh YS, Reddy SR, Ananthakrishnan AN. Analysis of safety, medical resource utilization, and treatment costs by drug class for management of inflammatory bowel disease in the United States based on insurance claims data. Adv Ther 2019;36(11):3079–95. doi:10.1007/s12325-019-01095-1.
[9] Perera S, Yang S, Stott-Miller M, Brady J. Analysis of healthcare resource utilization and costs after the initiation of biologic treatment in patients with Ulcerative Colitis and Crohn's disease. J Health Econ Outcomes Res 2018;6(1):96–112. doi:10.36469/9791.
[10] Kuenzig ME, Benchimol EI, Lee L, et al. The impact of inflammatory bowel disease in Canada 2018: direct costs and health services utilization. J Can Assoc Gastroenterol 2019;2(Suppl 1):S17–33. doi:10.1093/jcag/gwy055.
[11] Panaccione R, Colombel JF, Travis SPL, et al. Tight control for Crohn's disease with adalimumab-based treatment is cost-effective: an economic assessment of the CALM trial. Gut 2020;69(4):658–64. doi:10.1136/gutjnl-2019-318256.
[12] Park KT, Ehrlich OG, Allen JI, et al. The cost of inflammatory bowel disease: an initiative from the Crohn's & colitis foundation. Inflamm Bowel Dis 2020;26(1):1–10. doi:10.1093/ibd/izz104.
[13] Santiago M, Dias CC, Alves C, et al. The magnitude of Crohn's disease direct costs in health care systems (from different perspectives): a systematic review. Inflamm Bowel Dis 2022;28(10):1527–36. doi:10.1093/ibd/izab334.
[14] Tsai L, Nguyen NH, Ma C, Prokop LJ, Sandborn WJ, Singh S. Systematic review and meta-analysis: risk of hospitalization in patients with ulcerative colitis and Crohn's disease in population-based cohort studies. Dig Dis Sci 2022;67(6):2451–61. doi:10.1007/s10620-021-07200-1.
[15] Samaan M, Campbell S, Cunningham G, Tamilarasan AG, Irving PM, McCartney S. Biologic therapies for Crohn's disease: optimising the old and maximising the new. F1000Res 2019;8. doi:10.12688/f1000research.18902.1.
[16] Hafizi D.M.D,. Thompson W., Young C., Chao Y.-S., Loshak H., et al. Cadth technology review: optimal use 360 report appropriate pharmacotherapy for inflammatory bowel disease. 2019.
[17] Al-Bawardy B, Shivashankar R, Proctor DD. Novel and emerging therapies for inflammatory bowel disease. Front Pharmacol 2021;12:651415. doi:10.3389/fphar.2021.651415.
[18] Panaccione R, Steinhart AH, Bressler B, et al. Canadian association of gastroenterology clinical practice guideline for the management of luminal Crohn's disease. J Can Assoc Gastroenterol 2019;2(3):e1–e34. doi:10.1093/jcag/gwz019.
[19] Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing crohn's disease. Gastroenterology 2021;160(7):2496–508. doi:10.1053/j.gastro.2021.04.022.
[20] Ma C, Moran GW, Benchimol EI, et al. Surgical rates for Crohn's disease are decreasing: a population-based time trend analysis and validation study. Am J Gastroenterol 2017;112(12):1840–8. doi:10.1038/ajg.2017.394.
[21] Feagan BGSW, Gasink C, Jacobstein D, Lang Y, Friedman JR, et al. Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2016;375(20):1946–60. doi:10.1056/NEJMoa1602773.
[22] Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: three-year efficacy, safety, and immunogenicity of ustekinumab treatment of Crohn's disease. J Crohns Colitis 2020;14(1):23–32. doi:10.1093/ecco-jcc/jjz110.
[23] Sandborn WJ, Rebuck R, Wang Y, et al. Five-year efficacy and safety of ustekinumab treatment in Crohn's Disease: the IM-UNITI trial. Clin Gastroenterol Hepatol 2022;20(3) 578-590 e4. doi:10.1016/j.cgh.2021.02.025.
[24] Obando C, Ding Z, Muser E, et al. Persistence, dose titration, and health care resource utilization among crohn's disease patients treated with ustekinumab: a real-world analysis in the United States. Adv Ther 2020;37(5):2127–43. doi:10.1007/s12325-020-01276-3.
[25] Rahme ENH, Afif W. Cost of refractory Crohn's disease before and after ustekinumab utilization. J Can Assoc Gastroenterol 2019. doi:10.1093/jcag/gwz025.
[26] Banon T, Weil C, Borsi A, Chodick G, Shakked Z, Barit Ben-David N. Treatment patterns, persistence with therapy, and outcomes of ustekinumab in Crohn's disease: real-world data analysis. JGH Open 2022;6(2):120–5. doi:10.1002/jgh3.12670.
[27] Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980;1(8167):514. doi:10.1016/s0140-6736(80)92767-1.
[28] Vermeire SSS, Sandborn WJ, Dubois C, Rutgeerts P. Correlation between the crohn's disease activity and harvey-bradshaw indices in assessing crohn's disease severity. Clin Gastroenterol Hepatol 2010;8:357–63.
[29] Bessissow T, Narula N, Ma C, et al. Real-world effectiveness and safety of ustekinumab in bio-naive patients with moderate-to-severe Crohn's disease: a Canadian multi-center study. Dig Liver Dis 2023. doi:10.1016/j.dld.2023.08.042.
[30] Ontario Case Costing Initiative (OCCI). Available at: https://data.ontario.ca/dataset/ontario-case-costing-initiative-occi. Accessed May 25, 2022.
[31] Clopper C.J. and Pearson E.S. The Use Of Confidence or Fiducial Limits Illustrated in the Case of the Binomial. 1934;26(4):404–13. DOI: 10.1093/biomet/26.4.404.
[32] Biemans VBC, van der Meulen-de Jong AE, van der Woude CJ, et al. Ustekinumab for Crohn's Disease: results of the ICC Registry, a Nationwide Prospective Observational Cohort Study. J Crohns Colitis 2020;14(1):33–45. doi:10.1093/ecco-jcc/jjz119.
[33] Plevris N, Fulforth J, Siakavellas S, et al. Real-world effectiveness and safety of ustekinumab for the treatment of Crohn's disease: the Scottish ustekinumab cohort. J Gastroenterol Hepatol 2021;36(8):2067–75. doi:10.1111/jgh.15390.
[34] Forss ACM, Myrelid P, Strid H, Söderman C, Wagner A, et al. Ustekinumab is associated with real-world long-term effectiveness and improved health-related quality of life in crohn's disease. Dig Dis Sci 2022. doi:10.1007/s10620-022-07501-z.
[35] Straatmijer T, Biemans VBC, Hoentjen F, et al. Ustekinuma b for Crohn's disease: two-year results of the initiative on crohn and colitis (ICC) registry, a nationwide prospective observational cohort study. J Crohns Colitis 2021;15(11):1920–30. doi:10.1093/ecco-jcc/jjab081.
[36] Parra RS, Chebli JMF, Queiroz NSF, et al. Long-term effectiveness and safety of ustekinumab in bio-naive and bio-experienced anti-tumor necrosis factor

patients with Crohn's disease: a real-world multicenter Brazilian study. BMC Gastroenterol 2022;22(1):199. doi:10.1186/s12876-022-02280-3.
[37] Viola A, Muscianisi M, Macaluso FS, et al. Ustekinumab in Crohn's disease: real-world outcomes from the Sicilian network for inflammatory bowel diseases. JGH Open 2021;5(3):364–70. doi:10.1002/jgh3.12502.
[38] Barre A, Colombel JF, Ungaro R. Review article: predictors of response to vedolizumab and ustekinumab in inflammatory bowel disease. Aliment Pharmacol Ther 2018;47(7):896–905. doi:10.1111/apt.14550.
[39] Gisbert JP, Chaparro M. Predictors of primary response to biologic treatment [Anti-TNF, Vedolizumab, and Ustekinumab] in patients with inflammatory bowel disease: from basic science to clinical practice. J Crohns Colitis 2020;14(5):694–709. doi:10.1093/ecco-jcc/jjz195.
[40] Targownik LE, Benchimol EI, Witt J, et al. The effect of initiation of anti-TNF therapy on the subsequent direct health care costs of inflammatory bowel disease. Inflamm Bowel Dis 2019;25(10):1718–28. doi:10.1093/ibd/izz063.
[41] Bokemeyer B, Picker N, Wilke T, Rosin L, Patel H. Inadequate response, treatment patterns, health care utilization, and associated costs in patients with ulcerative colitis: retrospective cohort study based on german claims data. Inflamm Bowel Dis 2022;28(11):1647–57. doi:10.1093/ibd/izab330.
[42] Ma C, Smith MK, Guizzetti L, et al. Assessing national trends and disparities in ambulatory, emergency department, and inpatient visits for inflammatory bowel disease in the United States (2005-2016). Clin Gastroenterol Hepatol 2020;18(11) 2500-2509 e1. doi:10.1016/j.cgh.2020.01.023.
[43] Af Bjorkesten CG, Ilus T, Hallinen T, et al. Objectively assessed disease activity and drug persistence during ustekinumab treatment in a nationwide real-world Crohn's disease cohort. Eur J Gastroenterol Hepatol 2020;32(12):1507–13. doi:10.1097/MEG.0000000000001831.
[44] Chaparro M, Baston-Rey I, Fernandez-Salgado E, et al. Long-term real-world effectiveness and safety of ustekinumab in Crohn's disease patients: the SUSTAIN Study. Inflamm Bowel Dis 2022;28(11):1725–36. doi:10.1093/ibd/izab357.
[45] Chien TH, Puig A, Khuong T, Kouhkamari MH, Che S, Huang TH. An Australian real-world study of treatment persistence of Ustekinumab in Crohn's disease. Biologics 2021;15:237–45. doi:10.2147/BTT.S310076.
[46] Ding Z, Obando C, Muser E, Kozma C, Slaton T. Real-world persistence, maintenance dosing, and pre-post corticosteroid and opioid use among Crohn's disease patients with prescription claims for Ustekinumab in the USA. Drugs Real World Outcomes 2021;8(4):565–75. doi:10.1007/s40801-021-00264-5.
[47] Sipponen T, Af Bjorkesten CG, Hallinen T, et al. A nationwide real-world study on dynamic ustekinumab dosing and concomitant medication use among Crohn's disease patients in Finland. Scand J Gastroenterol 2021;56(6):661–70. doi:10.1080/00365521.2021.1906315.
[48] Teeple ASJ, Mallampati R, Adams C, Waters D, Muser E. Persistence, dosing, and other treatment patterns among Crohn's disease patients initiating biologics in United States. Crohn's Colitis 360 2021;3(4). doi:10.1093/crocol/otab076.

Exhibit "F4"

This is Exhibit “F4” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

_____

A Commissioner for Taking Affidavits, etc.

Arash Rouhi

Janssen Inc.

19 Green Belt Drive
Toronto, ON M3C 1L9

www.janssen.com/canada

April 30, 2018

Re: Green Shield Canada Pilot Program to Remove Funding from Existing REMICADE® Patients

Dear

Recently, you may have been made aware that Green Shield Canada has launched a pilot program to test its new Biosimilar Switching Policy. As a Janssen BioAdvance® patient insured by Green Shield Canada, we wish to notify you that if your employer has agreed to be part of this pilot, these changes may force you to switch from your current REMICADE® treatment to an infliximab biosimilar.

Janssen is aligned with Health Canada in that the decision to switch a patient should be made by the treating physician in consultation with the patient after taking into account available clinical evidence. We do not support Green Shield Canada's new policy because it takes away funding from previously covered patients, without a medical reason for doing so, and because, as a result, it may remove treatment options for physicians and their patients.

Janssen has tried to reach an agreement with Green Shield Canada to preserve treatment choice but has been unsuccessful to date. We are therefore informing you of this change in Green Shield policy and notifying you that as a result, if the Green Shield Canada Biosimilar Switching Policy affects your coverage, Janssen will not provide you with financial support for your REMICADE® treatment. Janssen also does not offer the Janssen BioAdvance® Program to patients who are not on, or who are switched off, a Janssen product.

To confirm your status with Green Shield and to find out how the pilot program may impact you, we suggest that you contact Green Shield Canada or your employer's benefits administrator.

Sincerely,

Andy Williams
Vice President, Immunology
Janssen Canada

Exhibit "F5"

This is Exhibit “F5” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

The BioJAMP Dedicated Team

Amélie Faubert, VP, Institutional Affairs & Specialty Products

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[redacted]

Exhibit "F6"

This is Exhibit “F6” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

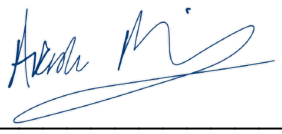
A Commissioner for Taking Affidavits, etc.

Arash Rouhi

REDACTED

Exhibit "F7"

This is Exhibit “F7” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.



A Commissioner for Taking Affidavits, etc.

Arash Rouhi

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

Johnson & Johnson To Host Enterprise Business Review

EVENT DATE/TIME: DECEMBER 05, 2023 / 3:00PM GMT

DECEMBER 05, 2023 / 3:00PM GMT, Johnson & Johnson To Host Enterprise Business Review

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PRESENTATION

Operator

Ladies and gentlemen, at this time, we ask that you please turn all cell phones and electronic devices on silent. And please note that recordings, photography and screenshots of any kind are prohibited throughout the program. Thank you.

Welcome to the Johnson & Johnson 2023 Enterprise Business Review Meeting. Please note that today's presentation includes forward-looking statements and non-GAAP financial measures. We encourage you to review the cautionary statement included in today's presentation, which identifies certain factors that may cause the company's actual results to differ materially from those projected. These factors are described in our SEC filings, which are available at investor.jnj.com in addition to reconciliations of any non-GAAP financial measures used in today's presentation.

Additionally, several of the products and compounds discussed today are being developed in collaboration with strategic partners or licensed from other companies. These slides acknowledge those relationships.

(presentation)

Operator

Ladies and gentlemen, please welcome Vice President, Investor Relations, Jessica Moore.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

Hello. Welcome, everyone. Thank you for joining us today, both in person and virtually. On behalf of the entire leadership team, it is my pleasure to welcome you to Johnson & Johnson's first-ever Enterprise Business Review, highlighting both Innovative Medicine and MedTech. We have a great day ahead of us, and we are excited for our many incredible leaders to provide you with insights into our long-term strategy.

When preparing for today, we did benchmarks of industry standards. MedTech companies tend to provide an outlook that's 2 to 4 years out. While pharmaceutical companies tend to provide an outlook that is 5 or more years. Given this, we will be providing long-term views for our MedTech business through 2027 and for our Innovative Medicine and enterprise as a whole through 2030. While we'd be quoting several financial figures throughout today, unless otherwise stated, financial figures represent non-GAAP measures and exclude the impact of currency.

Now looking at today's agenda. Joaquin will kick us off with an enterprise overview. You will hear from our MedTech leaders, including the opportunity for Q&A. Next, we will have a 1-hour break where we welcome those of you attending in person to visit our leaders at the live exhibits.

Exhibits can be found in both Siebert Hall and Freedom Hall on the 6th and 7th floors, where you'll also be able to enjoy lunch. For those of you that are joining us online, we encourage you to take advantage of our summaries for each exhibit available at our Investor Relations website.

Following the break, you will hear from our Innovative Medicine leaders, including the opportunity for Q&A. Joe will then walk you through our long-term financial goals and capital allocation strategy. We will conclude with enterprise Q&A. Following the Q&A, the exhibits will open for one last time. For those of you attending virtually, questions can be submitted for any Q&A session through the Ask a Question feature on our webcast page.

For your convenience, all exhibit summaries, the presentation material or any other content from today's session can be found on our Investor Relations website. When we conclude, many of you will receive an e-mail asking to complete a short survey. Your feedback is important to us so we can continuously improve, so we appreciate if you could take your time. Thank you all again for joining us today and your continued interest in Johnson & Johnson.

It is now my distinct honor to hand it over to Joaquin Duato, Chairman and CEO of Johnson & Johnson.

Operator

Ladies and gentlemen, please welcome Chairman and Chief Executive Officer, Joaquin Duato.

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

Hello, everyone, and thank you very much for joining us today. It is an incredible moment for our company. This morning, we were proud to be able to ring the bell of the New York Stock Exchange, and I felt it as a symbolic moment for our company. In many ways, this was the starting bell for the new Johnson & Johnson.

We have entered a new era, one that is exclusively focused on medical technology and innovative pharmaceuticals. We remain the largest and most diversified health care products company in the world. We are an innovation powerhouse. And with the separation of our consumer business, we have a stronger growth and margin profile, and we are more focused and more agile.

You know, I have been at Johnson & Johnson for more than 30 years. And let me tell you, I have never been more excited about the future of our business. The breadth of our portfolio, the depth of our pipeline is unique in our industry. So what does that mean? It means that we can innovate across the entire patient pathways in ways no other company in the world can. It's our work in oncology, in vision, in robotics, in cardiovascular, areas where we are transforming care across both our Innovative Medicine and MedTech businesses.

This is also an incredible time for our industry. As you have heard me say before, I believe that science and technology will advance human health more in this decade than we have seen in the last century. We're going to see more effective and more personalized treatments, earlier intervention and smarter and less invasive health care. And I'm convinced that Johnson & Johnson, it's going to be the company leading in the next wave of innovation.

As we evolve as a company, our purpose and our credo remain the foundation. Our commitment to our credo is stronger than ever. That's why I was so proud to have all our credo stakeholders represented at the podium in this morning's bell ringing. We had our patients, doctors, nurses, employees and also some of you, our investors.

So today, alongside of many of our talented leaders, I'm excited to talk to you about our company's vision and our confidence in our future. We are going to cover the areas that you told us you wanted to hear about. What's our overarching strategy, vision and path forward as the new Johnson & Johnson, our capital allocation priorities and approach to M&A and how we will accelerate growth in the back half of the decade.

So let me start with some of the top headlines. For the first time today, we are announcing guidance for 2024 with anticipated full year operational sales growth of 5% to 6% and adjusted operational earnings per share growth of 7.3% at the midpoint. This pace of growth reflects the strength of our portfolio and the progression of our pipeline.

We also expect to grow operational sales by more than 3% in 2025, which is the first year of STELARA biosimilar entrants in the U.S. This is a claim that few other companies can make when a product of this size faces biosimilar competition. And looking further ahead, we are projecting an operational sales compound annual growth rate of 5% to 7% from 2025 to 2030.

And here's how we will achieve this remarkable growth. In MedTech, you know my ambition is to make our MedTech business our best-in-class performer, and we are doing just that. We will accelerate growth at the upper range of our MedTech markets through commercial execution, differentiated innovation and by moving into higher-growth markets like you saw last year with the acquisition of Abiomed. We are increasing MedTech R&D investment and have doubled the value of our pipeline since 2018. And with 1/3 of our MedTech revenue expected to be generated by new products by 2027, we have confidence in the trajectory of our MedTech business.

I know you are also interested in the exciting pipeline of our Innovative Medicine business and how it will translate to growth in the back half of the decade. So let me also give you some headlines about Innovative Medicine. By 2030, our industry-leading pipeline and portfolio is expected to deliver more than 10 assets that have the potential to generate over $5 billion in peak year sales and further, 15 assets that have the potential for $1 billion to $5 billion in peak year sales.

Let me now move to our pipeline. By 2030, we expect to deliver more than 20 novel medicines and more than 50 product expansion filings. Our portfolio reflects our rapid shift to areas of high innovation and high growth, which you're already seeing with our progress in cell therapy, multispecific antibodies, gene therapy and with our oral peptide.

Our confidence is built on a strong foundation, something that our investors have come to expect from Johnson & Johnson. We are deeply committed to maintaining a robust credit profile, strong cash flow generation and a healthy balance sheet. This enables us to execute our capital allocation priorities and invest strategically to unlock accelerated growth for our business over the long term. This also is what has enabled us to deliver 61 consecutive years of increased dividends. When coupled with share repurchases, in total, we have returned more than 60% of 5-year free cash flow to shareholders.

Globally, we are powered by an incredible team of 130,000 people. That includes more than 26,000 people working in R&D, innovation and engineering and approximately 6,000 people in data science and digital who are embedded across our business. It's their work

which is accelerating our innovation.

In the past 5 years, our business development teams have assessed thousands of opportunities to innovate, investing more than $30 billion in M&A and upwards of $2 billion in licensing deals. These investments and collaborations continue to strengthen our pipeline with new investigational assets like our targeted oral peptide, CD20 targeted CAR-Ts, and with breakthrough innovations that have already reached patients like MONARCH, VELYS or CARVYKTI.

And our organic investment is significant with over $60 billion invested in R&D over the last 5 years, making us one of the top R&D investors in all of life sciences. You will be hearing more about our capital allocation strategies and M&A strategy from Joe this afternoon. Fundamentally, our approach remains unchanged. Our business development and innovation investments are assessed through a scientific, strategic and financial lens.

Our financial strength allows us to execute deals of all sizes. And from day 1, we are focused on delivering on the promise of a transaction like we are doing today with Abiomed. Our innovation engine has delivered 18 new medicines in the last decade and nearly 100 new MedTech product introductions since 2018. It is an engine that makes us the only company that can simultaneously advance robotic solutions across endoluminal, orthopaedics and general surgery. It is an engine that has produced a broad and diverse portfolio with 26 products and platforms that each generate more than $1 billion in sales annually.

The plans that you will see today will enable us to deliver strong and competitive growth. It will help us accelerate value creation. They will lead us into the next wave of innovation and they will transform health care. As you can see, we are evolving. We are driven because we believe health is everything. Our teams are determined to make an impact, and we are fueled by breakthrough science and transformational technology. Thank you, again, for joining us today on a journey into the future of medicine.

(presentation)

Operator

Ladies and gentlemen, please welcome Executive Vice President, Worldwide Chairman, MedTech, Tim Schmid.

Tim Schmid ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, MedTech***

Hello, everyone. It is a pleasure to be with you at such an incredible moment in our industry. I've been with Johnson & Johnson in MedTech for 30 years, in fact, my entire career. And during this time, I've experienced firsthand how MedTech as an industry has grown, driven considerably by the work we do at Johnson & Johnson. Now I am truly passionate about people and about health care. My mother was a palliative care nurse who worked well into her 60s, working with patients during their most vulnerable moments. And it was through her that I found my own calling and developed an affinity for health care and the important purpose that we all share here at Johnson & Johnson.

I started working right on the front lines of MedTech as a clinical sales specialist in Canada. And that's where I first learned that our job in this industry is ultimately helping to make clinicians better at what they do, which is improving and saving lives. And it's with this spirit of partnership in mind that I've worked closely with clinicians throughout my career to help build multibillion-dollar MedTech businesses here in North America, in Europe, and most recently in Asia, where I was at the forefront of establishing Johnson & Johnson MedTech's #1 market leadership position in that region.

Now I am proud, along with the talented team you will meet today to have been part of Johnson & Johnson MedTech's growth story and that turnaround over the last 5 years. And I'm honored to be here to represent the work of our dedicated associates around the world. You've already heard Joaquin speak about building a best-in-class medtech company, and that is exactly what we are doing.

As I step into this new role, I'm committed to building even further on the progress we've already made. And while I recognize, like you, that we have more work to do, I'm focused on further advancing our impact and our competitiveness. Our goal is clear and it is to be #1 or #2 in every market that we compete.

So let's get on with it. Today, we will ground you in the robust opportunity we enjoy in MedTech. We will review our accelerated business performance, and we will also show you how we plan to deliver operational growth in the upper range of the markets in which we compete moving forward.

You know, more than ever before, the world is demanding greater medical intervention. COVID-19, as you all know, really put the importance of public health directly in the spotlight and made people more connected to their personal health and well-being.

We also know that a rapidly aging global population is driving a growing disease burden. And as a result, health care spending is at an all-time high. At the same time, the world is expecting more from medical intervention. People want medical technology to be smarter, less invasive and more personalized to them individually. With our trusted portfolio, our global reach and scale and our differentiated pipeline, Johnson & Johnson MedTech is uniquely positioned to meet this demand, which will grow our business while also bringing life-changing and life-saving technologies to patients all around the world.

As you know, today, we are the second largest medtech company globally. Our end markets are more than $100 billion, growing at a weighted average of 5% to 7%. And we expect our business to grow operationally in the upper range of the markets in which we play. Within this dynamic segment, we're focused on continuously increasing our exposure to higher-growth markets where we can tackle the most pervasive and complex health challenges, and in doing so, impact even more patients.

So as you know, we've been on a journey to accelerate our growth and enhance our competitiveness. Our highly diversified business consists of 12 $1 billion platforms. In fact, 4 of those platforms deliver more than $2 billion annually.

In addition, most are either 1 or 2 in the markets in which we compete, and over the past 5 years, a majority have either maintained or gained market share. And 5 of our priority platforms have double-digit market share leads over our nearest competitors.

Across Johnson & Johnson MedTech, we have accelerated our performance over the last several years to become more competitive, and we will continue to be absolutely relentless here. For the third straight year, we expect our organic sales growth to be at least in line with or ahead of our competitive composite, which as you all know, is a group of peer companies that we reference in our annual report.

And when you compare our third quarter 2023 year-to-date adjusted operational sales growth of 7.4% to full year 2017 when we grew 1.5%, you'll see that we delivered, on average, 1 point of incremental growth each and every year. Now let's face it, this is no small feat for the second largest medtech company globally, particularly when most of the companies in our competitive composite are half of our size. Also, while we have, like our peer set, seen a positive impact resulting from COVID-19 procedure recovery, it is important to note that this has not been the main driver of our performance. Instead, our performance is a result of our commitment to innovation and our continued focus on shifting our portfolio into higher-growth markets. This, along with robust commercial execution and our expansion into higher-growth geographies, especially in Asia.

Now let me dive a little deeper into the role organic innovation is playing in the evolution of our portfolio to higher-growth markets. Our world-class scientists and engineers are partnering with leading clinicians around the world to deliver greater impact for patients. And our goal is to continue investing heavily in research and development and to increase its productivity. In fact, last year, we invested $2.5 billion in R&D, one of the highest overall R&D spends among our competitive composite. And we've increased our investments as a percentage of sales from 6.5% in 2018 to 9.1% last year. This commitment to R&D has allowed us to launch, as you heard from Joaquin, nearly 100 new products since 2018.

We've also doubled the value of our pipeline. And as a result, we expect that 1/3 of our revenue in 2027 will be generated by new products. We've also, as you know, increasingly employed inorganic innovation to accelerate the shift of our portfolio into high-growth markets. In the last 5 years, we've invested $22 billion in M&A, and at the same time, exited lower-growth markets. With nearly 40 venture capital investments, we're working aggressively to identify new opportunities to address critical unmet needs. For example, as you know, cardiovascular is one of health care's highest unmet needs and one of the fastest-growing global markets in medtech. This is an area of focus for us within our Interventional Solutions portfolio, and we have now successfully integrated Abiomed, the world leader in heart recovery into our portfolio, and we are tracking ahead of our deal model.

Building on this commitment to cardiovascular, we also announced last week the acquisition of Laminar, a company focused on eliminating the left atrial appendage to prevent stroke in AFib patients. These 2 investments in truly differentiated innovation, coupled with our existing global market leadership position in electrophysiology further reinforces our commitment to growing Johnson & Johnson's position in cardiovascular.

So you may ask, what's been the net result of this commitment to both organic and inorganic innovation? Well, half of our portfolio is now projected to be in higher-growth markets this year. That's compared to roughly 20% in 2018, and you can rest assured we intend to build on this momentum. Okay. So I've talked now about where we've come from and what we've accomplished over the last several years. Let's now focus on what you can expect from us moving forward.

Our MedTech business aims to further improve our financial performance and ultimately create more value for Johnson & Johnson by enhancing our focus on 3 key value drivers: number one, advancing our differentiated pipeline and continuing to shift our portfolio into high-growth markets; two, expanding our reach and scale around the world; and three, building operational resilience across our portfolio. With this, we expect to grow operationally in the upper range of the markets in which we play.

Let's now take a deeper look at these 3 key value drivers. First, we know that incremental innovation alone is insufficient to achieve our goals. We have a balanced approach to innovation and that we're focused on differentiated product upgrades while also placing big bets on building a pipeline of truly differentiated innovation to address significant unmet needs. You'll hear shortly from Ahmet Tezel, our Head of R&D, but first, let me share some highlights.

Johnson & Johnson has been at the forefront of surgery from the very early days of our company founding, and we remain the global market leader in surgical technologies today. And we continue to innovate across open, laparoscopic and robotic surgery to ensure our continued leadership.

As recently announced, we plan to submit an Investigational Device Exemption to the FDA in the second half of 2024 for OTTAVA, our soft tissue robotics platform. In orthopedics, we keep nearly 7 million people moving each year. We continue to advance differentiated programs with the potential to change the current standards of care, including smart plating systems and the continued expansion of VELYS, our robotic-assisted solution.

And we are advancing our Interventional Solutions portfolio, especially, as I mentioned earlier, in cardiovascular. For example, we expect to maintain our position as the clear market leader in electrophysiology through updates to our carto system and our pipeline of solutions in pulsed-field ablation.

We're also very excited about our entrance into heart recovery with Abiomed. Cardiovascular disease is a leading cause of death worldwide, and all forms of the disease lead to heart failure. Abiomed has made heart recovery possible, and J&J is now the undisputed world leader in heart recovery.

Our product pipeline has 3 additional Impella heart pumps under development or in clinical trial as we work to make the Impella pumps smaller, smarter and even more connected.

And in our Vision business, we meet the eye health needs of 40 million patients around the world every year. Today, we are the global market leader in contact lenses with ACUVUE. We're also working to control myopia progression with our therapeutic contact lenses and to enhance vision quality for cataract patients through our TECNIS intraocular lenses.

So to summarize, our differentiated pipeline, combined with continued inorganic innovation will further shape our portfolio to maximize growth, create value and penetrate high-growth end-state markets.

Our next key growth driver, continued global expansion. Today, as you probably know, 50% of our revenue is driven outside of the U.S. And while the U.S. will remain an absolute priority for us, given that it is the largest medtech market, continued global expansion will

prepare our growth into the future. And to facilitate this growth, we will continue to disproportionately deploy resources into countries where we have the highest potential for growth.

And we know how to compete globally, and there is still tremendous opportunity. This is where the scale of Johnson & Johnson really matters. For example, in the Asia Pacific region, this has been -- we have significant unmet needs and a vast and growing health care sector. In fact, today, 60% of the world's population, and as a result, 60% of the world's patients call this region home. By 2050, 1 in 3 will be over the age of 65, and as a result, highly active consumers of health care. We are the #1 MedTech company in this region, which is home to the second and the third largest health care markets in the world, China and Japan.

So you may ask, well, what sets us apart as a global player? Well, we have several key differentiators. Firstly, a global network of trusted relationships with clinicians. We have highly trained clinical sales expertise across multiple segments. We have deep regulatory capabilities which are critical to market access.

And finally, world-class professional education, which is fundamental to technology adoption in MedTech. Together, these capabilities enable us to penetrate more markets around the world faster with our highly differentiated premium products. For example, we'll help recover more hearts globally by expanding Impella heart pumps. Today, 80% of our Abiomed sales come from the U.S. Now Johnson & Johnson's global infrastructure is opening doors for rapid expansion.

Likewise, in robotics -- in robotic surgery, last month, our MONARCH platform became the first minimally- invasive robotic-assisted technology approved for peripheral lung procedures in China. There are more than 2 million patients diagnosed with lung cancer each year around the world, and nearly 40% of these patients live in China. Also, in just 2 years since we began the commercialization in the U.S. of our VELYS robotic assisted solution, more than 35,000 procedures have been performed globally. It's already commercially available in 15 markets, including the U.S., Europe and Asia Pacific and will continue to expand in 2024 with the recent CE Mark approval.

Shifting now to our high-growth electrophysiology platform. Globally, less than 5% of patients who would benefit from cardiac ablation actually have access to it. We're working to further expand treatment pathways to ensure more patients get access to this life-changing intervention.

Now finally, let me touch on the theme of operational resilience, which I know is incredibly important to you. We are proud of the progress we have made accelerating growth. That said, we also understand that building further resilience in our operations will be key to navigating a dynamic macro environment while also advancing our competitiveness and improving our operating margins.

Firstly, we are big and complex, and we will work even harder to meaningfully simplify our ways of working, to accelerate our speed of decision-making, to reduce costs and remove operational barriers that may have the potential to slow our people down. Secondly, we are reimagining our operations and supply chain capabilities to support both the top line growth that we're expecting but also to improve margins and generate cash flow to fund our future.

We're also strengthening product reliability and customer loyalty by localizing manufacturing, sourcing and innovation where it makes sense. And finally, the continued digitalization of our business will underpin absolutely everything we do across the product life cycle and customer journey from the way we develop new innovations to the way we engage with customers and patients. For example, we're harmonizing our IT systems to reduce complexity and increase overall efficiency and productivity.

We are in an incredible moment in our industry because medical technology is fundamentally transforming health care. Johnson & Johnson MedTech is on a path to even stronger performance, which means better outcomes for all of our stakeholders, for patients, for clinicians, for our employees and, of course, for our shareholders. And many of our global leaders are here today to tell you how we expect to continue to grow operationally in the upper range of our markets.

We have a highly competitive team united by our purpose to improve and save lives. You know, throughout Johnson & Johnson's history, this purpose, along with the values embodied in our credo have guided us, and they will continue to drive us to tackle the most pervasive

and complex health challenges. Thank you.

Operator

Ladies and gentlemen, please welcome company Group Chairman, MedTech R&D, Ahmet Tezel.

Ahmet Tezel ***Johnson & Johnson - Company Group Chairman, MedTech R&D***

Good morning. Medtech is fundamental to a new era in health care, and Johnson & Johnson MedTech is fundamental to the industry where devices are smarter, less invasive and more personalized. A year ago, I took on the privilege of leading R&D at Johnson & Johnson MedTech, where teams have been progressing in health care for over a century through deep medical and engineering expertise. Working alongside physicians, surgeons, hospital systems and payers, we've gained strong understanding of providers' needs, their patients' needs and the global health ecosystem. And this expertise is more important than ever.

Globally, we know that health complications and diseases are only growing, putting enormous pressure on health systems and governments. And at the same time, patient expectations and rightfully so are becoming more demanding. As patients, we all want better access to care that allows us to get back to our daily lives faster and easier. And that's why we turn to medical technologies to help deliver on what the world needs from health care. Johnson & Johnson is uniquely positioned to deliver those technologies with a best-in-class MedTech segment.

Our R&D organization is driving market-leading innovation with clinical capabilities, regulatory know-how and technical depth that only Johnson & Johnson can deliver. It's the breadth of our portfolio, our global reach and the connection to health care professionals. It's also our scale. As the second largest medtech company, we invest $2.5 billion in annual R&D spend, and nearly 15% of this investment goes to preclinical and clinical evidence generation.

There are many qualities that set Johnson & Johnson MedTech apart, like our broad footprint around the world with more than 35 global innovation hotspots. Across Europe and Middle East, we have strong IP and expertise in 3D printing, biomaterials, sensors and software development.

In China, we are driving localized R&D with deep reach to physicians and patients through collaborations with key hospitals and advocacy groups. And across the U.S., we are developing the next generation of robotics and designing next-generation capital equipment.

The broad footprint across the R&D organization allows us to deliver differentiated innovation, and this is how we do it. We drive complex product development. The number of U.S. Class III development programs in our pipeline is now more than 15. Class III products require the most rigorous FDA evaluations, critical to developing innovative solutions for patients with also higher barriers to entry for other competitors.

We unlock the potential of data science. With the use of AI and computational modeling, we have been able to analyze large data sets. We then take those insights to refine our innovations for better performance and for better patient outcomes.

And we collaborate with the world for the world. We are agnostic about the source of innovation in our portfolio, constantly scanning the market for the next groundbreaking medical pathway. Since 2020, we have initiated 21 JJDC investments and closed 18 early-stage collaborations through J&J innovation, ensuring a strong network of external partners and giving us access to a new frontier of innovation.

Across the industry, we know that R&D organizations are feeling more pressure to deliver innovations in a complex regulatory, clinical and supply chain landscape. You know, it reflects our strength that through these pressures, we have nearly doubled the R&D productivity since 2018 against an increasing pipeline value.

We have launched nearly 100 major products since 2018. And in 2022, we had more than 80,000 patents across our platforms, the most IP in the medtech industry.

We are growing R&D investments faster than our sales and have doubled the value of our pipeline since 2018. And as we look to the future, we believe the momentum will continue. Nearly 1/3 of our 2027 revenue expected to be generated by new products. And we will drive stronger integration and collaboration across our engineering, regulatory, clinical and supply chain teams to accelerate our robust pipeline of market-shaping innovation.

In each of our core areas, we are seeing exciting innovations that are delivering smarter, less invasive and more personalized solutions. We believe these innovations will sustain our top-tier growth over the next horizon.

Let me start by talking about our CARTO 3D mapping system, the command center for electrophysiology procedure navigation. It uses 4 million lines of code to guide our advanced catheters to help identify ablation targets and pinpoint treatment for heart arrhythmias like AFib and tachycardias, which affect more than 38 million people worldwide. Version 8 of this system is the first version supporting machine learning algorithms to automatically map the anatomy. It also provides hospitals with post-case analytics and clinical insights.

Besides CARTO, we have also developed CARTONET, a cloud-based application which has gathered more than 75,000 cases to date, including details about the ablation location, the force, the stability and duration. The more data we collect, the better the outcomes we can help support. This is the promise of a connected medtech. The investigational pulsed-field ablation portfolio you saw in the previous pipeline will also integrate with CARTO 3D mapping system, elevating our leadership in electrophysiology to new heights.

In orthopedics, we have a comprehensive biomaterials portfolio with solutions like FIBERGRAFT, the first bone graft substitute using boron-based bioactive glass to enhance cell proliferation for bone growth and bone health. This is really important for patients to heal properly after surgery.

We're also excited about the potential to bring new robotic offerings in the spine and partial knee space. And as we look to the future of orthopedics, we're building embedded sensors, smart end effectors and AI-based planning to deliver that personalized enabled tech.

In our Surgery business, we're expanding the indication of MONARCH, the first and only flexible robotic platform cleared for the use of bronchoscopy and urology procedures. MONARCH's recent approval in China for lung procedures is a first for the country. China has one of the highest incidents of lung cancer with over 40% of the world's cases. This is a huge opportunity for us to address a critical unmet need.

As Tim mentioned, we shared more information about the time line and design features for OTTAVA last month. This system will have the exclusive access for our Ethicon Instrumentation, where we have been the market leader for more than 100 years. You will hear more about these innovations from my colleagues and be able to see some of them firsthand at our booths.

We're also advancing underlying capabilities that will support a number of our innovations. For example, advanced visualization will be critical for the future of surgery. Our advanced visualization capabilities will enable things like anatomical measurements or critical structure identification, which effectively lights up structures like veins and can even identify tumors.

In our Orthopedics business, our TELIGEN system that you see here allows surgeons to see into the implant cavity in minimally invasive spine procedures. This means surgeons will see a never-before-achieved level of visibility of a patient's specific anatomy, enhancing their intraoperative decision-making.

Let me close by underlining the significant opportunity Johnson & Johnson MedTech has to lead the way in delivering smarter, less invasive and more personalized solutions for today and in the future. Johnson & Johnson MedTech can bring together a mix of clinical capabilities, regulatory know-how and the technical expertise at scale.

Our differentiated portfolio of market-shaping technologies is going after the biggest unmet needs and high-growth areas like cardiovascular, vision correction and robotics. And we are well positioned for top-tier revenue growth with game-changing innovations, including OTTAVA, MONARCH, VELYS, PFA, Impella ECP and ACUVUE Abiliti, that will raise the standard of care for patients and drive

the future of health care for the next decade and beyond. Thank you.

Operator

Ladies and gentlemen, now joining us via video, please welcome company Group Chairman, Cardiovascular and Specialty Solutions, Celine Martin.

Celine Martin ***Johnson & Johnson - Company Group Chairman, Cardiovascular & Specialty Solutions***

I'm sorry to not be with you in person today, but I'm pleased to have the opportunity to share my excitement for our electrophysiology business. Cardiovascular disease is the #1 cause of death globally. And as Tim mentioned, we're keen to expand our portfolio in high-growth cardiovascular markets. Last year, we completed the acquisition of Abiomed, the world leader in heart recovery. And just last week, we are pleased to announce the acquisition of Laminar, a company focused on eliminating the left atrial appendage to prevent stroke in AFib patients. And when it comes to AFib, our mission is clear, to cure atrial fibrillation.

We're proud to be #1 in the electrophysiology space. This is a $7 billion market that is expected to grow 11% to 13% over the next 5 years. And this is a market we've shaped with over a decade of double-digit growth, winning share and delivering innovation for patients around the world. AFib is a growing epidemic. It is a condition that affects nearly 38 million people worldwide today. And by 2050, 5 million new patients will be added to the pool each and every year. So why does it matter?

Well, it means that 1 person out of 4 over the age of 40 would experience AFib in their lifetime, and AFib patients are 5x more likely to experience a stroke and their mortality risk that's increased twofold. Fortunately, there is a cure for AFib. It is called cardiac ablation. Yet less than 5% of AFib patients receive an ablation today. As a market leader, we have a responsibility to reach more patients and elevate standards of care. And that's exactly what we've been doing.

Over the last 10 years, through an impressive cadence of innovation, we've been able to increase success from 66% to now 86%, and 86% is considered best-in-class clinical success. This was only made possible with our latest RF ablation catheter, QDOT MICRO, which is known for its very high-power short duration ablation.

We've also made remarkable progress reducing procedure time going from what used to be 3.5 hours in the past to less than 1 hour today. And we are eliminating exposure to radiation with the only FDA-approved zero fluoro workflow. You can only get that when you use the CARTO navigation system. This is best for patients but also best for clinicians who no longer have to wear heavy protective gear when they work in the lab every day.

Another way to help patients is faster access to therapy. Why? AFib begets AFib. The longer patients wait, the worse the outcome will be. With our ER to EP program, we'll be partnering with health care systems to optimize referral pathways for patients presented to the emergency room with AFib. And on average, we're seeing a 70% decrease in time to ablation where such programs are in place. This is a win-win for health care systems and for patients.

We're also proud of the momentum we have with programs like Get Smart About AFib. We've created the world's largest online AFib patient community where we share vital information on the signs and symptoms of AFib, and we educate on the benefits of cardiac ablation.

You know I'm often asked, what is the secret sauce that has made J&J MedTech so successful in the field of electrophysiology? And at the end of the day, it comes down to our products, our people, and our close partnership with the AFib community.

So how do we do it? First, we take a very focused approach to innovation. We're solving for unmet needs, locate where to ablate, deliver better lesions, simplify the procedure and eliminate fluoroscopy. And we work with EPs every step of the way in our development process. Then we use our unmatched scale to deliver innovation to the marketplace. We have the biggest reach on access of any company in the EP space. We have the world's largest installed base of mapping systems. We have the largest network of mappers, twice the size of our nearest competitor.

Our CARTO mappers are highly trained professionals known to be trusted partners to EPs. They share best practices and they enable consistency in workflows and outcomes. And finally, underpinning all of this, we have the most comprehensive professional education in the medtech industry. We expect pulsed-field ablation or PFA to be the next chapter in elevating standards of care.

So let me explain how we plan to tackle it. First, we are delivering a PFA ecosystem, one that is, from the get-go, fully integrated with our CARTO 3 mapping system. 3D mapping has been the cornerstone of any cardiac ablation procedure over the years. Why? Because when you're operating inside the heart, you need to know where you are and where you're going. CARTO is the only system that integrates parameters such as tissue proximity indicators, contact force measurement and ablation index. These tools provide Eps with real-time feedback that have proven to be critical for lesion durability and long-term outcomes in RF today and we expect it will be the same for PFA.

Next, looking at our catheters. We're advancing a full portfolio of options, multi-electrode, focal, large focal and single shot, all designed to tailor therapy to patient anatomies and physician preferences. And here again, we're learning from our experience, it drives clinical success.

So let's zoom in on each catheter. First to market will be the VARIPULSE multi-electrode catheter. We shared interim 12-month data from our inspIRE study in Europe, showing 79% clinical success and our full results look even better. We'll share more about it next month.

Next up, and where we expect to see the most rapid uptake in our PFA portfolio is our Dual Energy THERMOCOOL SMARTTOUCH SF Focal-tip Catheter. We completed enrollment in our EU study in June, and we are now in the 12-month follow-up period. We are particularly excited about this technology. It has the same look and feel as the RF-only version, which is currently #1 in the category.

And it is important because ablation involves a lot of muscle memory, and this is a technology EPs already know and trust.

We're also progressing OMNYPULSE, our large tip focal technology, which is currently enrolling in our European study. And last but not least, we're making strides in the development of our next-generation single-shot PFA technology. We're making tremendous progress towards our commercial launch readiness. And I'm pleased to share that the TRUPULSE system has just received CE Mark, truly paving the way for PFA solution to enter the market in Europe.

Here is the big takeaway. We're very bullish about the AFib market for 3 key reasons: number one, this is a growing underpenetrated markets while we have real opportunities to deliver life-changing ablation solutions for AFib patients; number two, we are the undisputed market leader today. Through a focused approach, we are developing groundbreaking innovation that delivers best clinical outcomes, short procedure times and zero fluoro workflows.

Finally, we're ready to win in PFA. We're delivering a differentiated PFA ecosystem that is integrated with CARTO from the get-go, coupled with our unmatched network of CARTO mappers to support electrophysiologists, we are well positioned to win. Millions of patients with cardiac arrythmias are waiting and counting on us to make a difference in their lives. Together, we'll help patients with AFib live the lives they want.

Operator

Ladies and gentlemen, please welcome Global Head, Heart Recovery Michael Bodner.

Michael Bodner ***Johnson & Johnson - Global Head, Heart Recovery***

Abiomed is more than the leader in heart recovery. Abiomed created the field of heart recovery, and our innovation has a demonstrated record of double-digit growth. Together, alongside the industry-leading work you just heard about in electrophysiology, J&J MedTech is poised to lead in the high-growth cardiovascular space. Coronary artery disease and heart failure are global epidemics, so here's the opportunity we have today within our 5 core geographies.

We are currently treating less than 3% of the total addressable market of 2 million patients, and heart failure remains one of the highest

unmet need categories. It's also one of the most expensive to treat. Abiomed's Impella heart pumps offer safer and less invasive treatments for this growing patient population. Heart failure, is pump failure, and it's the end stage for all cardiovascular disease.

So our goal is to drive therapy adoption and expand beyond our core geographic markets. And Abiomed is proud to pursue this goal as a part of Johnson & Johnson where we are already performing ahead of our deal model expectations. Our portfolio today addresses a large patient population of high-risk PCI and cardiogenic shock.

Next, we'll move into other manifestations of heart disease like acute decompensated heart failure and chronic heart failure. So now let me share more about Impella. When we injure a muscle in our body, we take the time to rest so we can heal. The same is true of our heart, except it's our most important muscle. It also needs to rest and recover, especially after a trauma like heart failure. And Impella makes this possible by providing temporary circulatory support. It's inserted percutaneously in the cath lab or surgically with a small incision in the operating room. It's placed in the left or right ventricle of the heart. It's turned on and it takes over the heart's pumping function until it's turned off and removed. It sounds simple but blood is very fragile. It's extremely challenging to safely pump blood with enough force to circulate it around your body. That's the magic of Impella. It moves blood safely.

Currently, we have 3 Impella heart pumps on the market. Impella CP and Impella 5.5, they support the left side of the heart. Impella RP supports the right side of the heart. For more than 20 years, we've continually improved Impella heart pumps, building on the strong foundation laid by our founding scientists who are still driving our innovation today. We have no direct competitors, and the IP behind these pumps is protected by nearly 5,000 patents.

Let me give you 2 examples of the types of patients Abiomed supports. Grant Queen is a husband, Marine and former school teacher from North Carolina. Last year, Grant's heart was so weak, he couldn't even walk through his house without having to stop and rest. But Grant was turned down for heart surgery because his comorbidities made him too high risk. Instead, Dr. Samuel Turner inserted Impella CP to protect the pumping function of Grant's heart while he placed stents and open Grant's arteries. One day later, Grant returned home and is back to his regular routine. This type of high-risk procedure makes up nearly half of Impella cases.

We also treat patients who have experienced a severe type of heart attack known as cardiogenic shock. When you go into cardiogenic shock, your heart can't pump enough blood to your brain and kidneys, and they start to die. That's what happened to Hillary Stefan, a wife and mother from Oregon. She was only 34 years old when she contracted COVID-19 and then developed myocarditis. Hillary slipped into cardiogenic shock and physicians implanted the Impella 5.5. She was so sick that her medical team began discussions with their family about a heart transplant, but after only 12 days supported by Impella, Hillary's heart had rested and recovered. Impella was removed and Hillary returned home to her family with her native heart.

Here is the unfortunate data. 50% of cardiogenic shock patients die. But with best practice, including early use of Impella, cardiogenic shock patients can have a survival rate greater than 80%. Our priority is to make Impella life-saving technology available to more patients around the world. And here are our 4 key growth drivers: one, indication expansion; two, geographic expansions; three, physician training; and four, new product introductions.

First, indication expansions. We are investing significantly in randomized controlled trials to drive adoption and make Impella the standard of care. STEMI DTU is studying if Impella can reduce heart muscle damage after a serious heart attack. The study is estimated to complete enrollment in late 2024 or early '25. If successful, this will lead to a new treatment option for nearly 200,000 patients in the U.S. alone. PROTECT 4 and RECOVER 4 are on-label studies powered for Class I indications to make Impella the standard of care for high-risk PCI and cardiogenic shock.

We also estimate the PROTECT 4 will complete enrollment in late 2024 or early '25. And RECOVER 4 enrolled its first patient just this quarter. Class I indications will significantly increase the number of patients receiving Impella as a therapy for these disease states.

Second, with the scale of J&J, we're expanding to new geographies globally. Currently, 80% of procedures take place in the U.S. Our goal is to make Impella available to more patients around the world. Third, we have a large and expanding clinical team that is training and educating health providers on the benefits and optimal use of Impella pumps daily. And finally, we are developing new products that are

lower profile, easier to use, smarter and more connected to increase adoption.

I'd like to highlight 4 of these new products in our pipeline. Impella ECP is the world's smallest heart pump. It's 35% smaller than Impella CP and is designed for improved safety and ease of use. It just completed its pivotal study with FDA submission anticipated next year.

Impella RP Flex is the newest version of our right-sided pump. It's designed to be easier to insert and we plan for a full commercial launch in the U.S. next year, and right heart failure affects about 50,000 patients per year in the U.S.

Impella BTR is in development as a bridge to recovery pump. The vision for Impella BTR is to create a minimally invasive, long-duration pump that allows a patient to go home on support with the potential to disrupt the $1 billion-plus LVAD market. We are currently conducting an early feasibility study, and we anticipate these products will help to unlock expanded adoption. We also have another product in development that's not a heart pump.

preCardia is a new therapy for the 300,000 persistently congested acute decompensated heart failure patients who don't respond well to pharmaceuticals. Our goal is to reduce the length of stay and rehospitalization rates of these patients to improve their quality of life. In 2021, preCardia received FDA Breakthrough Device status and is currently in an early feasibility study.

So as you can see, we continue to define and redefine the field of heart recovery. Abiomed continues to innovate for the field of heart recovery with a robust pipeline of products and clinical studies to address the large global unmet need in the cardiovascular space. And as we tap into the vast resources of Johnson & Johnson, we'll continue to expand in the U.S. and internationally, raising the standard of care in heart recovery for patients all around the world. Thank you.

Operator

Ladies and gentlemen, please welcome company group Chairman, Vision, Peter Menziuso.

Peter Menziuso ***Johnson & Johnson - Company Group Chairman, Vision***

Sight is our most dominant sense. 80% of what we perceive in the world around us comes through sight. This is why our mission is to help every person see their world clearly. Johnson & Johnson is a significant force in eye health. Every year, we improve and preserve sight for more than 40 million people around the world, and we see the opportunity to reach even more.

Let me tell you where we're headed because we're just scratching the surface. There are more than 2 billion people around the world that need a vision correction, and this number continues to rise every year due to an aging population and digital lifestyle trends. As a result, the vision market is growing at 5% to 7% annually with an estimated value of $20 billion by 2027. We are growing faster than the market today, and we expect to continue to do so with our differentiated innovation.

Our portfolio is broad, and it addresses eye health needs across a patient's lifetime from childhood myopia and the pediatric eye to investigational gene therapies to treat geographic atrophy and age-related macular degeneration.

Today, I'm going to focus on 2 of our core growth platforms, contact lenses and intraocular lenses, also known as IOLs. First, the contact lens market is valued at $10 billion today and is projected to grow 5% to 7% annually through 2027. We are the #1 leader in this space, the global market leader in contact lenses with our ACUVUE family.

So consider this, even with 120 million people that are wearing soft contact lenses today, the market is only reaching 10% of prospective wearers. Why? Well, there's 3 reasons. First is discomfort. New wearers often find lenses uncomfortable, and anyone who's ever transitioned from spectacles to lenses like myself, you understand what I'm talking about. Second, there's a lack of solutions for people that are living with astigmatism. Astigmatism is where the eye is shaped like a football versus round like a basketball. And we know that 40% of patients who need vision correction having astigmatism in at least one eye. This is a big opportunity. And third, patients drop out of lenses if they develop presbyopia. This is a condition where middle-aged and older adults have trouble seeing things up close, especially in low-light situations. But most people who have this experience, they don't know that multifocal contact lenses, like I'm wearing today, are an option.

We address these challenges with our latest innovation, ACUVUE OASYS Max 1-Day. It provides proven max comfort and max clarity versus our competitor. Now Max actually works with your eyes natural tear film, locking in moisture to maintain that superior comfort. Max also proves to have the highest level of blue violet light filtering, which is helping to design in today's world that digitally intense requirements that are in front of us.

Since launching across the U.S. and EMEA, we have seen rapid uptake, yielding unprecedented growth in our multifocal segment that's addressing presbyopia. This gives us confidence to launch in even more markets.

We also aim to launch MAX for people living with astigmatism in the coming years to meet that huge unmet need for so many patients. We do anticipate above-market growth and we've worked hard to ensure that we've made the right supply chain improvements across our entire fleet to meet all of our patient needs. So that's how we're driving innovation in contact lenses.

Now what I'd like to talk to you about is how we're driving innovation to treat cataracts. Cataracts are the leading cause of treatable blindness in the world. For most of us, developing a cataract is not an if, it's a when. Cataract is when your natural lens gets too dense and light can't easily get through. Today, a surgeon can remove a cataract and replace it with an IOL, with patients typically experiencing improved sight that same day. Cataract surgery is the #1 surgery performed around the world, 28 million procedures, but only 10% to 15% of people are getting advanced optical IOLs, specifically designed for astigmatism and presbyopia.

Given the global population that is aging, the patient need in this category is high and continues to grow. And the IOL market is valued at $3 billion today and is projected to grow 5% to 7% annually. We are proud to say that through TECNIS, our family of IOLs, we hold the #2 position in the surgical vision segment, and we have grown market share for the third consecutive year in a row. We anticipate growing the size of the market and closing the gap to #1. And here's how we're going to do it.

Today, when choosing an IOL, surgeons and patients must make trade-off decisions. For example, you can have a lens that is going to offer clear sight at all distances without spectacles but at the possible cost of glares and halos. Our technology combats these issues and improves the overall outcomes for both patients as well as surgeons. Our TECNIS family of IOLs offers a broad range of products tailored to a patient's lifestyle and individual needs. TECNIS Eyhance, our monofocal lens has become the new standard of care for patients who are looking for clear distance vision with improved intermediate vision as versus other monofocal lenses.

We've also recently launched advanced innovations with TECNIS Synergy and TECNIS Symfony OptiBlue, providing best-in-category low-light performance with increased range of sight for patients wishing to be spectacle-free. We are really pleased with the impact of these launches OUS, and we see significant opportunity to grow the global IOL market.

In the next 2 years, we expect to see full market launches of our next-generation lenses, TECNIS PureSee and TECNIS Odyssey. TECNIS Odyssey is suited for patients who want outstanding visual clarity near and far and who want to live without spectacles. It has great visual clarity at multiple distances, with low and manageable incidences of visual side effects like halos and glares.

For patients who are sensitive to visual side effects and are bothered by halos and glares, we've developed TECNIS PureSee, which minimizes those visual side effects while still providing outstanding middle and far distance vision. The combination of the clarity of vision, reduced visual side effects, ease of use, sets TECNIS Odyssey and TECNIS PureSee apart from currently available products.

So look, here's the bottom line. Our portfolio spans the lifetime of sight. We are winning in the contact lens and IOL markets today and have differentiated innovation for myopia management. We also have gene therapies that are in late development to treat geographic atrophy and age-related macular degeneration. Our expertise in optics, material science, innovative medicines and technology, all backed by the power of Johnson & Johnson positions us to lead the growing category of eye health into the future.

Innovation is who we are. We are creating whole new categories of eye health, including the first disposable contact lens and for presbyopia, the first contact lens and the first IOL. This strong legacy of first-to-market innovation gives us unprecedented brand trust among eye care professionals and patients. And we have deep equity with our preferred customer partners and are using data-enabled

experiences to better serve patients and improve outcomes.

So you can see we are well positioned to be the world's leader in eye health. And for Johnson & Johnson, success is where high science and high unmet need intersect, delivering the best for our patients now and into the future. This is what it looks like to make vision possible. Thank you.

Operator

Ladies and gentlemen, please welcome Company Group Chairman, Robotics and Digital, Hani Abouhalka.

Hani Abouhalka ***Johnson & Johnson - Company Group Chairman, Robotics and Digital***

At Johnson & Johnson, our robotics and digital ecosystem will support more personalized, more intelligent and less invasive health care. Today, I'll build on the information we shared in November around OTTAVA, including our time line and the system's unique characteristics. I'll also share more about the MONARCH platform and our vision for a connected digital ecosystem.

I want to start by saying that we are not new to digital innovation. We are building on work that has been ongoing across MedTech. For instance, our teams are showcasing our in-market robotic solutions, the MONARCH platform and VELYS robotic-assisted solution. Our teams are also showing a number of digitally enabled solutions in our portfolio like CARTO that are harnessing the power of data for more connected care. We are building on this innovation and leveraging our strength in science and technology to deliver what's next.

Robotics brings key capabilities to improve surgery, things like visualization, dexterity, ergonomics and stability. But after 20 years, there are still challenges with robotic surgery. At J&J, we understand the importance of listening to surgeons, and we've heard 3 key themes. First, surgeons are asking for increased availability and flexibility in robotic surgery. We need to address these challenges with scheduling, procedure throughput and workflows.

Second, surgeons and surgical teams need help to lighten the physical and mental load. And then lastly, digital is critical for what's next in surgery. Disease is connected, data should be, too. We believe that if we address these challenges, we can deliver an experience that is more human, more adaptive and more connected for the benefit of patients. OTTAVA, our soft tissue robotic platform, is our answer to these challenges. In November, we shared our plans to submit an IDE to the FDA in the second half of 2024. We remain firm and confident in this time line.

Our team is conducting periodic meetings with FDA to continue alignment and inform our plans. We are well underway to be ready for the clinical study. So you might ask, what makes OTTAVA different? As we said in November, due to intellectual property, we're not yet sharing every detail of the Ottava system. But what we are sharing is incredibly exciting. First, Ottava is the only robotic system with unified architecture. This means the 4 robotic arms are incorporated in the surgical bed. When the arms aren't in use, they stow invisibly. This allows surgeons to use the OR for any procedure and deploy any number of arms before or during a procedure.

Our unified architecture means there's no need for large booms or carts as with other systems. The robot is part of the surgical bed. This design creates space in crowded ORs and reduces the friction between surgical teams and the robot. The unified architecture also allows for clinically relevant features.

With OTTAVA, the robotic arms move naturally when the table is moved, and surgeons don't need to stop operating while this movement is happening. We call this feature, twin motion. This addresses a critical need and adds some of the flexibility and freedom missing in robotic surgery today.

We are bringing also the best of Ethicon to OTTAVA. Many surgeons around the world know the performance and trusted experience of our Ethicon instruments. More surgeons use Ethicon staplers than any other stapler on the market. Placing our trusted advanced Ethicon Instrumentation only on OTTAVA delivers consistency of experience across all surgery.

Robotics is an early market still taking shape. Fewer than 5% of all surgeries globally are completed using a robotic system. Current estimates suggest 20 million procedures are robotically relevant. But based on our research and our leadership in laparoscopic surgery,

we believe this number for OTTAVA is closer to 40 million. Procedural penetration in the U.S. is deepest and broadest, which is why we're starting here first.

We are also working a parallel path to approvals in key markets outside the U.S. like Japan and Europe to quickly scale globally. This market is ready for competition and choice. Based on our time line and our confidence to deliver, we expect OTTAVA to contribute meaningful revenue towards the end of the decade.

Flexible robotics is a strategic market, is less than 1% penetrated. MONARCH is the first and only multispecialty flexible robotics platform cleared for use in bronchoscopy and urology. The MONARCH platform for bronchoscopy addresses an unmet need in the diagnosis of lung cancer.

As you heard, lung cancer is the leading cause of cancer-related death worldwide, and earlier diagnosis increases the long-term survival rate for patients. I am excited about the adoption of this technology in the U.S. And as Ahmet mentioned earlier, in November, we announced regulatory approval for China.

The MONARCH platform for urology supports the treatment of kidney stones and received FDA approval in 2022. Kidney stones is a pervasive and painful condition that sadly also requires retreatment. Minimally invasive robotics has the potential to address that condition. Across lung biopsy and kidney stones removal, MONARCH has the potential to address nearly 7 million procedures globally. Our strength as J&J also means that MONARCH is a platform for future innovation. We are bringing together MedTech and Innovative Medicine to develop transformative interventional oncology solutions by delivering pharmaceuticals directly into tumors.

J&J MedTech will continue to innovate with robotic for what's next in surgery. We deliver on this promise with differentiated products and solutions and by connecting it all with POLYPHONIC, our digital ecosystem for surgery. Through this ecosystem, we are supporting the acceleration of robotics. We're also addressing unmet needs surgeons experience in areas like surgical video, education and collaboration. This is a strategic journey and a vision for what's next in surgical software as we continue our leadership in surgery. Thank you.

Operator

Ladies and gentlemen, please welcome Tim Schmid, Ahmet Tezel, Hani Abouhalka, Michael Bodner, Aldo Denti, Jass Brooks, Peter Menziuso and Sarah Wood.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Thank you. So before we get started, just a few logistics on how to participate in the Q&A. For those who are here with us live, you'll see in front of you at the tables, you have push-to-talk microphones. Once you're selected to ask your question, please push the button. You'll know it's on when you see a red light come on. Feel free to ask your question. Once you ask your question, please push the button again so that we don't hear anything else you say.

For those who are joining us virtually, we appreciate and want to hear your voice as well. Within the virtual platform, please type your question into the checkbox. We ask that you limit to just 1 question. We have limited time. We want to get through as many questions as possible.

One last item. On the virtually recorded video, what you heard today, unfortunately, Celine Martin is not able to be here with us live. She's not feeling well. But we do have Jass Brooks, the President of Electrophysiology, with us today and ready to address your questions. So with that, we will open it up.

QUESTIONS AND ANSWERS

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Yes, Rick. Please state your name and your firm. Sorry, I forgot to mention that.

Frederick Allen Wise ***Stifel, Nicolaus & Company, Incorporated, Research Division - MD & Senior Equity Research Analyst***

Rick Wise, Stifel. Just to start off, Hani, on the field of robotics. Maybe just help us think through at a high level how you're going to create a platform in Ottava that can be rapidly adopted. You're late to the game, I say respectfully. That's an opportunity as well to bring new technology. But talk us through more the diseases you're going to target, your priorities and maybe how you're going to leverage all of the company's strengths with actually what was a very impressive, incredible system that I was lucky enough to see on California.

Hani Abouhalka ***Johnson & Johnson - Company Group Chairman, Robotics and Digital***

Well, first, thank you for coming to California. We are very, very excited and confident about our Ottava program. We believe, first and foremost, it's early innings in the robotic market. As you know, globally, it's around 5%. What we heard from surgeons that they need someone to come in and play in this market and take robotic surgery forward, I think our team is very excited in creating what's next in surgery.

And if you think about it, it's going to be around a connected, more adaptive and human experience. Why are we going to win? First, we are leaders in surgery today. We have incredible teams working on things like wound closure and by surgery and the rest of surgery. But when it comes to Ottava specifically, a few things excite us the most. First, it is one-of-a-kind unique architecture. This unified architecture that I mentioned allows us to really remove friction in OR, give space back to surgeons to allow them to really work better for workflows. That unified architecture incorporates the arms into the table, also allows us to give something that surgeons talk to us about, which is the ability to really have the table move natively without any software or integration or stopping workflows or actually removing the carts or the booms. That's what we call twin motion, is going to be really differentiated for us.

The last 2 things I'll say, I think on instruments only on Ottava is a big deal. This brings standard experience across laparoscopy and robotics. I know surgeons would tell me today that while doing robotic surgery, they do manual firing using Ethicon trusted instruments. We are the leaders in stapling.

And the last, and Tim alluded to it, our presence globally not only gives me confidence that we'll be able to be by the side of surgeons to train and advance but also we have great commercial teams in the U.S. and globally. We're excited. I hope you saw it with us in California, and we'll be able to share more as we go into next year and beyond. And thank you.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Shagun?

Shagun Singh ***RBC Capital Markets, Research Division - Research Analyst***

Shagun Singh from RBC Capital. I know someone has to ask this question so I thought I'll ask just on GLP-1s. Tim, what is your view on the impact of GLP-1s just across your businesses? We've heard about it from cardiovascular to orthopedics across the board, pediatrics. How do you handicap that risk in the near, medium, longer term? Perhaps talk about the TAM.

Tim Schmid ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, MedTech***

Sure, Shagun. And let me maybe start at the highest level and then we'll get into the areas that I think have been brought up as potential areas of concern. Now firstly, let me say that we are thrilled by the continued innovation in the space and the opportunity that it provides to patients around the world. And the fact that this is shining an even brighter light on obesity as a major world challenge is a good thing for patients.

We are a broad business covering many different specialties, and we think we have a good read on the trends that are hitting our industry. I can categorically say that we do not anticipate any material impact to our business over the mid or long term as a result of GLPs.

And I think the 2 areas that have been brought up as the major areas of potential concern are surgery, specifically bariatrics, and then orthopedics. And so one, we dive a little deeper into those with our leaders of those business, maybe starting with surgery, Hani, and then we'll go to ortho.

Hani Abouhalka ***Johnson & Johnson - Company Group Chairman, Robotics and Digital***

I mean, I'll start by where Tim started. We're patient-first. Anytime there's advancements in treating obesity as a disease, this is something that we're excited about. It gives surgeons another tool in the toolbox. The second thing I'll say, if you look at it, obesity globally, it has some sort of a stigma. Having this be an option to allow surgeons to have dialogue with their patients, that's also very, very positive.

I don't see this having a long-term impact on bariatric surgery for the following reasons. First, around 30% of patients are not responding to GLP-1s. GLP-1s are not for all patients. The second thing is I started my career in actually bariatric surgery, 20 years ago when I saw first time the impact surgery has on patients and on surgical teams. And what I can tell you since then the data has shown is the long-term durability of bariatric surgery.

So at the end, what I think will happen is, this will be another tool for surgeons to discuss with patients. I think this will be incredibly positive for patients, great for our business, especially where some patients are, right now, maybe a bit certain obesity were not safe to do surgery. This might also help them and be more suitable for surgery. But I know, Aldo, this is something on your mind for orthopedics.

Aldo M. Denti ***Johnson & Johnson - Company Group Chairman, Orthopaedics***

Absolutely. So first and foremost, I think in orthopedics, you have to consider a few things. If you have a BMI over 40 and you speak to orthopedic surgeons, your complication rates in total hip arthroplasty and total knee arthroplasty go up. So if you're speaking to surgeons, the first thing they're going to tell you is weight loss is a good thing for orthopedics. So actually, as I see it, it actually opens up the funnel for more orthopedic care. So that's a good thing.

Second, if you've had and suffered from osteoarthritis, GLPs are not going to solve that problem. If you're in the funnel of orthopedics already, you're going to need surgery at some point. And the last point I'd make is if you look at osteoarthritis rates in the different countries across the globe, they're not very different. Countries like Japan, the United States don't show significant rates of differences in osteoarthritis. So as I said, for us in orthopedics, we believe it's actually going to increase the funnel in the short term. And then we'll have to see in the long term, how this plays out in terms of the other applications.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Josh?

Joshua Thomas Jennings ***TD Cowen, Research Division - MD & Senior Research Analyst***

Josh Jennings from TD Cowen. A question for Tim. Just the 5% to 7% revenue growth CAGR. Getting to the top end of that, that's enticing. And just thinking about the margin expansion potential for the business with getting that volume benefit, maybe you could help us think through some of the headwinds and tailwinds. And just from a high level, whether the MedTech unit should be delivering expansion in gross and operating margins.

Tim Schmid ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, MedTech***

Sure. Yes. Thank you. So firstly, we feel very confident that we will be able to deliver sales in the 5% to 7% range. We're not going to be specific there, given many variabilities in our sector, but we feel very confident about that. At the same time, as I mentioned in the strategies that I highlighted earlier, while top line growth is something that we're very proud of, we're not alone. In fact, our entire industry has been hit by some fairly significant headwinds on the back of COVID inflation, which has put pressure on margins.

And so we are being very clear and carefully balancing sales growth with margin improvement. And how we're doing that, I mentioned this is really primarily around how we look to build more resilience in our operations. And it's going to take some tough choices, to be honest, but we are going to be looking to continue to further simplify our organization, to accelerate speed of decision-making, to simplify our portfolio, which also creates complexity and cost.

We are also reimagining our supply chain while supporting our top line growth, really looking at operating margins and how we can free up more cash. And then finally, digital is a wonderful enabler of more efficiency across our business. And so we will continue to deploy that in every way possible.

We do expect continued improvement as it relates to actual margins. When Joe speaks a little later, we'll actually be telling you about what that means at the enterprise level. We don't typically report operating margins at the segment level but we'll certainly touch on that a little later in the enterprise dialogue.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. And Aldo, I know we recently talked about some opportunities within orthopedic space to look at our portfolio. Do you want to talk a little bit about the activities that will help with markets there too?

Aldo M. Denti ***Johnson & Johnson - Company Group Chairman, Orthopaedics***

Yes, sure. I want to kind of rewind back to 2019. I've told most of you that we're in a multi-part journey in orthopedics. We've always said that step one was to bring clinically specific sales forces across the globe. We have done that. Number two, we said we will reignite our innovation engine. We have done that. We've launched 55 products since 2019, most of those in high-growth segments and closed gaps in pretty much everything we had that we needed to close. The third step that I said was that we would focus on the places where we have the right to win.

Orthopaedics, as you saw from Tim, is a $50 billion market. $40 billion of that is controlled in 12 countries. So our focus is to go there and to scale where we can. The second step is to get out of our legacy products and focus on the innovation we brought to market. That's part of the restructuring plan as well. And lastly, like Tim said, we are no different than any other business. We've looked at, obviously, the margin compression we've had as a result of the headwinds. And what we're doing now is using a network strategy to address some of that. So that's the 3 parts of our restructure. And as you know, we've announced that recently, we're implementing those as we speak.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Okay. And Larry?

Lawrence H. Biegelsen ***Wells Fargo Securities, LLC, Research Division - Senior Medical Device Equity Research Analyst***

Larry Biegelsen, Wells Fargo. Tim, it's the first time I think we're hearing from you. Welcome to your new role. So my question for you is how do you see the strategy evolving under your leadership? How are you going to put your stamp on the business? And how are you thinking about inorganic opportunities? The Laminar deal was more dilutive than people expected. Does that mean going forward, you're going to focus more on revenue generating profitable M&A?

Tim Schmid ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, MedTech***

Thank you, Larry. After 30 days in the role, I'd like to be a little measured. And what I'm doing, Larry, is frankly spending a lot of my time not in New Brunswick, but frankly, out in the markets with our customers and with our people. And so I'll be a little measured in declaring exactly what we're going to change.

But I can tell you that this team you see on stage and our leadership team, we've all been a part of the resurgence of Johnson & Johnson MedTech. We're super proud of the accelerated growth that we've shown you today. And to think that back to 2017, we were growing 1.5%. If you look at our results through the third quarter, 7.4%, in fact, 8% on a pro forma basis. And so we've all been a part of that.

We've also been a part of actually continuing to shift the portfolio into higher-growth markets from 20% in 2018 to 50% today. And so let me tell you what's going to continue is firstly, that strategy around shifting the portfolio into higher-growth segments is an absolute priority. And how we do that is through 2 things: continuing to drive more productivity out of our organic engine, and then it's also looking at inorganic opportunities. And thanks to the support of Joaquin and our Executive Committee, we're committed to winning in MedTech. And I think the acquisition of Abiomed is a good example of that.

Laminar is a good example of really probably more in line with the typical types of deals that we do.

If we look at the last 20 years of Johnson & Johnson, we've typically focused on more tuck-in deals. About 90% of our transactions have been below $1 billion and that's where we will focus. At the same time, for truly accretive opportunities that allow us to get into adjacent opportunities, we are more than open to looking at those as well.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

And Jass, given that Larry's question included Laminar and some who are online or in the room may not have seen our release on that, do you want to talk just a little bit about what Laminar brings us and why we're excited about it?

Jasmina Brooks ***Johnson & Johnson - President, Electrophysiology***

Yes, certainly. So I think most of you may know that patients with atrial fibrillation are more likely to have -- 5x more likely to have stroke. With Biosense Webster and J&J Electrophysiology, our strategic focus is really to help those patients with atrial fibrillation deliver better innovations as well as elevate the standard of care. And Laminar's technology is differentiated as it is in this LAA space would perfectly fit with our Electrophysiology and intracardiac echo portfolio that we have today. And it's becoming really a cornerstone of electrophysiology because what we're seeing now that there are quite a few procedures that are happening where atrial fibrillation is followed by the left atrial appendage occlusion.

With Laminar specifically, what excites us about it is that's very different than the intra-catheter opportunities or the products that are available there commercially today. So instead of just taking the plug to occlude the LAA, what this technology does is actually uses the rotational motion to eliminate left atrial appendage.

So in general, we're excited about technology. We do have the FDA approval to start the IDE early next year, and we think it's going to fit really nicely with the rest of the portfolio in electrophysiology going forward.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Thank you. Danielle?

Danielle Joy Antalffy ***UBS Investment Bank, Research Division - Analyst***

Danielle Antalffy with UBS. Jass, just a question for you on the atrial fibrillation business. Obviously, you guys touched on PFA entering the market. I'm just curious about what's driving the 11% to -- I think you said 11% to 13% market growth. And why not faster? I mean, one of the things that PFA brings is higher throughput at the EP lab, a safer procedure that could drive higher referrals. So just curious about why just 11% to 13% and not potentially faster for the market?

Jasmina Brooks ***Johnson & Johnson - President, Electrophysiology***

I think if you look at atrial fibrillation in general, we know that 1 out of 4 people over the age of 40 is going to experience atrial fibrillation in their lifetime. So there's certainly a huge incidence of patients. And I think by 2050, we'll be adding about 5 million patients with atrial fibrillation to this pool. I think another thing that helps that is smart watches, right? So everybody is now diagnosing themselves with atrial fibrillation as well, so people are a lot more aware.

What we have seen, and Celine mentioned that in her video, that in the last 10 years, we have seen significant improvement in the efficiencies as well as the efficacy of this procedure. So we have gone from 3.5 hours procedure down to less than 60 minutes at our QDOT MICRO technology. We have seen the efficacy improve from 66% to 86%, again, with our QDOT MICRO technology. So what we're seeing is that patients and these procedures are becoming more efficient. They're becoming more effective. So we're hoping that we'll see more patients come through that pool and receive the atrial fibrillation ablation, cardiac ablation.

As Celine mentioned, and I think Tim alluded to it, only 5% of all of the patients that could be treated received the procedure. But what we're trying to make sure that these procedures are safer, which PFA has a promise to make them a lot safer. Not that the complication rate with RF is significantly higher, but there is the promise of improved safety with PFA.

We're also seeing the procedures are faster so maybe physicians can do more cases per day. And in the end, it's really going to be down to a number of electrophysiology labs and electrophysiologists that can perform these cases.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. And Alec, why don't we take a quick pause and see if we have any questions coming through on the virtual platform?

Alec Mast ***Johnson & Johnson - Investor Relations***

Yes. So there's a common theme of questions coming through currently in the platform around Abiomed. So the question around Abiomed is it looks like the integration has been a great success. Can you tell us a little bit more about your confidence in the ability to expand that business geographically?

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Michael?

Michael Bodner ***Johnson & Johnson - Global Head, Heart Recovery***

Thank you for the questions. 80% of the business today is in the United States, 20% is OUS, and that's predominantly in Germany and Japan. And if you look at the scale of Johnson & Johnson, we're deeply in more than 100 countries around the world. We've done this before. If you look at our Biosense business, Biosense scaled rapidly and became a very significant player in the electrophysiology space being able to tap into that infrastructure.

So we're confident on our ability to scale. It does take time to open up new markets, but we have the expertise, the capability not just commercially but also with deep resources for health economics, government affairs as well as training and educating physicians, which is most important in these nascent markets.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Thank you. Joanne?

Joanne Karen Wuensch ***Citigroup Inc., Research Division - MD***

Joanne Wuensch from Citibank. It struck me that Vision Care is the only of the 4 big sections that isn't holding a #1 spot, particularly in the surgical area. And I'm curious how you plan on moving it up towards #1 either through internal or external investment?

Peter Menziuso ***Johnson & Johnson - Company Group Chairman, Vision***

So we're sitting in a #1 position in our contact lens platform and #1 in our monofocal platform as well. On the specialty side of the market, as I talked about, 10% to 15% of the market is being penetrated with specialty lenses. As we continue to advance our TECNIS family of intraocular lenses, working on: one, visual acuity but also visual disturbances, we do see ourselves very positioned to move that segment of our portion more closer to our #1 spot.

We're really confident on the 40 million people that we're serving today, and we know that we're -- there is significant under penetration of the market that we want to serve as a leader in eye health.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Matt?

Matthew Stephan Miksic ***Barclays Bank PLC, Research Division - Research Analyst***

Matt Miksic from Barclays. I had a couple of follow-ups for Aldo and Jass. So I mean, you talked about the drivers of improving MedTech growth. Obviously, enabling technology has been a big part of that and has always been a part of Biosense and is now a bigger part of ortho. So Aldo, if you could maybe talk just about when we're going to see that hit Spine and start turning that business more towards market growth? And for Jass, just if I could ask them both at the same time. I think Celine was talking about we're the market leader, and that's an advantage.

I think some folks would say you're the market leader and maybe that makes you more vulnerable to grow at or below market share, with these folks nipping into your heel. So maybe talk a little bit about how this new PFA rollout and other competitors coming is something that you're going to be able to turn and power through.

Aldo M. Denti ***Johnson & Johnson - Company Group Chairman, Orthopaedics***

Yes. So I'll answer the question for Orthopaedics first. So our goal in Spine has always been to drive adoption in MIS, to be leader in MIS and also to be the leader in complex spine. In order to do that, we really need the foundation of any spine company as a historical lumbar system. You saw on the slide from both Ahmet and from Tim, we are in the process of launching TriALTIS. We have received 510(k) approval. TriALTIS is a modern thoracolumbar system that is specifically designed for robotics.

So step one, get our foundation right with our thoracolumbar system. We're in the process of doing that. Step 2, now that we have a thoracolumbar system that is designed for robotics, is launch a spine robot. In Q1 of next year, I have plans to share an update on where our spine robot is. And the combination of those 2 allows us not only to penetrate the MIS market or the degenerative market and, more importantly, also the complex mark with a foundation of the thoracolumbar system.

In MIS, you saw Ahmet speak about TELIGEN, which is the only system of its kind which allows for minimally invasive access to the spine in combination with a TLIF procedure. So we plan to lean on that as well. We've initially launched TELIGEN. The feedback is superb, and we're very, very pleased with that. So that foundation allows us now to accelerate our growth in spine.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Jass, if you want to talk about how we're going to maintain our leadership in electrophysiology.

Jasmina Brooks ***Johnson & Johnson - President, Electrophysiology***

Certainly. So we know that this market has been growing double digits, mostly because of the prevalence of atrial fibrillation disease globally. Biosense Webster and J&J electrophysiology have been the market leader over the last 2 decades, and we have been able to maintain the market share and grow that market share over the last couple of years. When it comes to PFA and where we are with that technology, we're extremely excited about the PFA ecosystem that we are working on. So we're not only focusing on the catheter technology specifically, which I'll talk about a little bit, but also how it integrates with the CARTO system.

Celine mentioned in her presentation, we have over 5,000 CARTO system installed globally. And we know from everything that we have learned in radiofrequency ablation over the last couple of decades, it's very much applicable to PFA as well.

So we know that 3D mapping is going to remain the cornerstone of this ablation. We know that it goes beyond just the catheter technology, but it's also linked to the algorithms like ablation index, like contact force, like proximity indications of the catheter, allowing physicians to actually know where to go during these procedures.

We also know that PFA is very different where the signals disappear as soon as you deliver energy so this makes these types of algorithms and the 3D mapping even more important.

In addition, all of our technology, all of the catheters are connected to CARTO. But we're also looking at the different, I guess, broad range of catheters to address different anatomies of patients and really tailor the approach. While atrial fibrillation is out there in 38 million patients, not every patient is created equal.

So we're starting out with our VARIPULSE catheter platform, which is the multi-electrode platform. Celine mentioned we already have the CE Mark in Europe for the TRUPULSE generator, which is a must-have once he wants to launch the technology. And then the VARIPULSE catheter we're looking forward to receiving that CE Mark and launching it in early in 2024.

In addition, STSF dual energy catheter that Celine also spoke about is extremely important part of our portfolio. It's the #1 selling ablation catheter today. So we're simply adding PFA to something that they're already used to using in focal side of things.

We also do have OMNYPULSE, which is large focal, that gives you the ability to create maybe larger lesions, not so many point-by-point lesions, and we're working on a single-shot technology.

So the way that we're looking at it in PFA, while we're not first to market, we're going to be best to market, right? It's the entire ecosystem

of catheter of CARTO as well as our sales force and clinical application specialists that are there to train help support these cases and share the best practices as we launch it across the regions.

Sarah Wood ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. And I want to thank you for the wonderful questions. Unfortunately, we are out of time. I'd like to ask if Tim has any closing comments that he would like to share.

Tim Schmid ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, MedTech***

Well, thank you, everyone. On behalf of the entire MedTech team, we really appreciate your time and your thoughtful questions today. Like I said, we are at an incredible moment in our industry. And I hope you can see how passionate and committed we all are to meeting this moment.

Here's what I'd like to leave you with. Firstly, we have a robust market opportunity that we're positioned to capitalize on, thanks to the momentum over the last several years. For the third straight year, we expect our organic sales growth to be at least in line or ahead of our competitive composite.

Moving forward, we expect to deliver operational growth in the upper range of the markets with a focus on 3 key drivers: advancing our differentiated pipeline and continuing to shift our portfolio into high-growth markets, expanding our global reach and building operational resilience. We are confident in the promise of our portfolio. Our MedTech team is bringing life-changing and life-saving technologies focused on tackling the world's most pressing health challenges.

I hope that those of you who are here with us at the New York Stock Exchange will continue visiting our MedTech exhibits to learn more about the growth-driving innovations from Johnson & Johnson. Thank you.

Operator

Ladies and gentlemen, at this time, our exhibits are open in Freedom Hall and Siebert Hall. For those in the room, we invite you to enjoy lunch and our exhibit booths. Our program will resume at 12:50 p.m. Eastern Time. Thank you.

(Break)

PRESENTATION

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

Hello, everybody. Welcome back. Good afternoon. Hope you enjoyed the lunch and that you had the opportunity to explore some of the exhibits and hear from some of our incredible leaders about the breakthrough science and significant opportunities that are behind some of our most promising assets. The video you just saw highlights how our relentless focus on transformational medical innovation is enabling us to shape the future of health care. Simply put, we're leading where medicine is going.

So this afternoon, our talented team is going to give you a deeper understanding of where we're focusing and what will drive our growth, both in the near term and in the second half of the decade. So let's start with what we'd like you to take away from the discussion today. So first, we are confident that our in-market portfolio, including our recent launches, will enable us to achieve our 2025 target of $57 billion. Between 2025 and 2030, we expect to deliver above-market growth with a compound annual growth rate of 5% to 7% and growth in every year. By 2030, our industry-leading portfolio and pipeline will include more than 10 assets with $5 billion in peak sales potential and an additional 15 assets that have $1 billion to $5 billion in peak sales potential. And we expect to deliver more than 70 novel therapy and meaningful product expansion filings and launches.

We disproportionately invest in R&D. In 2022, we invested $11.6 billion in the discovery and development of new treatments and new cures. Based on the strength of our pipeline and the greatest opportunities that we see ahead, we're prioritizing our resources in oncology, immunology, neuroscience and select disease areas where there's high unmet need, actionable science and where we have deep scientific and commercial expertise.

Oncology will become our #1 therapeutic area, and it's going to reach #1 in the industry as we strive to make cancer a curable disease. And we'll achieve this through the strength of our multiple myeloma and prostate cancer portfolios, combined with our upcoming launches in lung and bladder cancers. Immunology will be driven by growth in psoriasis and inflammatory bowel diseases as well as launches in autoantibody-driven diseases. We'll also lead in neuroscience with a focus on depression, schizophrenia, myasthenia gravis and Alzheimer's disease. And we're excited about our opportunities to redefine treatment in thrombosis, retinal diseases and pulmonary hypertension.

We've got a great track record of delivering growth that surpasses the competition. This year, in fact, we'll deliver our 12th consecutive year of above-market growth. But it's not only what we do that makes us successful, it's also how we do it. For 10 consecutive years, we've been ranked #1 in the pharmaceuticals category on Fortune's World Most Admired Companies list. And we've ranked in the top 3 on the Access to Medicines Index for the past decade based on our efforts to make our medicines accessible in low and middle-income countries globally. Today, we're the #2 pharmaceutical company, and we're on track to becoming #1.

So how will we do this? Well, we've got a clear differentiated strategy to win. We're going to drive our marketed portfolio through market share gains and expanding into new patient populations. We're going to deliver an accelerated pipeline of transformational first-in-class and best-in-class medicines. And we'll develop our next wave of innovation, collaborating throughout the innovation ecosystem as a partner of choice. We're going to accomplish this through our relentless focus on transformational medical innovation, deep expertise in our disease areas of focus, our world-class capabilities. And finally, we're going to compete to win on behalf of patients and on behalf of our business.

So we're boldly investing in the areas that we think are going to advance our leadership. These include supply chain capabilities to support our specialty medicines and modalities, data science and enabling technologies to help us deliver innovative medicines with precision and speed, value and access to support broad reimbursement, and our people who are going to propel our evolving portfolio. Our path to $57 billion is clear with our strategic focus in oncology, immunology and neuroscience. We're going to maximize the value of our key marketed medicines, including our recent launches to deliver growth that exceeds the anticipated impact of the STELARA biosimilar entrants.

We're going to deliver significant additional growth for our key brands through market share gains and increased penetration as well as expansion into new indications, additional lines of therapy and combination regimens that advance the standard of care. In addition, our recent launches will contribute meaningfully based on their profiles and their competitiveness.

We're ending 2023 in a strong position. And when you combine that with the potential of our key brands and the timing for STELARA biosimilars, we're confident we will deliver our 2025 target. We anticipate strong above-market growth to continue throughout the second half of this decade. And the Inflation Reduction Act has been factored into our outlook. Our current portfolio of marketed medicines will continue to deliver growth. And since these products are approved and on the market today, we know their profiles, making our ability to drive strong growth significantly de-risked. We're also confident in today's promising pipeline assets, and we're confident they're going to contribute to future growth, and 70% of our expected pipeline revenue is coming from programs that are already in Phase III.

Put another way, we expect the growth of our key brands, our recent launches and our pipeline assets to outpace the market during the second half of the decade, even when you factor in the impact from STELARA and other potential routine end-of-life LOEs. This exciting growth is going to come from assets that have been recently launched like TECVAYLI, TALVEY, CARVYKTI, SPRAVATO as well as launches in lung cancer, bladder cancer, autoantibody-driven diseases and targeted oral treatments in immunology, all of which you're going to hear about this afternoon.

At our last business review in 2021, we talked about 5 pipeline assets that had $5 billion in peak sales potential. Well, through 2030, we now expect our portfolio and our pipeline to include more than 10 assets that have $5 billion in peak sales potential and more than 15 additional assets that have $1 billion to $5 billion in peak sales potential. We have never been more confident about the power of our portfolio and our pipeline to fuel our future growth.

So I'd like to finish where I started, with what we're planning to deliver through the rest of the decade. So first, we will achieve the $57 billion revenue target in 2025. Between 2025 and 2030, we expect to deliver 5% to 7% compound annual growth with growth in every year. By 2030, we expect to have more than 10 assets with $5 billion in peak sales potential and more than 15 additional assets with $1 billion to $5 billion in potential. So with our portfolio of marketed medicines, our pipeline of transformational therapies together, we're going to redefine care for some of the world's most serious illnesses. So at Johnson & Johnson, we are leading where medicine is going. Thank you.

Operator

Ladies and gentlemen, please welcome Executive Vice President, Innovative Medicine R&D, John Reed.

John C. Reed ***Johnson & Johnson - Executive Vice President, Innovative Medicine R&D***

Well, good afternoon. It is truly an honor to be here today, representing our incredible research and development organization at Johnson & Johnson Innovative Medicine. I've been with Johnson & Johnson a little more than 8 months now. And in that time, I have become deeply impressed with the quality of the pipeline and the people who make it possible. I'll share briefly about our strategy for building and delivering a high-impact pipeline of transformational medicines and what makes our R&D organization different.

Well, first, I want to start by emphasizing that we are building incredible pipeline momentum operating from a position of strength. Since 2021, Johnson & Johnson has over-delivered on what we promised you, delivering 5 novel medicines, an industry-leading average of more than 2 per year, plus multiple line extensions. The quality of the pipeline has also improved when we consider the number of molecules with so-called mega blockbuster potential and the different projects that have been awarded breakthrough or fast track designations.

Importantly, we've maintained an impressive degree of innovation where roughly 2/3 of our development-stage molecules have first-in-class potential. And our R&D engine is also operating with industry-leading efficiency, boasting one of the highest productivity indices in the industry. In fact, as Jennifer said, we see potential to deliver more than 20 novel therapies and numerous line extensions through 2030, placing J&J's pipeline among today's industry leaders.

Now J&J's strategy for delivering a high-impact pipeline is comprised of 6 pillars that operate interdependently and that we believe will accelerate us into the future. And I'll share insights today into a few of these strategic pillars in the next few slides, but you can find the details in your online materials.

First, our R&D strategy renews our commitment to first-in-class and significantly differentiated medicines, and our pipeline is replete with examples. RYBREVANT, for instance, is now emerging as the new standard of care in EGF receptor-mutant non-small cell lung cancer. Milvexian, an investigational oral Factor XI inhibitor, has potential to set new standards for thrombosis treatment. Nipocalimab, it's showing promise not only in rare autoantibody-driven diseases but also in common complex chronic inflammatory conditions such as rheumatoid arthritis. And then aticaprant shows promise in depression with broad potential for several neuropsychiatric conditions where anhedonia symptoms are prevalent.

As Jennifer explained, we believe several of these molecules have mega blockbuster potential with peak sales north of $5 billion. And that's because of their potential to be truly transformational in patients. Now one way we're able to deliver these innovations is with an agnostic view on where innovation is sourced. While our internal research productivity at J&J is industry competitive and even industry leading by some metrics, business development or M&A is fundamental to our pipeline strategy. And we have a very strong track record of spotting and acquiring many high-quality assets over the years. When it comes to partnering, we live by our credo, seeking mutually value-generating win-win agreements with external innovators, which makes J&J a preferred partner.

A key to our consistent pipeline success that I really want to emphasize is our deep and durable commitment to our so-called disease area stronghold or DAS structure. This is unique among large pharmaceutical companies, endowing J&J with exceptionally deep expertise and serving as a magnet for attracting and retaining the world's top experts. The DAS concept has really paid off, for example, in multiple myeloma, where we've delivered 5 industry-leading medicines, most of them first-in-class therapies. Our myeloma portfolio

addresses every line of therapy transforming the treatment of this malignant disease and accounting, in large part, for why J&J will soon rank #1 in hematological oncology.

A similar case can be made for our GI DAS, where we rank #1 in IBD therapies. J&J introduced the first biologics in immunology targeting TNF and then IL-23. And today, we are once again changing the practice of medicine, pioneering fixed-dose combinations of biologics and blazing new trails with our targeted oral peptide that blocks the IL-23 receptor. For the first time, we're going to be able to offer patients an oral option with both high efficacy but also potential for best-in-class safety. And in neuroscience, wherein J&J ranks #1 in psychiatry, my colleagues will share how SPRAVATO and our pipeline of novel antidepressants are building on this legacy of leadership.

Now while deeply committed to the DAS concept, some diseases carry such urgent need that we take calculated risks to explore new frontiers adjacent to our established areas, and you'll hear more about these today. And when you do, I'm confident that you will be impressed by advances in bladder and lung cancer and by our universal solution for autoantibody-driven diseases that affect millions of patients around the world.

Moving on to one of the other pillars of our strategy. When it comes to combating tough diseases, many times, unlocking complex disease biology requires access to diverse modalities. And on that score, J&J has made great progress in recent years. We can now point to several examples of industry-leading excellence. And today, we will showcase our leadership in bi- and tri-specific antibodies, for oncology in CAR-T cell therapy, and in oral lymphokine inhibitors for immunology.

Let me spend just a minute on data science and digital health, very popular subject these days. These technologies accelerate our R&D engine across the entire value chain from target discovery and patient segmentation to drug design and CMC process optimization to all facets of clinical development. With our data science experts fully integrated into our therapeutic areas, data science now accelerates nearly all our pipeline programs.

So in closing, at J&J Innovative Medicine, we never forget the words of Dr. Paul Janssen, who famously said, "Patients are waiting." With the momentum of our robust pipeline, I am confident that J&J's R&D engine will continue to drive us in the future with industry-leading science coming from our world-class talents, who are deeply dedicated to transforming the practice of medicine for the patients we serve. Thank you.

Operator

Ladies and gentlemen, please welcome Worldwide Vice President, Oncology, Biljana Naumovic; and Global Therapeutic Area Head, Oncology, Peter Lebowitz.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

All right. So it is an absolute pleasure today to discuss the tremendous progress of the Johnson & Johnson Oncology portfolio. So over the past decade, by any measure, we have had extraordinary success. Our progress has been driven by our mission, which is to eliminate this disease. And while many talk about cures, we actually have plans in place to actually drive to cures in our disease area strongholds. So our approach is we focus on deep disease understanding. We embrace open innovation. We strive to bring together curative and potential synergistic treatment regimens.

Our progress has allowed us to build an industry-leading pipeline now with nearly 2 million patients treated with a Johnson & Johnson oncology medicine. And our approach will continue to deliver. So I think it's important to take a moment to look at what we've accomplished as a team in the past decade. This has truly been a pioneering, innovative R&D group that has continued to deliver year after year. This includes 14 new medicines delivered since 2011. Many of these first and/or best-in-class. Many of them have changed the treatment paradigm and started us down the path to cures. So some examples, TALVEY, the first GPRC5D bispecific; TECVAYLI, the first BCMA bispecific; RYBREVANT, the first bispecific in lung cancer; DARZALEX, the first antibody ever in multiple myeloma; and CARVYKTI, a potential best-in-class BCMA CAR-T. Just a tremendous record of bringing forward one innovative medicine after another.

So on top of this amazing track record, 37 New England Journal of Medicine publications, 13 breakthrough therapies, one just came yesterday, and a number of drugs advancing that we think can further transform the trajectory of disease. These innovative medicines

have been transformational for many patients. And as a result, we've seen tremendous growth. In 2011, we were ranked #12 as an oncology company with about $2 billion in sales. This year, we expect to deliver more than $17 billion, ranked #3. And this has been done with excellence, both in internal capabilities as well as our open innovation approach. The proof point is first-in-class medicines that were discovered and developed internally. But then at the same time, we have incredibly successful collaborations that have delivered transformational therapies.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

We have made an incredible progress, like Peter said. And yet, there still remains a global health care crisis as we approach 2030. And we don't say this lightly. Within a decade, the cancer diagnosis is expected to increase by almost 70% worldwide. That's a mind-blowing statistic, which means that millions, millions more patients will continue to need our support. And because of that, we continue to develop breakthrough therapies in hematological and solid tumor malignancies. Every year, more than 5 million new cancer patients are diagnosed in the cancer types we work on. And some of them don't survive more than 5 years. So these mortality rates, coupled with the rise in incidents, tell us there will be a lot of more patients who need us.

So we think that our science portfolio and pipeline will provide us with the ability to make an impact in patients' lives. And only through that, establish our leadership and strengthen our leadership in hematological malignancies in prostate cancer, but we also see tremendous opportunities for growth in lung cancer and localized bladder cancer.

Now I have to say, overall breadth of our portfolio is tremendous. So Peter and I, some of you know as well, can stay here and talk to you a whole day. But we need to focus, so we'll focus on 3 things. We'll talk to you about multiple myeloma, we'll talk about lung cancer, and we'll talk about bladder cancer. But let's address the projections of the oncology market first. Market growth of nearly $90 billion with a CAGR of 8% between now and 2030 reflect truly the unmet need that oncology has and will still continue to have. So we have the opportunity to revolutionize the treatments by intervening earlier, combining and sequencing regimens, all in order to achieve deeper remissions and longer progression and overall survival. So as Peter says, as we strive to eliminate cancer, we want to give patients more time.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So I want to talk a little bit about what we told you in 2021 and where we are now. So in 2021, we stood on a similar stage, said that we were going to deliver 6 innovative therapies between 2021 and 2023. 6 new drugs, right? So just let that sink in for a second. Even for a large company with a top oncology R&D engine, that is a lofty goal. But this remarkable oncology R&D team delivered with 6 drugs. Some are truly first and/or best-in-class with CARVYKTI, TECVAYLI, TALVEY, RYBREVANT, lazertinib, AKEEGA, following close behind our novel targeted releasing system in bladder cancer. And on that topic, as I mentioned, we're thrilled to have received FDA Breakthrough Therapy designation yesterday for TAR-200. This is a big step for the program.

It's been a remarkable run of successful drug development that has had a huge impact for patients. So today, while we can't cover all the work, as Biljana said, we will cover some of the highlights and show our approach that has led to this remarkable success. We have dramatically expanded the depth and breadth of the oncology portfolio, and we continue to see tremendous opportunity looking forward. We expect to continue on our path of 2 novel therapies approved or submitted per year going forward. And we continue with our strategy of building regimens with the best science. This strategy has delivered across both the early and late-stage portfolio.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

So let's start with multiple myeloma, where we see a distinct opportunity to move from treatment to progression to treat to cure. Over the last 2 decades, we have seen incredible advances in the treatment of multiple myeloma with 11 new therapies being approved, nearly half of which come from Johnson & Johnson. But as these treatments have been approved, rather than displacing their predecessors, we have seen a complete evolution in the treatment of multiple myeloma by novel modes of action being combined in doublet, triplet and now quad regimens, improving outcomes for patients through their synergistic benefits, which means they extended patient lives, almost doubling the number of patients who are now living longer and able to receive additional lines of therapy.

Amongst other things, this has led to a $20 billion growth in the market since 2004. And even more, the market projections, even with REVLIMID coming off patent, where you know REVLIMID represents 30% of the market value today, will continue to grow significant

going forward. But simply put, the market will continue to grow because there is ample opportunity to do better for 70,000 patients that live today with multiple myeloma because 1/3 of them will not survive more than 5 years. The portfolio we have created has the potential to transform multiple myeloma into a curable disease with our complementary modes of action and our approach to combination in sequencing.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So this is what moving towards cures looks like in this slide. On the left, over the past 70 years, there's been dramatic improvement in the survival for patients diagnosed with this disease with the introduction of novel therapies, many of which were J&J therapies. J&J has been at the forefront of this. The figure on the right gives you an idea of how this all comes together, and we are attacking multiple myeloma cells in orthogonal ways. So instead of treating and then waiting for resistance to emerge and then treating with something else, we're coming in with an approach to the disease where tumor cells cannot escape. And this is how we begin to drive to cures, and this is what we aim to do.

So now I'd like to go through some of the data. CARVYKTI, we believe, is a potential best-in-class cell therapy, probably the most active therapy that we've ever seen in multiple myeloma. With nearly 100% overall response rate, a stringent complete response rate of 83%, this is the best complete response rate we've ever seen in a multicenter study in this setting.

In addition, we have 2 novel CD3 redirector molecules. And one might ask, why do we need all these therapies in this disease? And again, if you're going to get to cures, physicians need multiple weapons in their arsenal. So one of those weapons is TECVAYLI, the first-ever approved BCMA CD3 with activity that is remarkable, a response rate of 63%. Most of these responses are very deep with VGPR, very good partial response, or complete response. We also introduced TALVEY, a completely novel CD3 drug with a new target that has shown a 72% response rate. Again, most of these are deep responses.

So let me just be clear with these. Each one of these drugs alone has the potential to transform the treatment paradigm of the disease. But having these together with the expertise and the development capabilities to build regimens will truly revolutionize approaches to this disease and we believe can potentially lead us to curative treatments.

So we've already made a lot of progress in starting to build these regimens. I'm showing some examples here, and there will be more combinations and sequence in future studies. So on the left in this slide, you see DARZALEX plus either TECVAYLI or TALVEY. Both of these regimens now have combination response rates that look superior to the single agent numbers. These combinations are now both in Phase III studies. On the right side, you see an even more innovative approach, combining 2 different CD3 redirectors with TECVAYLI and TALVEY that target different molecules on the multiple myeloma cell. So it's important to point out here that a loss of target can be a mechanism of resistance to these therapies. So by hitting both targets at the same time, it is a way to prevent this resistance.

So here are some results. We treated the highest-risk multiple myeloma patients, those who have extramedullary disease, meaning they have a solid plasmacytoma. And these patients don't respond well to standard therapies. So in these patients, TECVAYLI and TALVEY as single agents are active compared to conventional agents with about a 30% to 40% response rate. But when we combine these 2 drugs together in this high-risk population, we now once again get a 70-plus percent response rate, a really dramatic improvement. So this regimen is now also planned for Phase III studies, not just in extramedullary disease but in other populations as well. So these examples that we've shown here give you an idea of what we mean when we talk about building regimens. With 4 major first or potential best-in-class therapeutics, we can redefine the future of how we treat this disease.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

So how are we advancing the multiple myeloma paradigm? Our focus is on advancing therapies into earlier settings with future cures in mind through our deep disease area expertise and portfolio strengths across all lines of therapy. In the near term, we have transformative therapies in every line that will drive our exponential growth. DARZALEX will become even more a frontline treatment with the approval of PERSEUS. CARVYKTI will be available as a second-line option upon the launch of CARTITUDE-4. And we will maximize the adoption of our bispecifics, TECVAYLI and TALVEY, across all patient subtypes in the later settings.

In the midterm, we're moving the combinations to the second-line setting and CARVYKTI to the frontline setting. First, to

transplant-ineligible patient population starting with CARTITUDE-5. And soon after, to patient-eligible patient population with CARTITUDE-6. You know we are the first bold company to aim to replace transplantation in multiple myeloma. So within this decade, as our studies read out, we will have a regimen in every line of therapy in sequence, and we will be the only pharmaceutical company with a full spectrum of offerings for multiple myeloma.

We already have an industry-leading portfolio that will deliver more than $20 billion in peak sales. And we expect that with it, more than 50% of patients in multiple myeloma will be treated by a Johnson & Johnson medicine. And by the end of next year, we also expect to be #1 pharmaceutical company in hematology. With our industry-leading portfolio, we aim to transform the treatment and cure more than 50% of patients with multiple myeloma within this decade.

So let me now transition to lung cancer. We are working to create a future where we deliver the same level of transformation for lung cancer that we just described in myeloma. It has been a sadly uneventful 7 years in EGFR-mutated lung cancer space. And our aim is to disrupt that by delivering novel multi-targeted therapies, as evidenced by our pivotal head-to-head data recently presented at the European Society of Medical Oncology. We believe we can shaken the ground. But this is why it matters. Lung cancer is the leading cause of cancer mortality worldwide, killing almost 2 million people each year, and the incidence is rising. Because of that, within the decade, the market for lung cancer is expected to grow the most compared to any other oncology market, rising to a whopping $60 billion in value.

More than 70% of patients initially diagnosed with lung cancer do not survive more than 5 years. Even with innovations in immunological and targeted therapies, we have only seen a dent in mortalities. So quite frankly, because of that, we have to use overall survival as the critical measure of success moving forward. And for this reason, we have designed most rigorous studies to advance the science. With 3 impressive Phase III studies we have delivered simultaneously, you have all seen the first impact that we already made. We have committed to bring forward transformative therapies. And with RYBREVANT and lazertinib, we're doing exactly that. These are dual targeted therapies with a novel bispecific antibody that works through immune path, combined with a third-generation efficacious and very well-combined TKI. And we're also progressing fast with subcutaneous formulation as well as protocols for best patient treatment in our COCOON trials.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So there is a massive opportunity to better treat this disease with RYBREVANT and lazertinib, and we feel we can make a significant impact. RYBREVANT is the first-ever fully human bispecific antibody to be approved in lung cancer and has a unique mechanism of action, targeting 2 major oncogenic driver pathways and bringing in an immune response through an activated Fc domain.

The clinical development plan for RYBREVANT plus lazertinib is extensive. So I'll first give you an overview, and then we'll look at some of the data. MARIPOSA is the Phase III study with RYBREVANT plus lazertinib in frontline common EGFR mutation, which read out in September. We presented results at ESMO, and we since have initiated a rolling submission to the FDA. Importantly, this is the first targeted combination study in this population. Also, the first regimen ever to show a survival trend head-to-head versus osimertinib. MARIPOSA-2 is a second-line Phase III study of RYBREVANT plus chemo in common EGFR mutation again in patients who have received osi upfront and have progressed. The Phase III PAPILLON study, for which we recently received FDA priority review, is RYBREVANT frontline in exon 20 insertion and combined with chemotherapy. And finally, PALOMA is a study where we're putting in place subcutaneous formulation and optimizing the regimen to improve convenience for patients.

So let's now take a look at some of the results of these 3 major Phase III studies, and I'll start with MARIPOSA. So on the left is a Kaplan-Meier curve for the progression-free survival. And as you see, highly positive, clinically and statistically significant difference in progression-free survival. But perhaps even more important is a notable overall survival trend. So this is critical in lung cancer. We want patients to be free of progression for sure, but it's even more important that they live longer as we begin to introduce combination regimens.

Importantly, MARIPOSA was not the only RYBREVANT study to show a survival trend. All 3 Phase III studies showed this trend. MARIPOSA-2, which had progression-free survival hazard ratio of 0.48 (corrected by company after the call), also had OS trend. PAPILLON has a ratio of 0.39 for progression-free survival, also had an overall survival trend. So very important results in all 3 studies,

positive trials with secondary endpoints all going in the right direction. And we have high confidence that with continued follow-up, these overall survival trends will become statistically significant as well.

So with these remarkable results, we believe we are in a place to have best-in-class EGFR portfolio across all lines of therapy. As you see in this graph, we started in a small population, moved into larger population. We also moved to frontline to change the treatment paradigm. It's also important to point out that over the next year, we believe the MARIPOSA regimen and data will continue to look better. The overall survival results, we believe, will end up getting to statistical significance. Our mitigation approaches for side effects will improve the patient experience, and we will introduce the subcutaneous formulation.

Finally, we're also exploring RYBREVANT in other areas where EGFR and cMET oncogenic pathways are important drivers. This includes an ongoing study in colorectal cancer.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

So why are we doing all this? The standard of care today in this space is far from good. 18-month progression-free survival and under 3 years overall survival for young, mostly working women with families. There's just no way that's good enough.

So there are a few different opinions and options of the path moving forward. Recently, we have seen an attempt to bring back chemotherapy in the frontline setting. On the surface, there have been positive results of the study that showed improvements in progression-free survival. But that's actually the problem. Combining both lines of therapy in the frontline setting provides detrimental to overall survival, as shown in the World Conference on Lung Cancer.

So the question becomes, is bringing back chemotherapy in the frontline setting the right thing to do for patients? Well, we have asked the patients, and the answer is no. Now here's what we have with RYBREVANT and lazertinib. A powerful, durable chemo-free regimen that brings not only much awaited and clinically meaningful progression-free survival but shows a trend for statistically significant overall survival. And on top of that, using RYBREVANT and lazertinib in the frontline, patients still have a standard line of therapy after progression.

So with its immune-driven effect shown in PAPILLON and the CNS protection shown in the MARIPOSA, RYBREVANT is set to become the standard of care in the frontline therapy and the backbone for the future. And we intend to bring it to as many patients as possible. As of now, we have treated 5,500 patients in 33 countries in almost 700 centers. And so with that, we think and looking forward to bringing these therapies to above its $5 billion peak year potential.

But our final topic is bladder cancer. It's a critical area of research. Any health care system finds bladder cancer to be the most expensive cancer type. In 2021 in the United States, only to treat bladder cancer patients newly diagnosed and those with disease recurrence, the costs were exceeding $6.5 billion. Well, this is because the treatment of bladder cancer is particularly intensive. But even more than that, it is a daunting, dreaded diagnosis.

Imagine this as a standard of care. Excruciatingly painful installations of BCG, described by patients as a tiger clawing from the inside. As a patient needs to turn their body from left to right to get the BCG fluid touching every wall of the bladder. And after that, eventually, the bladder is removed because BCG simply doesn't work in the long run. BCG has been an ingrained standard of care past 40 years, but every response is very short-lived.

Disease recurrence and BCG failures are common, and up to 80% of patients with non-muscle invasive bladder cancer progress within a year and require retreatment. It should not be a surprise that a refusal of BCG treatment is common. But despite of that, doctors still use it because there is no other option.

Today also, the majority of the pipeline agents being discovered are being investigated in bladder cancer with a combination with BCG, but they don't aim to replace it. That's not a future to look forward to if you're a patient. So with TARIS, our targeted releasing system, we think we will transform the standard of care for this large and currently underserved patient population.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

Yes. So after the past few years, every time I talk about our portfolio with you guys, I've told you that the TARIS is coming. And now the data has arrived.

So TARIS, as Biljana said, is a unique platform of drug and device that will transform the treatment of localized bladder cancer. The drug device system is inserted in the bladder in order to provide a sustained and controlled release of drug locally over months at a time. This means patients get highly active drug in the bladder, sustained exposure without systemic toxicity. The procedure of inserting and extracting is a straightforward urologic office procedure without a need for surgery or hospitalization. So this technology was really designed to deliver potential cures for localized bladder cancer.

With TAR-200 and TAR-210, we presented some truly transformational data, and our registration program is well underway. TAR-200 is a device that releases gemcitabine in the bladder, and the results in BCG-exposed patients are truly remarkable, 77% complete response rate. We have 3 major Phase III studies that we believe can replace the standard of care in high-risk non-muscle invasive bladder cancer and in muscle invasive bladder cancer.

TAR-210 takes the platform to the next stage with an innovative targeted therapy. This drug-device combination releases erdafitinib, our first-in-class FGFR inhibitor, to treat FGFR-mutated localized bladder cancer. Results in the intermediate risk non-small cell lung cancer, bladder cancer population, which is about 70% FGFR mutated, are astounding, approaching a 90% complete response rate. So we're now rapidly moving TAR-210 to Phase III studies as well. These 2 therapies cover different patient populations of unmet need, allow us to cover the full localized bladder cancer population.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

With these incredible study results, we are confident that we will truly transform the treatment for bladder cancer and displace BCG and chemo-radiotherapy as standards of care. We are dedicated to bladder-sparing regimens and bringing to patients and clinicians the first targeted therapy that we believe will redefine localized disease and improve the quality of life of nearly 400,000 patients living with bladder cancer today, and ultimately, bringing this therapy to above $5 billion peak year potential.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So as we mentioned before, it's impossible to fully cover all the programs in our pipeline. But I did want to highlight a few things that you should be aware of in the near term for our early pipeline.

As I mentioned, we plan to continue to deliver about 2 novel therapies per year over the next few years. Over the past few years, we've shown the strength of our internal discovery capabilities. It's important to note that our 3 approved bispecific antibodies were all discovered and developed internally. Our pipeline remains really strong. The external in-licensing environment is highly favorable. We expect our internal and external approach to continue to deliver at the same level of productivity.

So I just want to cover a few of the highlights of innovation from this early pipeline. We have next-generation trispecific antibodies already in the clinic showing some interesting data. We're going after cell therapy with novel approaches to CAR-T. We completed a couple of deals around ADCs with next-generation platforms as well as targets. We also have a menin program that we are really excited about as potential best in class that we're presenting our clinical data at ASH. We have a number of programs in the clinic that are novel approaches to prostate cancer with targeted biologics. And last, we have an oncolytic virus that we believe is best in class, and we have a clinical approach and indication that gives us high probability of success.

So we will finish where we started. Our success has been driven by a mission, strategy, execution and culture that has withstood the test of time. We're fierce in pursuing cures, but we are also humble. Innovation, we know, requires an open mind. So what comes next? We continue on the mission of cure, and we continue to deliver rapid progress.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

And we never rest in our determination to bring transformational medicine to patients. That is our inspiration, to boldly pioneer the field, and with it, establish Johnson & Johnson as #1 oncology company as we strive to get in front of and ultimately eliminate cancer. Thank you.

Operator

Thank you ladies and gentlemen, please welcome Worldwide Vice President, Immunology, Candice Long; and Global Therapeutic Head, Immunology, David Lee.

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

We are redefining the treatment of immune-mediated disease with transformational therapies. Since 2018, we have been on a journey to expand the reach and impact of our immunology portfolio with a focus on patient need, science and value. Today, Candice and I will walk through how we are delivering against our growth strategy with multiple first and best-in-class programs that are leveraging our deep expertise and proven track record. What you'll see here today is an industry-leading portfolio that is fueling the growth outlook for Johnson & Johnson.

Our vision has us focused each day on restoring health for the millions of patients living with immune disease. And our mission acknowledges that the vast majority of patients are still waiting. That gap defines our relentless dissatisfaction with the status quo. Today, we'll review the impact of our systematic and evidence-driven approach and our exclusive focus on achieving durable symptom-free remission.

Now why does this make us unique? While others are focusing on treatment response, we are raising the bar and focusing on durable symptom-free remission across our portfolio, a portfolio that has broad impact for patients at every stage of life. Ultimately, we are enabling patients to move from a hope for some day to an expectation that they can reclaim their lives every day. With this approach, we are ushering in the next wave of immunology innovation, building upon an already profound legacy.

With the introduction of REMICADE 25 years ago, we pioneered a revolution that defined a new standard of care. And since then, we have distinguished ourselves by consistently redefining that standard of care with medicines like STELARA and TREMFYA. Here, you see our growth trajectory of 9% CAGR over the last 11 years, representing 5 internally developed assets, 32 approvals and millions of patients whose lives have been transformed.

Finally, while our discovery engine continues to fire, we remain committed to the best possible science regardless of where it comes from. Through strategic collaborations, we further access the best in innovation.

Candice Long ***Johnson & Johnson - Worldwide Vice President, Immunology***

And truly understanding patient need lies at the heart of our strategy. There are 30 million people living with immune-mediated diseases in our areas of focus across the G8 countries. Only about 10% of these individuals are experiencing remission. A staggering statistic when you think about the scientific breakthroughs that have happened over the last few decades.

So for us to expand our reach and impact within our portfolio, we need to appropriately contextualize the patient need. About 25 million individuals are eligible for therapy. 75% seen here in the red portion of the pie, they are not receiving advanced therapies for a variety of reasons. That leaves about 3 million people, the blue segment, who have been diagnosed for diseases where there are no or extremely limited advanced therapies, and about 3 million people who have failed or lost response to the current advanced therapies seen here in the purple.

Our pathway approach takes each of these patient groups into account. For that 10% of patients that you see here in gray who have achieved durable remission, we are proud that our treatments have contributed to their positive outcomes. And it's important to point out that this segment is not a strategic focus area for our next-generation treatments. What's more, this 10% population is, in fact, the focus of companies making biosimilars. So as an innovation-based company, we are competing in completely different arenas. Where we

operate, the market growth is expected to be $50 billion through 2030.

Now to your left, you see the foundation on which we've built our legacy, all of which continue to fuel the growth of Johnson & Johnson. On the immediate horizon, we have our much anticipated programs, TREMFYA, JNJ-2113, nipocalimab and JNJ-4804, all of which are in Phase II or Phase III across multiple indications. What comes next? New mechanisms, new modalities, all of which are building from our experience and our expertise.

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

So this brings us to our pathway strategy. We invest deeply with a long-term view in our carefully selected pathways. This yields the differentiating depth of clinical and scientific insights we're talking about today. A key example is our work in the IL-23 pathway. We established the foundation for our IL-23 expertise with STELARA, the first anti-IL-12/23, which today is indicated for psoriatic and inflammatory bowel diseases. Leveraging our learnings and experience, we then deliver the next generation of innovation with TREMFYA, the first p19 directive selective IL-23 inhibitor with current indications in psoriatic disease and with inflammatory bowel diseases up next.

These treatments are both well known for their impressive efficacy, durability and clean safety profile. Now we continue to expand our leadership in IL-23 with JNJ-2113, our first and best-in-class targeted oral peptide; and with JNJ-4804, our first-in-class biologic combination. We're also expanding to other targets in this pathway, including JNJ-1459, a potentially best-in-class investigational targeted small molecule IL-17 inhibitor.

Candice Long ***Johnson & Johnson - Worldwide Vice President, Immunology***

So let's take a closer look at TREMFYA and how we believe that in addition to our clinical data, the design and the attributes of this molecule make an important difference for patients while also distinguishing us in the market. From a patient need perspective, TREMFYA checks multiple boxes with its biggest impact for patients with undertreated disease. TREMFYA has proven that the IL-23 pathway is strongly implicated in psoriatic disease and is currently helping more than 300,000 patients. It's demonstrated unmatched durability in psoriasis, sustained response for up to 5 years, superiority versus 3 other mechanisms of action.

And in psoriatic arthritis, TREMFYA is the only IL-23 inhibitor in the class that showed inhibition of structural joint damage in a Phase III trial. And we are very excited about our Phase III data for our TREMFYA IBD studies, which will be available in the first half of 2024. Our research has already demonstrated the differentiating benefits of TREMFYA in this space. And we know that not all IL-23 inhibitors are the same.

TREMFYA is indeed unique. TREMFYA is the only IL-23 inhibitor with high potency for blocking IL-23 signaling and for binding to both the IL-23 and the CD64, allowing it to localize the source of inflammation where the IL-23 is produced. In our Phase II study, TREMFYA achieved a 65% response rate, the best 1-year clinical remission rate to date in a Crohn's disease registrational program with the durability of response through 3 years.

What's more? TREMFYA is the only IL-23 inhibitor with the potential for the convenience of subcutaneous induction across both of our IBD indications. This will be a huge benefit for patients. Overall, we are anticipating TREMFYA peak year sales across psoriatic and inflammatory diseases to reach over $5 billion.

So let's pivot to the approximately 5 million patients living with moderate to severe psoriatic and inflammatory bowel diseases who are eligible but not receiving advanced therapies. Why? First, the current oral market is vastly underserved. Treatments are less effective than currently available advanced treatments. They come with significant safety trade-offs.

And in addition, despite the safe and effective injectable biologics, the most common reason cited for not using existing advanced therapies are, one, the method of administration and the overall perceived risk of intravenous and subcutaneous treatments. This tells us that if there was a once-daily pill option that delivered a durable symptom-free remission along with a demonstrated strong safety profile, you would redefine the standard of care for patients with immune-mediated diseases.

What's more? 75% of patients using injectables report that they would switch to a once-daily pill that offered high efficacy and proven safety. Finally, there is significant worldwide market growth for orals expected by the end of this decade. And this sets the stage for our new investigational targeted oral therapies.

We have potentially 2 transformational treatments in this space that are expected to launch by 2030. First, we will change the treatment paradigm with JNJ-2113, our potential first and best-in-class targeted oral peptide. Second, we have JNJ-1459, our investigational targeted small molecule IL-17 inhibitor, which has the potential to also be best in class.

IL-23 and IL-17 well-established mechanisms in psoriatic disease with substantial and growing market shares. Each of these assets will have a distinct role in our portfolio. What this means is that in addition to psoriatic disease, we anticipate that JNJ-2113 will also be extremely efficacious in IBD and that JNJ-1459 will be effective in other immuno-dermatologic as well as rheumatic diseases.

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

The results from our Phase IIb study in adults with psoriasis show that JNJ-2113 delivers an unprecedented profile. The treatment demonstrates complete skin clearance at levels comparable with current advanced injectable biologics, levels not seen in currently approved oral psoriasis treatments. JNJ-2113 also demonstrates an encouraging safety profile versus those currently approved orals.

So we kicked off our pivotal Phase III development program this quarter with 2 studies in adults with moderate to severe psoriasis. And in addition, 2 head-to-head studies will commence in the first half of 2024. For all of these studies, we will use a 200-milligram once daily dose. And we include a higher primary efficacy endpoint than the industry standard, again, raising the bar on remission. We also have initiated a JNJ-2113 Phase IIb study for adults with ulcerative colitis.

Now pivoting to JNJ-1459, our investigational targeted small molecule IL-17 inhibitor. We completed Phase I study -- our Phase I study and are launching a Phase II dose-ranging study in psoriasis and are evaluating other systemic inflammatory diseases next.

In short, we plan to lead the orals market. In fact, we see an estimated revenue potential of more than $5 billion in peak year sales across indications for JNJ-2113 alone. This is an increase from our $1 billion plus categorization we shared at our 2021 Pharmaceutical Business Review, which is the result of our phenomenal data.

Okay. Now let's talk about refractory patients, those individuals who have experienced inadequate efficacy or loss of efficacy from advanced therapies. This is a significant and growing population. And this brings us to JNJ-4804, our novel combination biologic that targets IL-23 and TNF to well-defined drivers of immune-mediated diseases. Our proof-of-concept study in ulcerative colitis showed compelling efficacy of 83.1% with a safety profile consistent with monotherapy.

We anticipate JNJ-4804 breaking through the monotherapy efficacy ceiling that exists and being able to do it across multiple diseases, including ulcerative colitis and Crohn's disease, which represent more than 500,000 people in the G8. JNJ-4804 also holds a promise for even higher efficacy in longer-term maintenance dosing.

And we plan to explore this asset in disease modification as well. Our deep expertise and broad portfolio of assets uniquely positions us to identify effective combinations. In fact, JNJ-4804 is our first of 3 combination therapies. With 4804, we are first in class, and no one is in our rearview mirror, meaning JNJ-4804 has the potential to become the leading treatment for these refractory patients. Now to put the value of this in context, in IBD alone, we expect peak year sales to be in the $1 billion to $5 billion range.

Candice Long ***Johnson & Johnson - Worldwide Vice President, Immunology***

Auto- and alloantibody diseases represent an area of immense need, affecting 240 million people worldwide who live with more than 80 different diseases, most of which have few or no safe, effective, approved or targeted treatments. These diseases are caused by pathogenic IgG antibodies made by one's own body that detect critical organs and tissues. In pregnancy, alloantibodies from a pregnant person can attack their developing fetus.

Nipocalimab is a differentiated anti-FcRn that we believe will define the standard of care of auto and alloantibody diseases. Nipocalimab

is the only anti-FcRn with proof of mechanism across 3 key segments: rare autoantibody, maternal-fetal and prevalent rheumatic diseases. The addressable population for nipocalimab in our initial 10 indications is just over 2 million people. And the total estimated revenue potential is more than $5 billion based on peak year sales.

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

So let's dig a little deeper into why the unique molecular structure of nipocalimab may hold the key to differentiated efficacy and safety among anti-FcRns. First, nipocalimab binds to FcRn with one of the highest affinities of any anti-FcRn. And this translates into nipocalimab's potential best-in-class IgG profile lowering.

Second, our proprietary crystal structures demonstrate nipocalimab's binding is highly specific to the IgG binding site without overlap on the albumin binding site. This is potentially why nipocalimab has been found to have no clinically significant impact on albumin and lipid levels at the current doses being evaluated for chronic disease. Of note, due to its pH independent binding to FcRn, nipocalimab blocks placental IgG transfer without entering the fetal circulation. Thus, it's the only anti-FcRn being studied in pregnant populations.

In addition to the unique molecular structure of nipocalimab, there are other key factors contributing to its potential best-in-class designation such as efficacy, optimized safety profile, convenient dosing and device paradigm and its unparalleled position in the maternal-fetal space.

So let's turn to these results. In our rare autoantibody segment, we have transformative Phase II data in moderate to severe generalized myasthenia gravis. Existing advanced therapies for this disease are either suboptimal in terms of safety and tolerability or do not offer patients with this chronic disease a regular dosing schedule that keeps their symptoms under control.

At the dose we're studying in our Phase III program, we anticipate IgG reduction of up to 77%. And we expect our Phase III top line results to be ready to communicate in early '24. Now since myasthenia is a chronic disease, we are planning to ultimately meet patient needs with a convenient treatment administration delivered at home twice monthly with regular stable dosing in a differentiated subcutaneous device. Myasthenia gravis will be our first indication in rare autoantibody with warm autoimmune hemolytic anemia up next, where we will be first in class.

Candice Long ***Johnson & Johnson - Worldwide Vice President, Immunology***

In maternal-fetal immunology, nipocalimab is also the only anti-FcRn, meeting the needs of patients living with devastating illnesses where there are no approved medical therapies. We delivered groundbreaking clinical data earlier this year in hemolytic disease of the fetus and newborn, or HDFN, a rare disease where alloantibodies from the pregnant person crossed the placenta, attacking fetal red blood cells, which can result in the death of the fetus.

Pregnancies affected by this disease may require repeated intrauterine transfusions, which are invasive and risky. Our Phase II study demonstrated 54% of live births without the need for an intrauterine transfusion. This compares to less than 10% historically. We look forward to delivering the first transformative medical treatment in 50 years for this 2-person disease with very high patient need. Critically, having this unique data in maternal-fetal immunology differentiates nipocalimab from other agents since approximately 80% of rheumatology patients are female and up to half are of child-bearing potential.

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

Finally, we are excited by our first-in-class, first-in-disease data from our rheumatoid arthritis proof-of-concept study, which confirmed our intent to pursue a combination therapy. Here, we're looking at patients who have inadequate response to biologics. In rheumatoid arthritis, that's about 20% to 30% of patients. Our clinical study is the first time that selective reduction of IgG autoantibodies has ever shown efficacy.

Our analysis also confirmed that combining our anti-FcRn with an anti-TNF, again, hitting 2 complementary pathways that we know impact disease activity offers the potential to deliver a truly transformative therapy. And efficacy nearly doubled in a prespecified

autoantibody high subpopulation, which shows the potential for a true precision medicine approach. Our Phase II combination proof-of-concept study has launched, and we are excited to continue this program where we have a strong legacy of transforming patient lives.

Candice Long ***Johnson & Johnson - Worldwide Vice President, Immunology***

I'd like to leave you with a few parting thoughts. As Johnson & Johnson, our immunology legacy has set the foundation, and our pathway strategy is paving our way for the future. You heard the phrases best in class and first in class many times in this presentation. This is why we are so confident in saying that we will redefine the standard of care.

And finally, there's so much more to come. As we expand the reach and the impact of our portfolio, we will transform the lives of millions of patients, create unprecedented value for the organization and emerge the leader in immunology by the end of this decade. Thank you.

Operator

Ladies and gentlemen, please welcome Worldwide Vice President, Neuroscience, Peter Fang; and Global Therapeutic Area Head, Neuroscience, Bill Martin.

Bill Martin ***Johnson & Johnson - Global Therapeutic Area Head, Neuroscience***

Today, we are here to provide an update on our leadership in the precision neuroscience revolution to reduce the burden and disability caused by serious nervous system disorders. Our goal is to deliver breakthrough solutions for people with neuropsychiatric, neurodegenerative and neurological autoantibody-driven diseases. Our strategy harnesses scientific advances in 4 areas: human genetics, data science, biomarkers and clinical trials -- and digital health, sorry. We leverage these advances to enable precision approaches for target and patient identification, target modulation and therapeutic focus.

Peter Fang ***Johnson & Johnson - Worldwide Vice President, Neuroscience***

For nearly 7 decades, we have pioneered innovative medicines that have significantly advanced treatment for nervous system disorders. And our journey began with Haldol for the treatment of schizophrenia, which was invented by Dr. Paul Janssen in 1958. And since then, we have introduced over 20 industry-leading innovations. We've delivered over $6.8 billion in sales in 2022 and established ourselves as the #1 psychiatry company in the world. And most recently, we launched INVEGA HAFYERA, the first and only twice yearly treatment for adults with schizophrenia. And we also introduced SPRAVATO, marking the first new mechanism of action in more than 3 decades to treat 2 challenging types of depression.

However, the number of people affected by diseases of the brain continues to rise, driven by both the mental health crisis and the aging population. And despite progress in understanding and treating these conditions, significant unmet needs persist, impacting the lives of over 1 billion people. Half of all schizophrenia patients experienced partial improvement or unacceptable side effects, resulting in a significant economic impact.

In major depressive disorders, most patients experience residual symptoms even with standard of care and are expected to cost the global economy by up to $6 trillion by 2030. And in Alzheimer's disease, the economic burden is a staggering 12x that of cancer. And so given the high unmet need, we expect the neuroscience market to double and grow by almost 12% by 2030. And on the foundation of our expertise in schizophrenia and depression and by adding our precision neuroscience approach, we aim to become the #1 neuroscience company in the world.

Bill Martin ***Johnson & Johnson - Global Therapeutic Area Head, Neuroscience***

However, the heterogeneity of the 1 billion people impacted by these diseases demands a precision approach to neuroscience research. Today, most conventional therapies have a one-size-fits-all approach, leading to mixed outcomes. That is why our scientists at J&J are dedicated to relentless innovation in biomarkers, data science and clinical trials.

Our goal is to identify disease subtypes in patients, tie targets of interest to disease and predict which individuals will best respond to a particular medication. We aim to treat the right patient with the right treatment at the right time. We're working to bring greater precision to the development of an expanded differentiated portfolio of novel products.

Our robust pipeline is guided by our deepened understanding of mechanisms of key neurological disorders and our ability to identify distinct subtypes within these diseases. Each treatment is designed to target a subpopulation of patients by focusing on the underlying biology and symptoms of each patient. And it's exciting to share that we have 6 planned submissions by 2030 with 5 of them being first-in-class therapies. And now we will provide you with an in-depth view of our portfolio and pipeline.

Peter Fang ***Johnson & Johnson - Worldwide Vice President, Neuroscience***

As mentioned earlier, our legacy in psychiatry is unparalleled. Today, our leading INVEGA portfolio provides adults with schizophrenia the longest-term symptom control in a single dose. In fact, in a recent study, over 96% of patients who continued on INVEGA HAYFERA were relapse free in the open-label extension. And nearly 9 out of 10 patients completed 2 years of treatment. Our INVEGA portfolio has impacted nearly 6 million patient life years, delivered over $4 billion in sales in 2022 and has become the leading long acting injectables portfolio in schizophrenia.

In depression, SPRAVATO continues to gain momentum both in the U.S. and globally with approvals in over 70 countries and having treated more than 70,000 patients. Sales have experienced an increase of more than 80% when compared to the previous year. And a recent head-to-head study published by The New England Journal of Medicine showcased the efficacy of SPRAVATO compared to a commonly used adjunctive therapy.

Patients on SPRAVATO were 70% more likely to achieve and sustain remission. And these data validates SPRAVATO's first-in-class breakthrough innovation for people with challenging forms of depression. We believe with its sustained momentum, we anticipate SPRAVATO reaching peak sales from $1 billion to $5 billion.

Bill Martin ***Johnson & Johnson - Global Therapeutic Area Head, Neuroscience***

But what about our future portfolio? As Jennifer highlighted, we are leading where medicine is going. We know that major depressive disorder is a heterogeneous disease characterized by mechanistically distinct features such as anxiety, anhedonia and insomnia. Under current standard of care, 7 out of 10 patients experience residual symptoms. We are committed to developing therapies that specifically target the underlying mechanisms of disease and address these inadequately treated symptoms.

Our near-term portfolio includes aticaprant and seltorexant, both anticipated to enter the market in rapid succession within the next 2 years. A key future growth driver for us is aticaprant, which acts as an antagonist to the kappa receptors that control the processing of reward and when activated, contribute to anhedonia and depression.

Anhedonia, which is characterized by a loss of interest and enjoyment in activities, is present in approximately 60% of individuals with depression. It's the third most common residual symptom after first-line treatment. In a Phase II clinical trial in patients with MDD and inadequate response to standard of care, aticaprant as an adjunctive treatment showed greater reduction in overall depression symptoms compared to patients under standard of care alone.

The magnitude of the overall antidepressant efficacy was greater in those with elevated anhedonia with a more favorable safety and tolerability profile relative to other adjunctive treatments. Phase III trials are underway, and we anticipate aticaprant to achieve peak sales exceeding $1 billion.

Now like aticaprant, seltorexant targets a specific subgroup of patients with MDD. It antagonizes the orexin-2 receptor to reduce the wakefulness and hyperarousal associated with depression. Half of the people with depression experience sleep disturbances that are not fully addressed by current antidepressant treatments. Phase II studies show that patients who receive seltorexant as an adjunctive therapy improve their depression symptoms as well as sleep onset and maintenance. The Phase III program has yielded promising results, which we look forward to sharing in 2024. We expect peak sales for seltorexant to exceed $1 billion.

In Alzheimer's disease, we are applying precision approaches to improve care of targeted patient subpopulations at all stages of the disease. AD begins with the accumulation of 2 proteins, amyloid and tau. Our robust programs on tau aim to deliver potential best-in-class disease-modifying treatments. In the early stages with memory symptoms, we seek to intercept disease progression with a

monoclonal antibody directed against the pathological form of the tau protein in contrast to previous therapies directed against the end terminal portion of the protein.

Additionally, recognizing that 315 million people globally show signs of AD before symptoms, we aim to identify and treat them early, reducing irreversible brain damage and slowing or stopping the disease. Our collaboration with AC Immune on tau active immunotherapy targets a relevant epitope adjacent to the aggregation domain. And we have already demonstrated a maturation of the immune response towards antibodies with preferential binding to pathological phospho-tau aggregates.

If successful, this would mark a significant milestone as the first active immunotherapy targeting tau. For AD patients with neuropsychiatric symptoms, we're studying seltorexant to treat mild, moderate AD with agitation based on hypothesized dysregulation of the orexin system.

Posdinemab could potentially be available as early as 2028 with anticipated peak sales exceeding $5 billion. Our comprehensive approach to Alzheimer's disease is a concrete example of how we are leading where medicine is going.

Peter Fang ***Johnson & Johnson - Worldwide Vice President, Neuroscience***

We are at a pivotal moment for J&J innovative medicine for neuroscience. On our nearly 7-decade legacy in psychiatry and our precision neuroscience strategy, we are incredibly well positioned to make an impact to the over 1 billion people affected by diseases of the brain and double our sales by 2030. We have an exciting portfolio of innovative first-in-class therapies. And in the near term, we expect multiple late-stage data readouts, submissions and launches. And we will also continue to strengthen our pipeline with external innovation. And ultimately, we aim to deliver up to 4 blockbusters and 2 mega blockbuster brands across neuroscience in the foreseeable future.

In closing, our precision neuroscience strategy has set us on a trajectory to double our growth and become the #1 neuroscience company by 2030. And we are incredibly excited to bring these innovations to patients worldwide. Thank you.

QUESTIONS AND ANSWERS

Operator

Ladies and gentlemen, please welcome Jennifer Taubert, John Reed, Tom Cavanaugh, Peter Lebowitz, David Lee, Bill Martin, Biljana Naumovic and Raychel Kruper.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Thank you, everyone. So as a reminder, for those in the room, please use your push to speak microphones in front of you once I have called on you. For those online, please use the chat box to ask your questions. So with that, we are happy to take your questions. And I see Chris Schott.

Christopher Thomas Schott ***JPMorgan Chase & Co, Research Division - Senior Analyst***

Great. I guess my question was on CARVYKTI and maybe the broader multiple myeloma kind of outlook. Obviously, very impressive data for that asset. I'm just interested maybe in your views of what percent of the market you think could be ideal candidates for CAR-T, your latest views of when you'll have capacity to pursue those patients and maybe just any color you can provide of the $25 billion target. How much of that is CAR-T versus the other agents that you have?

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

Thank you, Chris. That's a great question. Let me start by saying that we don't provide that split of the brands in that $25 billion. And I can start first by saying that we're doing absolutely everything possible to increase the capacity. We have talked about that past full year, and you have seen the increases in capacity we have made. We have addressed it in a very systemic approach, going from the lentivirus, moving in in-house, addressing the capacity within increasing the number of slots and decreasing the number of out of spec. So we're doing everything that we can to increase the capacity. We do not comment on what the capacity can be because that definitely changes as we open and work on expansion.

As for the number of patients who could be eligible for CARVYKTI in the frontline setting, when you look from the perspective of the results that we expect to see from CARTITUDE-5 and CARTITUDE-6, if they mimic what we've seen in CARTITUDE-4, the question would be who is not a CARVYKTI patient in the frontline setting. But we will aim to get it to as many patients as possible in that setting.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

And Jennifer, I don't know if you want to comment to the $5 billion assets that are in multiple myeloma as well. So we have CARVYKTI, TECVAYLI, TALVEY and DARZALEX.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

I think you just answered that question.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Apologies.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

No, no, no. We really do have a leading multiple myeloma portfolio, and we're so excited about what we do have. And I think on CARVYKTI real quick, we've actually doubled capacity this year. We've set up a manufacturing site that's in the process of qualification in Europe. We brought on 2 external manufacturers as well, and as Biljana noted, brought lenti in-house. So based on the data that keeps coming out of the R&D team, we are more and more and more bullish on that. So excited.

And then when you take a look at not only DARZALEX and what we're doing in increasing penetration in the frontline setting, CARVYKTI, that will have a role to play as we continue to expand capacity there. And then with TECVAYLI and the TALVEY launches in the latter lines of therapy, we really do have a product for literally every patient at every stage of the disease.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Geoff?

Geoffrey Christopher Meacham ***BofA Securities, Research Division - MD***

Great. One question on lung and then one on myeloma. On lung for the PALOMA study, talk a little bit about whether you think that's needed to really drive an inflection in market share. I wasn't sure what the messaging is pre and post that data set. And then for CARVYKTI moving to first-line myeloma maybe for Peter, if you think about MRD negativity is previously not being an approvable endpoint, do you think that's needed in the first-line setting? And I'm assuming you'll be comparing yourself against REVLIMID or maybe VELCADE regimens. Talk about kind of the hurdle that you'll have to hit with respect to kind of blunting the cost-benefit conversation as those are obviously [beginning].

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

I could start with lung cancer. So look, in lung cancer space, especially in metastatic lung cancer space, you want to use your most efficacious therapy first. So in that setting, if we are bringing the broadest set of data and overall survival very soon, I think that will be the major driver of the prescription habits for any physicians because mainly the patients are going to be thinking with their legs.

When you look at the data from PAPILLON and MARIPOSA-2, we're already having to add RYBREVANT on the established chemotherapy to begin with. So intravenous therapy and having intravenous therapy in the setting where you already have chemotherapy will be a normal thing, and we think that based on the results that we have, the penetration is going to be extensive and very fast.

When we talk about the first-line setting, we really understand the need to be very patient-centric in that setting. And even though we understand that even coming with intravenous formulation is going to make a difference in patients' lives, coming with subcutaneous as soon as possible and having that convenience to the patients in the frontline setting will make all the difference as well. So that's how we see the play out between the IV and the subcutaneous.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So regarding CARVYKTI, look, we believe CARVYKTI is a frontline drug, right? Remember, frontline multiple myeloma is transplant. So replacing transplant is what we always aim to do, and we believe that that's going to be -- CARTITUDE-6 is going to be a positive study. We've already gotten that started. So we don't see it as a major hurdle to get that into frontline. It's the most active therapy that we've ever had. That's where it should sit.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Terence?

Terence C. Flynn ***Morgan Stanley, Research Division - Equity Analyst***

Terence Flynn, Morgan Stanley. Maybe a 2-part question for me. I was just wondering, as we think about the oral immunology market and IL-23, how should we think about sequencing here with TREMFYA and oral IL-23? And then the second question relates to milvexian. You expressed confidence in this asset. A competitor recently had somewhat of a setback. So maybe just remind us why you're still confident here in differentiation relative to the buyer asset.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. So maybe we start with Tom. If you want to begin?

Tom Cavanaugh ***Johnson & Johnson - Company Group Chairman, North America Innovative Medicine***

Yes, with the immunology. Sure. So first and foremost, I think as you heard from Candice, we believe both can play in this marketplace for the 5 million patients that are currently not receiving treatment or advanced therapies is a prime spot for the orals, both the 2113 and our oral IL-17. So I would say both have a play in the marketplace. There's a significant unmet medical need there and a need for what we would say high efficacy. So complete skinning clearance, a safe profile and an oral delivery.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. And then John?

John C. Reed ***Johnson & Johnson - Executive Vice President, Innovative Medicine R&D***

Yes. I'll take the milvexian question. No, we remain entirely confident, and I'll tell you why. We knew from the Phase II studies we had done and through modeling of dose response relationships that for the atrial fibrillation indication, which is more like a venous side, low-volume situation where there's slower flow that we would need to hit the target harder. So you'll notice in our studies for AFib, if you compare it with the secondary stroke prevention and the ACS, which are more arterial side, high pressure systems, you'll notice that for AFib, we have 4x the dose. So that was done very specifically because of our modeling and our data taught us that that's what you'd have to do for AFib.

The other study you mentioned, they didn't do that. There are speculations as to why. I won't get into that. But that leaves us still very confident that AFib is a great indication for us. On top of that, I would say through a biologic to Factor XI that's been tested in the market and gone head-to-head against oral Factor X with a specific question of superior safety, not efficacy but safety, that experiment has been done. And that further substantiated the hypothesis that Factor XI could be a safer target than Factor X. So between those 2 things, we are as bullish as ever about our program.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

Yes. And I would add in. So AFib is the largest of the 3 indications. So if you take a look, there's ACS, secondary stroke prevention and AFib. AFib is the biggest. And so now we're in a case where we're going to be first and maybe only. And so that also gives us an additional advantage in the marketplace. So we feel good about the program going forward.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Okay. Louise?

Louise Alesandra Chen ***Cantor Fitzgerald & Co., Research Division - MD & Senior Research Analyst***

Louise Chen from Cantor. So I wanted to ask you about your path to become a #1 neuroscience company in 2030. How much of that is buy versus build? And do you have any interest in rare but high unmet need in neuro disorders?

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. Bill?

Bill Martin ***Johnson & Johnson - Global Therapeutic Area Head, Neuroscience***

Yes. So thanks for that question. So I think that what you see in laying out today for the first time is we have multiple post-proof-of-concept assets in Phase III that we have high confidence in delivering within this time frame. We have other assets internally that are in the Phase IIb setting, which we believe have mega blockbuster potential by 2030.

Now as we've highlighted, as John captioned nicely, we remain agnostic to source of innovation. So while we have a tremendous internal pipeline, we've maintained our commitment to the external space, have done several smaller licensing deals over the last couple of years, and we'll always continue with humility to look for where there's breakthrough innovations that we can source to supplement the growth of the internal pipeline.

Trung Huynh ***UBS - Analyst***

Trung Huynh from UBS. Just another on multiple myeloma. We're looking forward to the PERSEUS data being presented at ASH later. Could you just tell us currently what the penetration is in that eligible transplant population? And where do you think it could go to post this data? And then I'm curious on your thoughts on the eventual goal to replace stem cell transplants with CAR-T. How is that going to affect DARZALEX?

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Sure. Biljana?

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

Yes. Thank you for the question. So look, we have seen the GRIFFIN data last year as well, and the excitement for the quad regimen is very high. Ultimately, what we get with PERSEUS data is confirmation of the efficaciousness of the regimen combined with the fact that there is maintenance therapy that brings tremendous benefit for the patients. So once we discuss the data on ASH, we think that we will expand into the frontline setting.

Mind you, we have not penetrated 50% of the frontline setting where we could be. So ultimately, there is ample opportunity, especially when we think of the maintenance therapy with DARZALEX going forward.

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

So just to mention how replacing transplant works with CAR-T, remember, in CARTITUDE-6, it's a DARZALEX regimen. So the idea here is, as we've sort of gone through, is in order to cure this disease, we need all these pieces in place. And again, our goal is to create these regimens to actually treat to cure. So DARZALEX will be included in that regimen.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Alec, any questions from online?

Alec Mast ***Johnson & Johnson - Investor Relations***

Yes. So one question coming from online was around nipocalimab. Can you share a bit more insight into why you're so confident in this asset's future success, particularly its ability to compete in the myasthenia gravis space as well as the opportunity you have in RA?

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Okay. David?

David M. Lee ***Johnson & Johnson - Global Therapeutic Area Head, Immunology***

Maybe I'll start. Tom, you can amplify. So we have a high degree of confidence in nipocalimab based on the data that we've demonstrated so far, its molecular profile. It's got among the highest affinity bindings to the FcRn, therefore, lowering the pathogenic disease-causing autoantibodies. We know its binding site is exquisitely specific for IgG. Therefore, at the doses we're using, we're not hitting some of the safety profiles with albumin and lipids that others are seeing, and then as we go forward and we demonstrate the ability to dose chronic diseases with continuous reliable therapies that are convenient and safe. Those are all great reasons why we're going to be, again, leading in that space.

And by the way, I would mention we're just getting started in those rare autoantibody. We also have proof of concept in maternal-fetal and prevalent rheumatology now. So again, expanding the aperture for where this drug is going to be transformative even more broadly than has been shown by others so far.

Tom Cavanaugh ***Johnson & Johnson - Company Group Chairman, North America Innovative Medicine***

Yes. I'll just -- I'll piggyback on that a little bit, and you heard it earlier, underscore the population by which we're targeting. Many of these diseases are chronic in nature. So not only efficacy is important but also safety and convenience. And from a safety factor, many of them, unfortunately, are women and women of child-bearing potential. So that unique characteristic of nipocalimab versus the other FcRns is critically important, and we're going to stress that as well as the delivery. You heard from David the ability to administer through subcutaneous formulation.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Okay. Guggenheim?

Arseniy Shabashvili ***Guggenheim Securities, LLC, Research Division - Associate***

Arseniy Shabashvili on for Vamil Divan from Guggenheim Securities. A question on the Inflation Reduction Act. How's the new legislation affecting your internal R&D priorities and the external opportunities you're looking at?

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

So Tom, do you want to start? And then to you, John?

Tom Cavanaugh ***Johnson & Johnson - Company Group Chairman, North America Innovative Medicine***

yes, I can start. I think first and foremost, we continue to believe that the IRA's drug price provisions are damaging to the innovation ecosystem, and they will inhibit patient access as well as choice and quality of care. With that said, it's early in the process, both from an industry perspective and working along with CMS. We have built all of that into our models with the statutory requirements, and the products that are currently under review right now are not major catalysts or growth drivers in the second half of the decade. So we are very confident in our ability to deliver the $57 billion in 2025 as well as the 5% to 7% compound annual growth rate through 2030. So we've taken that into our models that we know today.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

John, anything on the R&D side?

John C. Reed ***Johnson & Johnson - Executive Vice President, Innovative Medicine R&D***

No, I think it's clear. But I think some of the frustrations we have with the IRA are if you just look at -- take oncology as an example, where one tends to start late lines of therapy where patients had little to -- where we have little to offer and you gradually work your way into earlier lines with that first approval in late line, that's when the clock starts ticking. And many times, it's not even a full approval. It's an accelerated approval, and you still have to wait for overall survival data to get full approval.

But all the while, the clock is ticking, and then the incentive for investment is getting lower and lower as your time is running out. So I think it's going to be particularly frustrating for diseases like oncology. I mean if you think about the adjuvant space where you're trying to prevent tumors in the early localized, I mean those are long studies that cost -- they require large investment in those. The business case for those is going to be tough now with this IRA principle.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

So if you think about if IRA goes into effect as it's currently designed, what do you need? You need companies to go big early to develop that full indication set and to get to market quickly and have fast time to peak. That's exactly where we play and how we win. And so our R&D team does do that, builds out that broad indication set from the get-go. We run lots of trials all at the same time. We try to get in a launch, and we actually lead the industry as well in terms of speed to time to access as well as driving to peak.

And so I think that under these circumstances, as Johnson & Johnson, we're poised to win in there. And so we're continuing to adapt and position ourselves to make sure that we're going to be winning for the future as well.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Maybe another from the webcast?

Alec Mast ***Johnson & Johnson - Investor Relations***

Yes, sure. So exciting to see the strong early results from TAR-200 and TAR-210, and the TAR-200 was just granted U.S. FDA Breakthrough Therapy Designation. How quickly do you think you'll be able to get these on the market? And how do you think about the competition in this setting?

Peter F. Lebowitz ***Johnson & Johnson - Global Therapeutic Area Head, Oncology***

Yes. So with TAR-200, there is -- and SunRISe-1, there is a clear validated FDA path to an accelerated approval. And so that trial is underway. We're enrolling patients, and it's all a matter of how that trial -- number of patients we need on discussions with the FDA. So a clear path there.

With TAR-210, it's possible also to get to an accelerated path, and that's something we're exploring now. But the results with that are so spectacular that the team has already gotten going with the late-stage development. But there -- we believe there might be a path there as well.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

And look, from the opportunities that we see with TARIS that we just see a huge blue ocean, the asset that works so magnificently in a localized setting, where you just give it in a simple procedure, 2 minutes in, 1 minute out, and you have a durable responses that even increase over time. Nobody has seen this in bladder cancer before.

Tom Cavanaugh ***Johnson & Johnson - Company Group Chairman, North America Innovative Medicine***

And I would just add. Where it is attractive is in the urology setting, and we know this market very well. We have a well-established products and leadership position with prostate cancer. So we'll be able to deliver TARIS. No problem.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

So we have time for one last question. Matt?

Matthew Stephan Miksic ***Barclays Bank PLC, Research Division - Research Analyst***

Matt Miksic from Barclays. Just maybe a follow-up to Jen, your comment on like ramping quickly. It was upstairs at the AI and digital science booth. And talk a little bit about the progress you've made since the last meeting. And if anyone on the stage here can talk about how that's been leveraged effectively to kind of get through trials faster and maybe identify molecules earlier, that would be super interesting to hear about.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

Yes, absolutely. And we're investing a lot. I think you saw at the beginning Joaquin. He was talking about the 6,000 people we have across Johnson & Johnson that are working to really, what I'll call, empower our business across all aspects, really starting with R&D, working through supply chain, all through commercial. And John, maybe if you want to start in really how we're using data sciences.

John C. Reed ***Johnson & Johnson - Executive Vice President, Innovative Medicine R&D***

Yes, we could spend a lot of time on it, but just you mentioned about how we can get through clinical trials faster. I mean one of the things we've been using -- developing machine learning algorithms to predict which of the clinical sites would be the best recruiters of patients as well as meeting our clinical trial diversity goals as well for patient diversity. So that has really helped us a lot now to pick sites that really deliver as opposed to those that you activate the site. You spend all the money, and then they enroll 1 or -- 0 or 1 patients.

So we've been having great success with that. And actually, we just ran a trial, a test of it with our milvexian study. And the sites that were predicted to be higher enrolling indeed had about 3x more patients than the ones that were predicted to be lower enrolling. So we're kind of using the data as they go to refine the algorithm. So that's just one example of the kind of things we can do.

And then in drug discovery, we use machine learning practically in every project these days at some level, various dimensions of that, whether it's structure based or not, to hopefully accelerate the progress, maybe get to the lead compound with fewer trials. So -- but we're kind of all in when it comes to these digital technologies, from finding targets to precision medicine, to drug design, to the clinical trial development and even -- and also novel endpoints like, Bill, you're trying new cognition endpoints with sort of smartphone gamification. Even that will really surpass the dodgy old not terribly quantitative measures we use like now for like the ADAS-Cog-12 in Alzheimer's.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

I mentioned in my talk that we disproportionately invest in R&D. And what that means is on the commercial side, we've got to be really efficient so that we can put all the money in John's shop. And so we're using it really throughout the commercial space and globally to figure out how do we get to the right customer at the right time with the right message and the right means that are going to be most impactful to them.

And so we're taking all kinds of data sets and putting them together to take our precious commercial resources and make sure that we're getting to the customer in that way and then also that we're able to pair up with that right patient at the right time to really help accompany them through their journey with that right information and exactly what they need to help them both get on and stay on therapy.

So significant advances. And we always take a look, and we're always trying to do better and better, but we're also quantifying. And we've seen noticeable lifts in our sales based on the efforts that we've done. So definitely more to come, but we really have it really throughout all aspects of our business. You can ask Jim more about that when he's on the panel later, Jim Swanson, our Head of IT.

Raychel Kruper ***Johnson & Johnson - Sr. Director, Investor Relations***

Great. So thank you so much for all of your questions. With that, I will turn it over to Jennifer to close this out.

Jennifer L. Taubert ***Johnson & Johnson - Executive Vice President, Worldwide Chairman, Innovative Medicine***

Okay. Well, great. Thank you, everyone. It has been an incredible session today, and thank you to all of my colleagues for really the great job. I hope that you've got a deeper understanding of our strategy and how we plan to continue to lead in the industry.

So our currently marketed medicines are going to drive really meaningful growth through market share gains and expansion into new patient populations. And when you combine that with our promising pipeline assets, we anticipate our portfolio is going to deliver between 5% to 7% compound annual growth rate from 2025 to 2030, with growth in every year.

And by 2030, okay, our portfolio is going to have 10 or more assets that each have $5 billion in peak sales potential. And you can add on top of that another 15 assets that have -- will have between $1 billion and $5 billion peak sales potential. So we really think our portfolio, our pipeline, breakthrough science and our truly talented team give us enormous confidence for our future. So after this afternoon session, I hope that you share in our excitement as well. So thank you very much.

PRESENTATION

Operator

Ladies and gentlemen, please welcome Executive Vice President and Chief Financial Officer, Joe Wolk.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

Hello, everyone. I hope you share our excitement today, which represents the energy and optimism of the 130,000 colleagues worldwide across Johnson & Johnson. Today, you've heard from Joaquin as well as our MedTech and Innovative Medicine leaders about how we will succeed, innovate and execute to bring transformational new treatments to patients. These plans give us confidence in our ability to achieve sustained competitive revenue growth and profit commensurate with that growth.

So let me walk you through what you've heard thus far today and how that translates to Johnson & Johnson's future financial performance. This slide provides an overview of what we believe we can achieve at the enterprise level in the near term. To make my comparisons easy, consistent with how we guide, my comments on past results as well as any forward projections will exclude revenue related to the COVID-19 vaccine as well as any future not yet acquired in-process research and development charges. In addition, we do not speculate on future currency movements. Therefore, any references to reported financials reflect a euro spot rate as of last week at 1.09.

Let's start with our outlook for 2023. We continue to expect adjusted operational sales growth in the range of 7.2% to 7.7%. The transaction with Laminar is one that is clearly aligned with our strategy of moving our MedTech portfolio into higher-growth areas. The accounting for an acquisition of this type, consistent across our industry, requires an in-process research and development charge and cannot be considered special item non-GAAP treatment.

As a result of the acquisition, we anticipate operating margin to be flat versus 2022 as there is an impact of approximately $0.17 on an adjusted operational earnings basis, which is now expected on an earnings per share basis to be in the range of $9.85 to $9.91 or growth of 10.6% at the midpoint. It's important to call out that since January, we've been able to increase our guidance throughout the year for a cumulative increase of $3 billion on operational sales and approximately $0.10 on adjusted operational earnings per share basis, even after absorbing $0.27 for our licensing deal with Cellular Biomedicine Group as well as the acquisition of Laminar.

Turning to 2024. We expect operational sales growth for the full year to be in the range of 5% to 6% with minimal impact from currency on reported sales. We anticipate adjusted operational earnings per share to grow at 7.3% at the midpoint for a range of $10.55 to $10.75. Our 2024 EPS guidance range encompasses dilution of approximately $0.15 associated with the Laminar transaction as well as anticipated impact from OECD Pillar Two on our tax rate, as mentioned during our Q3 earnings call. We will provide more information on other elements of our 2024 financial guidance during our Q4 earnings call in January.

But let me briefly touch upon the topic of operating margin for 2024 at this time. We are certainly proud of our historical operating margin performance. Excluding the 2023 Laminar IP R&D charge I just referenced, operational improvement this year has been achieved despite inflationary pressures as well as the dyssynergies related to the Consumer Health separation. For 2024, we believe the appropriate call at this time is flat, maintaining the 2023 levels, which locks in those efficiencies that we've been able to achieve in the last 2 years.

Now that does not mean we won't continue to strive for improvement. Specifically, as you heard from Tim, we continue moving to higher growth markets and optimizing our supply chain in MedTech. We will also continue to digitize our business, leveraging technology and AI to accelerate a more streamlined operating model. But there are some obvious headwinds that counter those improvements.

As seen annually in our U.S. transparency report, our Innovative Medicine business grows through innovation, not through price, and that will not change. Second, STELARA, being a mature product in addition to our largest product, enjoys one of the best margin profiles within our portfolio. So as such, there is a disproportionate margin effect on sales lost, which we now anticipate to begin outside the U.S. in mid-2024.

And finally, we manage for the long term. You have heard numerous examples today of exciting assets that address critical unmet health care needs. We will invest to ensure that these assets are fully funded for both clinical as well as commercial success. But you can count

on us to continue to look for and act upon efficiencies to improve margin when warranted over the long term.

Now let's take a look at each of our business segments, starting with MedTech. With our differentiated pipeline, continued global expansion and move to higher growth spaces, we expect revenue growth in the upper range of our markets, which are projected to grow 5% to 7% through 2027. This projected performance is premised on catalysts highlighted throughout today, such as maintaining our leadership in electrophysiology with the introduction of QDOT as well as our suite of pulse-field ablation products.

We continue to build on our position as the leader in heart recovery with 3 additional Abiomed heart pumps under development for heart failure and high-risk PCI. In Vision, we will attain above-market sales growth by delivering next-generation contact lens and cataract solutions that enhance vision for patients. And we will advance our robotics platforms, including OTTAVA, MONARCH and VELYS, into higher growth segments of the MedTech market.

Turning to Innovative Medicine. We are confident in our ability to meet the 2025 Innovative Medicine operational revenue target of $57 billion. Few companies, if any, would target growth in a year in which a biosimilar entrant is competing against the largest product. But that's exactly what Johnson & Johnson is planning to do.

In relation to 2025, one question we often get is what the step down of STELARA sales will be due to the biosimilar entry in Europe of 2024 as well as the U.S. at the beginning of 2025. When modeling the impact, we see the Humira erosion curve as a relatively good proxy, with the assumption that STELARA's erosion could be slightly less steep in that first year post biosimilar launch. I will caveat, strongly caveat that there are many dynamics at play, which could result in a slightly different curve.

Longer term, I'll simply double down on what you heard from Joaquin and Jennifer. We expect compound annual operational sales growth from 2025 to 2030 in the range of 5% to 7%. And yes, this operational sales CAGR does account for the impact from the STELARA biosimilar entry as well as other composition of matter patent expiries associated with XARELTO, IMBRUVICA, OPSUMIT, UPTRAVI and SIMPONI. It also, as you heard earlier, considers the impact from the Inflation Reduction Act, as you heard earlier today.

The highlights from the Innovative Medicine presentation are clear: an industry-leading portfolio of more than 10 assets with the potential for more than $5 billion in peak-year sales; an additional 15 assets having the potential to generate between $1 billion and $5 billion in peak-year sales; and a pipeline expected to deliver more than 20 novel therapies and more than 50 product expansion filings by 2030.

Now another question Joaquin and I are often asked, what value is the Street missing relative to our pipeline and our portfolio? One admittedly simple way we thought to address that question was to identify disconnects between Street estimates and what we believe some of our newer assets will deliver in revenue. We recognize the Street estimates are risk-adjusted, science is unpredictable, but this slide attempts to illustrate some notable differences from the estimates we have seen in those models, specifically for the year 2027.

As you've heard from our oncology leaders, the introduction of CARVYKTI, TECVAYLI and TALVEY have completely revolutionized treatment for multiple myeloma patients, with each asset having the potential to deliver over $5 billion in peak-year sales. Based on current adoption, anticipated approval in earlier lines of therapy and combination regimens, our estimates for CARVYKTI and TECVAYLI are at least 25% higher and TALVEY, at least double.

We also heard about significant opportunities to become the standard of care in lung cancer with RYBREVANT and lazertinib, which also has the potential to be a $5 billion-plus asset. Our forecasts are at least double that of the estimates we have seen in market models. With TARIS for bladder cancer, we see another opportunity for revenue over $5 billion. And based on TAR-200 and TAR-210 studies, coupled with the high unmet need, our forecasts are at least 50% higher.

In depression, SPRAVATO has the potential to reach peak sales between $1 billion to $5 billion. Our forecast is at least 50% higher than the estimates we have seen in the market models. Now to be balanced, market estimates are a bit more optimistic on nipocalimab in 2027 as we expect to need a bit more time to address delays we incurred during the pandemic. However, we do anticipate closing that gap shortly after launch.

All this translates to Johnson & Johnson enterprise operational sales growth of at least 3% operational sales growth in 2025, the first year the STELARA biosimilar entry occurs in the U.S.; and 5% to 7% operational sales CAGR from 2025 to 2030, despite the impact of STELARA biosimilar entrants, which we estimate is approximately 200 basis points.

Turning to free cash flow, which is clearly a critical element to any business and really the foundation of Johnson & Johnson's capital allocation strategy. Now we're incredibly proud of the track record of generating free cash flow in a robust way. It supports our business needs. And as a percent of sales, over the last decade, we averaged about 22%.

Due to a series of tax disbursements related to the benefits of 2017 U.S. tax reform, unprecedented inflation, litigation payments, that number in the last 2 years has dipped. But even with that dip, our strong free cash flow has enabled us to act upon all 4 of our allocation -- capital allocation priorities in each of those years.

Looking ahead, while some of those dynamics causing the dip will persist, by 2026, we are targeting free cash flow returning to at least our historical average and meet, in absolute terms, levels we had attained even when the Consumer Health business was part of our portfolio. We expect this improvement in free cash flow to be driven by an increased focus on inventory management within MedTech, driven by supply chain optimization efforts that you heard earlier from Tim as well as comments we made on our Q3 earnings call. We will see a sunsetting by 2026 of payments related to TCJA as well as opioid settlements. And we are proactively acting across all parts of our organization to improve working capital.

Now some of you may be wondering about potential future talc litigation and payments associated with that. Erik Haas is part of our final Q&A panel to share how those recent settlements you may have read about fit into the 4-pronged approach that he outlined on our last earnings call. But it is important to note here that we don't foresee any of those settlements or others that may emerge materially impacting our ability to execute upon our capital allocation priorities.

Speaking of capital allocation, our framework remains intact. We will continue investing in internal R&D, growing our dividend, executing strategic, financially sound business development and opportunistically initiating share repurchase programs. But let me provide you with a bit more insight into how we are thinking about each of those priorities.

We are committed to maintaining an industry-leading level of investment in R&D. It's critical to our future success. Regarding our dividend, in the last 5 years, we have returned $53 billion to shareholders. And we were pleased to maintain our dividend per share amount despite the Kenvue split-off, which we know is very important to our investors. We plan to continue to increase our dividend on an annual basis, as we have for 61 consecutive years.

So how will we leverage our strong financial position to deploy capital and accelerate long-term value creation through strategic, financially sound partnerships and acquisitions? When we look at business development opportunities, we assess them through a scientific, strategic and financial lens irrespective of size, irrespective of segment.

In our Innovative Medicine business, we have been particularly successful with partnerships on early-stage assets. In fact, several of our largest products today have come through creatively structured partnerships. One notable example clearly is CARVYKTI with Legend. That does not mean we are averse to a later-stage opportunity if strategic and financial criteria are met.

MedTech can be a bit different. Generally, we tend to focus on acquisitions that have commercialized assets, accompanied by a robust innovation platform, much like we did with the acquisition of Abiomed. However, here, too, we are agnostic. If a great opportunity presents itself for an earlier-stage asset, we will act as demonstrated with the Laminar transaction. Whatever the strategic approach, we know that we are accountable to earning a rate of return that compensates our shareholders for the risk that we are bearing on their behalf.

And lastly, our capital allocation framework includes executing share repurchase programs from time to time. In early 2023, we completed a $5 billion program that we announced late in 2022. And just months ago, through the Kenvue separation, we reduced

Johnson & Johnson's outstanding share count by 191 million shares, approximately 7% without the use of cash and in a tax-free manner.

So yes, we are confident in the future performance of Johnson & Johnson and our ability to deliver profitable growth. We plan to achieve this through continued acceleration of our in-market portfolio in key disease areas such as oncology, immunology, neuroscience, interventional solutions, vision and robotics. We will deliver our robust Innovative Medicine pipeline with several first and best-in-class therapies, of which 70% of the assets incorporated into our 2025 to 2030 CAGR have already advanced to Phase III.

Third, our broad and differentiated MedTech pipeline with upcoming launches in high-growth spaces and continued geographic expansion with several market-leading platforms. And finally, robust free cash flow generation that solidifies our already strong financial foundation.

Taken all together, we are confident in our ability to achieve near- and long-term financial targets, delivering sustainable long-term value creation for shareholders. Thank you.

It is now my pleasure to invite other members of Johnson & Johnson's leadership for a final Q&A panel focused on the enterprise.

QUESTIONS AND ANSWERS

Operator

Ladies and gentlemen, please welcome Joaquin Duato, Bill Hait, Jim Swanson, Joe Wolk, Erik Haas and Jessica Moore.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

All right, enterprise Q&A. Similar to the other Q&A sessions that we've had throughout the day, please utilize your microphone, you have the chat feature for those of you who are online, please remember to say your name, your firm. And as a reminder, one question please so that we can get through as many of the analysts as possible. Joanne?

Joanne Karen Wuensch ***Citigroup Inc., Research Division - MD***

Joanne Wuensch from Citibank. Congratulations on the spin-out of Kenvue, but I frequently get the question if that's just Phase I, and Phase II would be to spin out of the MedTech and Innovative Medicine piece of it. And if you do choose to keep it together, what are you getting out of having the 2 parts in 1 house?

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

Thank you, Joanne. Great question. Thank you for starting with that one. So we all firmly believe that MedTech and pharma belong together. They have the same diseases, cardiovascular, oncology, trauma that you have seen today. It's the same physician. It's the same patient. It's the same hospitals. It's the same payer. It's the same regulatory agency. So we believe that by having capabilities both in MedTech and in pharma, we can be in a better position to serve the entire patient journey than any other company. Sometimes we use the example of lung cancer.

We can diagnose lung cancer with our bronchoscopy-assisted robotic system. We can perform surgery and remove the mass with our smart instruments. And we can treat it with our multi-specific antibodies. No other company in the world can do that. So we firmly believe that in order to be able to have a real impact in those diseases, having that breadth of capabilities puts us in a better position moving forward.

I hope when you visited today our exhibits and you saw the breadth of what Johnson & Johnson can offer, you've got a better idea showing, not telling me, of what type of things a company can do. So we truly believe that MedTech and pharma belong together. And we think this is going to be a better position for us to be able to have a real impact and to deliver the growth targets that you have seen today and to create the value long term for shareholders that we always say.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

I just want to add from the standpoint of maybe a financial type of answer. There's a lot more synergies that are had because of the nature of MedTech and Innovative Medicine in terms of the regulatory environment, the clinical development pathways, the data generation. It's very different than what we experienced in the consumer separation.

Again, the strategic rationale was that the businesses had diverged, and the success criteria became very, very different. That would not necessarily be the case with a MedTech and Innovative Medicine separation. There's a lot of harmonization, as Joaquin just referenced, around disease states and patient journeys that allow for a lot of financial efficiency to be built into our model.

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

And with that, now to be more financial too. In order to be able to earn the right of having this company like the one we have today, then we have to be individually top-tier performer in Innovative Medicine pharma and in MedTech. So we earn the right of being this company that we are today by being top performer on both sides. So that's a clear goal for us. We have to be a top performer, both in MedTech and in Innovative Medicines.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

Jayson.

Jayson Tyler Bedford ***Raymond James & Associates, Inc., Research Division - MD & Senior Medical Supplies and Devices Analyst***

Jayson Bedford from Raymond James. Just maybe for Joe, on EPS growth, you're seeing some leverage in '24, but I think the slide indicated that EPS would be commensurate with revenue growth. So I'm just wondering why you wouldn't see a little bit of leverage and then just, did that same comment apply for '25 as well?

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

Yes. So I think in EPS growth, Jayson, we're seeing 7.3% next year with a sales growth of about 5% to 6% range. So there is a little bit of bottom line outperforming top line, which has really been a principle of ours over a number of years.

I would say as we get into 2025, I wouldn't handicap the team in that regard. I'd like to see the next year play out. We are looking for great efficiencies. And the commensurate is to make sure that folks understood despite the margin pressures that I outlined in my prepared remarks, that people should not have fears about us going backwards. I think that was some of the prevailing thought that we had.

So we'll always look to improve a little bit faster than our sales cadence, but we don't want to pigeonhole ourselves in any one particular year. I do feel maybe to show a little bit into the back half of the decade, feel pretty good about some of the opportunities we have for further margin enhancement.

Today, we don't talk about it a lot, but we're investing heavily in our technology environment, right? Maybe I'll even turn it over to Jim to talk about some of the efficiencies that -- when I say technology environment, that's kind of the, I'll say, the cost of doing business: our reporting, our financial systems, our human resources systems, our ERPs.

We're making significant investments, as you heard throughout the day, in capabilities for the future that should also add efficiencies. But Jim, maybe you want to talk a little bit about kind of our technology landscape?

James Swanson ***Johnson & Johnson - Executive Vice President, Chief Information Officer***

Yes. So we are a company that has been around for 135 years. As you can imagine, through all these acquisitions, we have a labyrinth of systems and capabilities. We have the opportunity, which we're taking full advantage of that, to standardize that backbone, the financial backbone and transactions across the whole enterprise, how we deliver products, how we commercialize those products. It's a lot of opportunity to create a foundational layer, and data becomes a really key part of that, which we think can innovate on top.

So with those foundational systems, it accelerates our innovation, it accelerates our ability to access data, it accelerates our ability to use

AI and ML across our enterprise, which we have infused in all aspects of our business. So those investments are really key to the future growth that we've been highlighting.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

And right now, Jayson, we anticipate those investments would kind of be less in '27, '28 than they are today.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

David.

David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD***

Yes. Dave Risinger from Leerink Partners. So regarding your 2025 through 2030 Innovative Medicine sales growth target of 5% to 7%. Using the midpoint of 6%, that yields $76 billion. So I was really struck by the comment that you're targeting Oncology segment revenue of over $50 billion in 2030.

That would imply, obviously, potentially 2/3 or more of the sales from Oncology. And obviously, that target for 2030 is also actually -- that over $50 billion is close to the $57 billion total Innovative Medicine segment target for '25. So that was quite striking. So I'm hoping that you could just provide some more context for that. And then in addition, if I might add on, how do you see M&A factoring into your long-term forecast?

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

Yes. So I think we need to get a little clarity on the numbers. I'm not sure exactly we said $50 billion Oncology. Biljana, Jennifer, you can correct me if I'm wrong here.

Biljana Naumovic ***Johnson & Johnson - Worldwide Vice President, Oncology***

I can comment. So if you were doing calculations based on peak-year sales, peak-year sales are not all 2030. We discussed peak-year sales on the assets and not everything will be peaking in 2030.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

So for the assets that we highlighted, it means that they would either be launched as of 2023 or filed with by 2030. So it doesn't mean that the peak-year sales happen in this range. The peak-year sales could happen any time after 2025 period. So it could be in 2030, 2032, 2033, but the asset would have been filed before 2030, with the potential to be peaked.

David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD***

And is that risk adjusted or unadjusted?

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

That is non risk-adjusted number, and it includes any partner revenue as well.

David Reed Risinger ***Leerink Partners LLC, Research Division - Senior MD***

Got it.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

We have nice footnotes in the deck as well just to make sure there's no misunderstanding.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

And just your second part of your question there, does it include acquisitions? That would be all organic growth as we projected today.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

Danielle?

Danielle Joy Antalffy ***UBS Investment Bank, Research Division - Analyst***

Okay. Got it right this time. Danielle Antalffy with UBS. Just a question, Joe, on capital allocation. It felt like you were maybe hinting or maybe this is me being a MedTech analyst that from a business development perspective, a little bit more focused now on the MedTech side of things versus the Innovative Medicine side of things.

Just curious, number one, if that's a fair characterization. Number two, where you see the biggest areas within MedTech that look interesting, where J&J currently isn't involved and whether it becomes more about buying scale versus buying individual technologies or into individual markets.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

Yes. So Danielle, I'm going to turn the question over to Joaquin because I think it's more appropriate for him to answer. But from my comments, you shouldn't refer that there is really a bias either way. We're looking for that next great opportunity.

One of the great things of being part of Johnson & Johnson is have an array, a plethora of really good decisions we can make. It's how do we choose the ones that are transformationally great that will really determine our success. But Joaquin, I don't know if you want to hand out our list.

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

Thank you. Thank you. When we look at an opportunity, we look at it with 3 lenses. One is strategic. To what extent we think it fits, whether it's in Innovative Medicines or in MedTech, it fits areas where we have internal capabilities and we will have knowledge. We have seen that there is a very good correlation with our success in licensing or in an acquisition when we have internal knowledge and capabilities in terms of how we create value downstream.

The second one is scientific. So we look at to what extent we believe this is going to be a significant improvement in the standard of care. We try to go to opportunities that are going to make a difference, that are first in class, that are going to make a significant change.

And the third one is financial, frankly. So we are very disciplined in our financials, and we want opportunities that are going to create appropriate return on the capital invested and that they start to do in day 1 as we are doing with Abiomed. We want to make sure that they start to deliver day 1.

Now historically, in the Innovative Medicine business, we have been very successful doing licensings and partnerships. As you have seen now, for example, we quoted today Legend that we did several years ago or this year, we did several biomedicines for CAR-T 19 -- CD19 and CD20.

In MedTech, oftentimes, the maturation of these opportunities take longer. So we want to shift into higher overall market, sometimes we have to do acquisitions like we did with Abiomed or sometimes we go earlier than we have done in Laminar. So there is flexibility in the approach we take depending on the situation. But we are agnostic, and we see M&A as an important tool in delivering growth moving forward.

Now I always remind everybody that our organic investment is the most important piece of our capital allocation. In the last 5 years, we have invested in internal R&D $60 billion. As I said earlier this morning, we are the largest investor in R&D in Life Sciences, and that's where the majority of the growth is going to come from because we are a company that sells at midpoint this year, $85 billion. 1% is $850 million of growth.

It's very difficult to have an opportunity which is going to create other than the step-up of the first year 1 point of growth for Johnson & Johnson. So by default, that takes us to the opportunities that are going to be earlier on, on the value creation cycle. And that's where we can put our capabilities in manufacturing, in clinical development, in commercialization to make it happen. I hope it addresses your question.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

Maybe we can take one from the web, Alec?

Alec Mast ***Johnson & Johnson - Investor Relations***

Sure. Yes. So a couple of questions on talc coming in. So with regards to the company's ongoing litigation, the 4-pronged strategy that you had highlighted during Q3 earnings, can you give us just an idea of what initiatives the company is taking currently, give us progress and kind of what next steps we should be looking for?

Erik Haas ***Johnson & Johnson - Worldwide Vice President, Litigation***

Yes. Let me start by saying we understand, we appreciate it. We've heard from the investors their interest in resolving talc and putting talc behind us so the company can get on with what it does, which is developing life-saving therapies.

And in that end, you might have seen on the news last night or early this morning that we have made recent progress over the last few weeks in resolving a number and a series of large mesothelioma portfolios with the goal to facilitate our pursuit of a consensual prepackaged bankruptcy resolution, which we announced on the last earnings call. So that plan is moving forward. And that's, first and foremost, the agenda item, and it's on track. It's on the exact same timing that we previously announced moving into 2024.

Now to the extent that there are individual law firms that do not want to resolve the cases, we are comfortable litigating with those entities because remember, we have won the overwhelming vast majority of the claims we tried because these claims are based on junk science. So you hear a lot in the press when there might be a trial in a particular jurisdiction in a state court. But at the appellate court, we tend to win in the end. And the overwhelming vast majority of those cases, we won. So we will litigate those. And right now, those settlements have resolved all but one of the cases that we're on schedule for 2023 and significantly curtailed those for 2024.

And with respect to the 4 prongs, the last issue is the bankruptcy appeal. The Third Circuit agreed to hear that appeal on an expedited basis at our request, knowing that it's an important issue and knowing that an issue likely will need to go to the Supreme Court for resolution. So in short, we're on track. We're moving forward, and we feel very positive on where we are.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

Louise.

Louise Alesandra Chen ***Cantor Fitzgerald & Co., Research Division - MD & Senior Research Analyst***

Louise Chen from Cantor. Just wanted to ask you a quick question. Do you have any interest in entering the obesity market?

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

Thank you. So there's how many companies now having GLP-1s in the market? Like more than 10. So I think there's enough companies working in obesity right now for now to be there. If in the future, there are alternative mechanisms or approaches that makes sense, we may look into that.

But certainly, we are not planning to get into the GLP-1. And there's enough companies already to my count, and this is not a joke. There's about a dozen companies that are working there that have assets that are in the clinic already. So it's too crowded for us.

We have opportunities in the Innovative Medicine area, as you have seen in these 3 areas: neuroscience, which I think it's a real frontier for pharmaceutical development. I think the needy mental health is significant, and society doesn't pay the same attention to mental health than it should, and then in oncology and in immunology as we have described.

So I think that we have enough for now. But if there were opportunities for something that were truly differentiated, complementary to what we have now, we may consider that. Thank you, Louise.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

All right. So I think we have time for one last question. So maybe Chris?

Christopher Thomas Schott ***JPMorgan Chase & Co, Research Division - Senior Analyst***

A lot of pressure. Sorry. I just want to follow up on talc a little bit more. I think we hear from a lot of investors this dynamic of it's an overhang on the stock. And I'm just trying to get a sense, maybe for Joaquin, your sense of urgency in that you're laying out what seems like a very robust growth outlook for the company, both the Innovative Medicine and MedTech segment. And I think it gets kind of lost a little bit with the talc dynamics over here.

So how do you balance, I guess, minimizing the capital outlays associated whatever needs to be done on talc versus creating a story that might be cleaner for a broader group of investors when you think about kind of going through that? So just hoping a little bit more color on how you think about that dynamic.

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

So let me start, and I will let Erik and Joe comment. Look, our intention with talc unequivocally is to be able to bring resolution to these cases and leave this situation behind so we can spend these days talking about what we do better, which is delivering innovation. And I think it would be better for everyone. I can assure you that 99.9% of the people at Johnson & Johnson is not thinking about talc. They're thinking about how we advance medicines and medical technologies for patients.

Now Joe said that before, when it comes to our capital allocation and the opportunity to be able to hit in all the pillars of our capital allocation, talc does not impact that ability under any circumstance that we are thinking about the resolution of these cases.

Joseph J. Wolk ***Johnson & Johnson - Executive Vice President, Chief Financial Officer***

So just to clarify, it's not a barrier. And if you just go back to the original bankruptcy structure, that was a series of payments over a number of years. That's why we're confident in making those statements. And that's fundamental to the settlements that Erik would be working on.

Erik Haas ***Johnson & Johnson - Worldwide Vice President, Litigation***

And just to supplement that, so the settlements that were contemplated are consistent with what we contemplated doing through the bankruptcy. So they're supplemental, they're collaborative, and they corroborate that.

The other thing to keep in mind in terms of what we've done to date, the amount that's been expended in the course of the bankruptcy is actually less than we probably would have otherwise spent had we not been in the bankruptcy proceeding. So we had a 2-year hiatus of claims where there were no litigations.

And now that we're back in the tort system hopefully temporarily, while we now come up with the next bankruptcy, we are incurring actually less on a go-run basis than we were before. So really, ultimately, the question is whether, overall, this strategy makes economic sense. And as Joe and Joaquin said, it has. And the contemplated resolution will not as of yet require any additional charges.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

So we're going to ask a bonus question because we can't end the day on talc. So Alec, maybe you can send us one from the web.

Alec Mast ***Johnson & Johnson - Investor Relations***

Yes. So Joaquin, you had talked about the interventional oncology space earlier, and we've heard a little bit about it today and some of the booths exhibits that we've seen throughout. Bill, might be a question more from your side of things. Can you provide us an update on where some of those initiatives stand today and where you see this space going over time for J&J?

William N. Hait ***Executive Vice President - Chief External Innovation and Medical Officer***

Sure. Fantastic question. It actually goes back to where Joaquin had begun and talking about the 2 sectors. When we first looked at an opportunity for a robotic bronchoscope, it was like robotic bronchoscope, okay. But when we put 2 teams together from the 2 different sectors, we said, this is actually not a robotic bronchoscope. This is a pulmonoscope. You can do for the lung what the colonoscope does to your colon.

And then we realized by getting anywhere in the lung, even to the tiniest nodules, we can diagnose cancers earlier with the Monarch scope using the diagnostic tool. But we could also, through that same instrument, treat the tumor directly with energy, like our NeuWave energy products, with our oncolytic virus that you heard John and Peter and the team mentioned, and with pharmaceuticals.

So suddenly, a relatively small opportunity robotic bronchoscope became a whole new area that we're investing in now across our company. So it was just an exciting initiative that Joaquin helped us tee up. And I think it's going to be transformational for patient care.

Jessica Moore ***Johnson & Johnson - Vice President, Investor Relations***

All right. Wonderful. So now to close the day, Joaquin will say some final remarks.

Joaquin Duato ***Johnson & Johnson - Chairman and Chief Executive Officer***

Thank you, and thank you for joining us. We truly appreciate all of you taking time and spending a day with us. So it's been fantastic. I think you've seen today how we have entered into a new era.

I hope you see today the benefits of being exclusively dedicating an innovation through medical technology and innovative pharmaceuticals. We remain the most diversified health care company in the world.

We have 26 platforms that each of them sells more than $1 billion per year. And we have high confidence on the power of science and technology to bring transformative solutions for patients in the future. And we believe that Johnson & Johnson is uniquely positioned to be able to lead in that next wave to lead where medicine is taking us.

So in closing, thank you for your interest in Johnson & Johnson. I hope we addressed all the areas that you wanted to cover. You told us you wanted to know about our vision and strategy for Johnson & Johnson. You told us you wanted to know about our capital allocation and M&A. And you told us you wanted us to give you visibility about the growth drivers of MedTech and innovative pharmaceuticals in the second half of the decade, and we tried to do that today.

I'm so very proud of the team that you met today. In total, you have 45 presenters from Johnson & Johnson on the stage and on the exhibits that shows you the talent depth that this company has. And I can tell you that today, I'm more confident than ever on the future of Johnson & Johnson. Thank you very much.

Operator

Ladies and gentlemen, that concludes our enterprise business review. Thank you for your attention. For those in the room, we invite you to continue to explore our exhibits. Thank you.

Exhibit "F8"

This is Exhibit “F8” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.

Arash Rouhi

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

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PRESENTATION

Operator

Good morning, and welcome to Johnson & Johnson's First Quarter 2023 Earnings Conference Call. (Operator Instructions) This call is being recorded. If anyone has any objections, you may disconnect at this time. (Operator Instructions) I will now turn the conference call over to Johnson & Johnson. You may begin.

Jessica Moore *Johnson & Johnson - VP of IR*

Good morning. This is Jessica Moore, Vice President of Investor Relations for Johnson & Johnson. Welcome to our company's review of the 2023 first quarter business results and full year financial outlook.

Joining me on today's call are Joe Wolk, Executive Vice President, Chief Financial Officer; and Ashley McEvoy, Executive Vice President, Worldwide Chairman of MedTech. Unfortunately, Jennifer Taubert, Executive Vice President, Worldwide Chairman of Pharmaceuticals, is not feeling well and is unable to join us today.

A few logistics before we get into the details. As a reminder, you can find additional materials, including today's presentation and associated schedules, on the Investor Relations section of the Johnson & Johnson website at investor.jnj.com.

Please note that today's meeting contains forward-looking statements regarding, among other things, the company's future operating and financial performance, product development, market position and business strategy and the anticipated separation of the company's Consumer Health business.

You are cautioned not to rely on these forward-looking statements, which are based on current expectations of future events using the information available as of today's date and are subject to certain risks and uncertainties that may cause the company's actual results to differ materially from those projected. A description of these risks, uncertainties and other factors can be found in our SEC filings, including our 2022 Form 10-K, which is available at investor.jnj.com and on the SEC's website.

Additionally, several of the products and compounds discussed today are being developed in collaboration with strategic partners or licensed from other companies. This slide acknowledges those relationships.

Moving to today's agenda, I will review the first quarter sales and P&L results for the corporation and highlights related to the 3 segments. Joe will then provide additional business and financial commentary before sharing an overview of our cash position, capital allocation priorities and updated guidance for 2023. The remaining time will be available for your questions. We anticipate the webcast will last approximately 60 minutes.

Now let's turn to our first quarter results. Worldwide sales were $24.7 billion for the first quarter of 2023, an increase of 5.6% versus the

first quarter of 2022. Operational sales, which excludes the effect of translational currency, increased 9.0% as currency had a negative impact of 3.4 points.

In the U.S., sales increased 9.7%. In regions outside the U.S., our reported sales increased 1.8%. Operational sales outside the U.S. increased 8.3% with currency negatively impacting our reported OUS results by 6.5 points. Excluding the net impact of acquisitions and divestitures, adjusted operational sales growth was 7.6% worldwide, 7.4% in the U.S. and 7.9% outside the U.S. with all 3 segments growing sequentially over the fourth quarter.

Turning now to earnings. For the quarter, net loss was $68 million, and basic loss per share was $0.03 versus diluted earnings per share of $1.93 1 year ago primarily driven by the $6.9 billion charge related to the talc settlement proposal. Excluding after-tax intangible asset amortization expense and special items for both periods, adjusted net earnings for the quarter were $7.1 billion, and adjusted diluted earnings per share was $2.68, representing a decrease of 0.9% and an increase of 0.4%, respectively, compared to the first quarter of 2022. On an operational basis, adjusted diluted earnings per share increased 3.0%.

I will now comment on business segment sales performance highlights for the quarter. Unless otherwise stated, percentages quoted represent the operational sales change in comparison to the first quarter of 2022 and therefore, exclude the impact of currency translation.

Beginning with Consumer Health. Worldwide Consumer Health sales of $3.9 billion increased 7.4% with an increase of 11.4% in the U.S. and an increase of 4.4% outside the U.S. Worldwide operational sales increased 11.3%. And outside the U.S., operational sales increased 11.3%. Results were primarily driven by global strategic price increases across all franchises.

Volume growth in OTC was due to an exceptionally strong cough, cold and flu season most pronounced in Europe coupled with some one-time retailer restocking primarily in the U.S. related to low inventory levels due to tripledemic demand. Skin Health/Beauty delivered double-digit growth driven by price actions lapping prior year supply constraints and current quarter restocking as well as strong NEUTROGENA and AVEENO e-commerce and club channel performance and new product innovations.

Moving on to our Pharmaceutical segment. Worldwide Pharmaceutical sales of $13.4 billion increased 4.2% with growth of 5.9% in the U.S. and 2.4% outside of the U.S. Worldwide operational sales increased 7.2% and outside the U.S., operational sales increased 8.6%. Excluding the COVID-19 vaccine sales, worldwide operational sales increased 4.9%. U.S. operational sales increased 7.1%, and outside the U.S., operational sales increased 2.4%.

Pharmaceutical growth excluding the COVID-19 vaccine was driven by our key brands and continued uptake in our recently launched products with 8 assets delivering double-digit growth.

We continue to drive strong sales growth for both DARZALEX and ERLEADA with increases of 25.7% and 40.3%, respectively. STELARA grew 9.6% driven by market growth and share gains in Crohn's disease and ulcerative colitis with gains of 2.2 points and 4.8 points in the U.S., respectively, partially offset by unfavorable patient mix and price. TREMFYA grew 11.0% driven by market growth and share gains in psoriasis and psoriatic arthritis with gains of 0.9 points and 2.1 points in the U.S., respectively, partially offset by unfavorable patient mix.

Turning to newly launched products. We are excited to disclose CARVYKTI and SPRAVATO sales for the first time this quarter. We continue to make progress on our thoughtful and phased launch of CARVYKTI and continue to expand access and reimbursement for SPRAVATO. Also, we are encouraged by the early success of our launch of TECVAYLI, sales of which are included in Other Oncology.

This sales growth was partially offset by the loss of exclusivity in REMICADE and ZYTIGA, along with a decrease in IMBRUVICA sales due to competitive pressures. IMBRUVICA maintains its market leadership position worldwide.

I'll now turn your attention to the MedTech segment. Worldwide MedTech sales of $7.5 billion increased by 7.3% with growth of 16.6% in the U.S. and a decline of 0.6% outside of the U.S. Worldwide operational sales increased 11%. And outside the U.S., operational sales increased 6.2%.

Abiomed contributed 4.6% to operational growth. Excluding the impact of acquisition and divestitures, worldwide adjusted operational sales growth was 6.4%.

Sales in the first quarter accelerated sequentially from Q4 for all 4 MedTech businesses driven by global procedure growth, continued uptake of recently launched products and commercial execution. As anticipated, in China, procedure volumes improved as the quarter progressed. Partially offsetting growth in the quarter was the impact of volume-based procurement in China as well as supply constraints.

The Interventional Solutions franchise delivered operational growth of 41.9%, which includes $324 million related to Abiomed. We are excited about the progress of the integration to which Joe will provide additional context. Excluding the impact of the acquisition, this franchise delivered another quarter of double-digit worldwide growth at 12.3%. As we continue to increase our reporting transparency, beginning this quarter, we are providing visibility to Electrophysiology sales. Electrophysiology continued to deliver double-digit sales growth in all regions with the exception of Asia Pacific, which reflects impacts related to volume-based procurement in China.

Orthopaedics operational growth of 5.1% reflects the strong procedure recovery and success of recently launched products especially digital and enabling technologies driving pull-through sales in areas like Hips and Knees. Growth was partially offset by the impact of volume-based procurement in China, primarily in Hips and Spine.

Global growth of 9.3% in Contact Lens and Other reflects continued penetration of our ACUVUE OASYS 1-Day family of products, including the recent launch of ACUVUE OASYS MAX 1-Day, strong commercial execution and strategic price actions. Growth in Contact Lens and U.S. Surgical Vision was tempered by continued supply challenges.

Now turning to our consolidated statement of earnings for the first quarter of 2023. I'd like to highlight a few noteworthy items that have changed compared to the same quarter of last year.

Cost of products sold deleveraged by 150 basis points driven by onetime COVID-19 vaccine manufacturing exit-related costs in the Pharmaceutical business and commodity inflation and acquisition-related items in the MedTech business.

Selling, marketing and administrative margins leveraged by 60 basis points driven by proactive management of costs given the current inflationary environment.

We continue to invest strategically in research and development at competitive levels, investing 14.4% of sales this quarter. The $3.6 billion invested was a 2.9% increase versus the prior year.

The other income and expense line was an expense of $7.2 billion in the first quarter of 2023 compared to net income of $100 million in the first quarter of 2022. The increase in expense was the result of the $6.9 billion charge related to the talc settlement proposal recorded in the first quarter of 2023 as previously disclosed.

Regarding taxes in the quarter, our effective tax rate was 90.8% versus 12.2% in the same period last year primarily driven by the $6.9 billion accrual for the talc settlement proposal. Excluding special items, the effective tax rate was 16.5% versus 13.3% in the same period last year. I encourage you to review our upcoming first quarter 10-Q filing for additional details on specific tax matters.

Lastly, I'll direct your attention to the boxed section of the slide, where we have also provided our income before tax, net earnings and earnings per share adjusted to exclude the impact of intangible amortization expense and special items.

Now let's look at the adjusted income before tax by segment. In the first quarter of 2023, our adjusted income before tax for the enterprise as a percentage of sales decreased from 35.1% to 34.2%. Pharmaceutical margins declined from 44.1% to 43.2% driven primarily by mix, partially offset by proactive management of costs. MedTech margins remained flat at 27.0% driven primarily by inflationary impacts, offset by proactive management of costs. Finally, Consumer Health margins improved from 22.1% to 22.3% driven

primarily by strategic price actions, partially offset by input cost inflation.

This concludes the sales and earnings portion of the Johnson & Johnson first quarter 2023 results. I am now pleased to turn the call over to Joe Wolk. Joe?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Thank you, Jess, and thank you all for joining today's call. We are pleased to report another quarter of strong operational performance across our business. The results reflect the strength and versatility of Johnson & Johnson and our commitment to improving health care outcomes around the world.

2023 has many important catalysts that can drive meaningful near- and long-term value for Johnson & Johnson shareholders. We remain focused on the successful separation of our Consumer Health business, Kenvue, which will position both companies to be more agile, focused and competitive. We are also expecting a number of pipeline advancements that will provide increased confidence in our Pharmaceutical and MedTech businesses.

Our Pharmaceutical segment delivered a strong first quarter. Growth from our Pharmaceutical business continues to be driven by key assets in our existing portfolio, including DARZALEX, TREMFYA, ERLEADA, INVEGA SUSTENNA and UPTRAVI as well as uptake from new launches such as SPRAVATO, CARVYKTI and TECVAYLI.

2023 is an important year of scientific innovation for our Pharmaceutical business. And in Q1, we announced that CARVYKTI, our BCMA cell therapy, met its primary endpoint in the CARTITUDE-4 study, a Phase III trial in multiple myeloma patients who have received 1 to 3 prior lines of therapy. We look forward to presenting these results in an upcoming major medical meeting.

Additionally, our partners at Protagonist Therapeutics announced positive top line results from the Phase IIb FRONTIER-1 study of our oral IL-23 in patients with moderate to severe plaque psoriasis. We look forward to sharing this data and future development plans at an upcoming medical meeting.

Finally, as we continually review our portfolio to prioritize the most transformational assets for ongoing investment and an assessment of the RSV vaccine landscape, the company made the decision to discontinue its investigational RSV adult vaccine program. This decision is part of a broader effort to make strategic choices for our pipeline and R&D investments to focus on medicines with the greatest potential benefit to patients.

Looking at the rest of the year, we expect important data from key pipeline assets such as nipocalimab and TREMFYA as well as the potential approval of talquetamab. Importantly, I want to mention 2 additional highlights. First, the MARIPOSA study of RYBREVANT plus lazertinib in frontline non-small cell lung cancer remains on track with the potential for final analysis later this year.

We are also excited to present data from the SunRISe-1 study of TAR-200 in muscle invasive bladder cancer at the American Urological Association's Annual Meeting this month, which demonstrated a promising complete response and safety profile.

Regarding our Pharmaceutical business, I'd like to reiterate some comments I recently made at the Cowen Investor Conference in March related to the strengthening of the U.S. dollar and the impact on the 2025 Pharmaceutical sales goal the team put forth during the 2021 Investor Day. While we don't speculate on currency, based on the current rates, the 2025 sales target of $60 billion is approximately $57 billion on a constant currency basis.

In 2022 alone, FX had a negative impact of roughly $3 billion in Pharmaceuticals. While that is the math qualitatively since 2021, a number of things have changed in our portfolio. On the plus side, we've seen acceleration of some current and potential upcoming launches like TECVAYLI and talquetamab. But to be balanced, we've also experienced competitive pressure on IMBRUVICA above what was anticipated in 2021. So many push and pulls, but we are striving to attain our operational goals. We are confident in our ability to exceed 2025 estimates The Street has out there today of approximately $54 billion.

MedTech delivered a strong quarter of sales growth. We continued to advance key pipeline programs. For example, within our electrophysiology business, we reached a few milestones this quarter related to our pulsed field ablation pipeline programs, including the European clinical study inspiRE, which achieved early success by meeting both primary safety and efficacy endpoints.

Additionally, we announced completion of the first procedures in the European SmartfiRE clinical study evaluating the safety and effectiveness of our investigational dual energy catheter, which combines both pulsed field and radiofrequency ablation capabilities.

As you know, we continue to prioritize investment in high-growth areas, as demonstrated by our acquisition of Abiomed, which closed this past December.

With Abiomed, MedTech now has 12 platforms with over $1 billion in annual sales. While it is still early days, we are pleased with the integration and performance of Abiomed.

Patient utilization of Abiomed technologies grew mid- to high teens in both Europe and the United States and over 30% in Japan. We continue to see strong adoption of newer technologies, such as Impella 5.5, and we achieved record quarterly enrollment in both the STEMI DTU and PROTECT IV pivotal trials as we continue to advance efforts in pursuit of Class I guidelines. For perspective, operational sales growth compared to the same quarter last year reported by Abiomed as a standalone company was 22%.

In Orthopaedics, just this month, we obtained CE Mark for the VELYS Robotic-Assisted Solution, positioning us to expand our international footprint with this differentiated solution in total knee.

Finally, the MedTech team is excited by the progress being made in regards to the OTTAVA general surgery robotic solution, and we remain on track to share more information in the second half of this year.

Our Consumer Health business delivered double-digit first quarter sales growth driven by strategic price actions, strong demand and some stock replenishment.

We remain on track to complete the separation of this business in 2023, assuming accommodative market conditions. Since the start of the year, we have been operating our Consumer Health business as a company within a company and continue to update our Form S-1 filing with the Securities and Exchange Commission, giving us the opportunity to pursue an initial public offering as a potential first step in the separation.

Standup cost and stranded costs remain consistent with what we have stated previously with an active program well underway to reduce the stranded costs.

Turning to notable enterprise events. I'd like to briefly touch LTL's refiling for bankruptcy on April 4th. Neither LTL's original filing nor this refiling is an acknowledgment of wrongdoing nor an indication that the company has changed its long-standing position that its talcum powder products are safe. Our goal continues to be for an equitable and efficient resolution of the cosmetic talc litigation against the company, and we believe this refiling represents progress towards that goal.

As a reminder, LTL's bankruptcy filing will not have an impact upon the Kenvue separation, and the talc liabilities in the United States and Canada will remain with Johnson & Johnson. As part of the refiling, we have proposed a reorganization plan that had significant support from claimants and includes a payment of $8.9 billion in present value over a 25-year period. LTL will continue to work through the process set forth by the bankruptcy court and expects to present the reorganization plan to the court in mid-May.

Our capital allocation priorities remain consistent. And in 2022, we successfully executed against all pillars. R&D investment remains our #1 priority and driver of long-term growth and value creation.

We know the value our investors place on our dividend, and we were pleased to announce this morning that our Board of Directors has authorized a 5.3% increase, marking our 61st consecutive year of dividend increases.

In addition, we continuously evaluate strategic business development opportunities that enable Johnson & Johnson to create value for patients, customers and shareholders. Our final priority is share repurchase programs when appropriate. In fact, this past quarter, we completed the $5 billion share repurchase program announced late last year.

We are confident in our strong financial position, including our AAA-rated balance sheet and our ability to deploy capital across all strategic priorities. We believe this strength differentiates Johnson & Johnson and enables us to pull the appropriate levers to set us up for long-term success.

Moving on to our full year 2023 guidance for the enterprise. Based on our strong start to the year, we are pleased to raise our guidance. We now expect operational sales growth for the full year 2023 up 1 percentage point in the range of 5.5% to 6.5% or up $1 billion in a range of $97.9 billion to $98.9 billion on a constant currency basis and adjusted operational sales growth up 1 percentage point in the range of 4.5% to 5.5%.

Our sales guidance continues to exclude contribution from the COVID-19 vaccine. As you know, we don't speculate on future currency movements. Last quarter, we noted that we utilized the euro spot rate relative to the U.S. dollar at 1.08. The euro spot rate as of late last week was 1.10. We continue to estimate there would be minimal impact from foreign currency translation on reported sales for the year as the dollar has strengthened versus other select currencies.

We are maintaining the guidance we provided in January for our adjusted pretax operating margin, other income and expense, interest expense and tax rate. We are also increasing our adjusted earnings per share guidance by $0.05 per share and tightening the range to $10.50 to $10.60 or $10.55 at the midpoint on a constant currency basis, reflecting operational or constant currency growth of approximately 3.5% to 4.5% or 4% at the midpoint.

While not predicting the impact of currency movements, assuming recent exchange rates I previously referenced, our reported adjusted earnings per share for the year would be favorably impacted by approximately $0.05 per share. This favorable currency impact, coupled with our strong operational outlook, results in an increase to our reported adjusted earnings per share for the year by $0.10 per share and tightening the range to $10.60 to $10.70 or $10.65 at the midpoint, reflecting growth of approximately 4.5% to 5.5% or 5% at the midpoint.

While we do not provide guidance by segment or on a quarterly basis, I'd like to provide some qualitative considerations for your modeling.

In Pharmaceuticals, we maintain our expectation of delivering above-market growth in 2023 driven by key assets and continued uptake of our newly launched products. This growth considers the potential composition of matter patent expiry of STELARA, which we currently assume will occur in late 2023 in the United States. Further, we continue to expect 2023 impact from other post-LOE products, including REMICADE, ZYTIGA and XEPLION as well as increased austerity measures across Europe. Regarding our COVID-19 vaccine, we do not anticipate material sales beyond that which were recorded in the first quarter as our contractual commitments are complete.

In MedTech, we expect continued competitive growth fueled by increased procedures and commercial uptake of recently launched products. We anticipate relatively stable procedure volumes and health care staffing levels for the remainder of the year with normal seasonality.

Regarding quarterly phasing, given the strength of our first quarter results, we now expect relatively consistent performance throughout the year from our Pharmaceutical and MedTech businesses.

When modeling Consumer Health growth rates in 2023, it is important to take into consideration prior year comparisons as well as the robust cough, cold and flu season and the onetime restocking that occurred in the first quarter. As a reminder, the first half of 2022 was impacted by supply constraints.

A few brief announcements before we take your questions. Continuing our efforts to increase our transparency and assist with your modeling, we are planning to post a patent table, including U.S. pharmaceutical patents, to our investor website in the quarter.

In addition, please mark your calendars for December 5th as we will be hosting an enterprise business review at the New York Stock Exchange focused on the new Johnson & Johnson, highlighting both our Pharmaceutical and MedTech businesses. We will provide additional details about the event in the coming months.

Before we turn to your questions, let me state how proud we are regarding our team's continued hard work and unwavering commitment. Our sights are set on the future, focused on delivering competitive growth for the new Johnson & Johnson. We are confident that our current plans position us for near-term success, long-term growth and value creation for our shareholders.

I'll now turn the discussion to the Q&A portion of the call. Kevin, can you please provide instructions for those wishing to ask a question?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question is coming from Chris Schott from JPMorgan.

Christopher Thomas Schott ***JPMorgan Chase & Co, Research Division - Senior Analyst***

Just maybe a 2-parter on the pharma side. First, on the $57 billion target for pharma, I think your comments are very clear in terms of your confidence of exceeding consensus of $54 billion. Are you still confident though in that $57 billion target as we think about kind of the pushes and pulls that you just outlined there?

And then maybe just a specific question on RYBREVANT. Just want to make sure the comments correctly there. I think you mentioned there's a final analysis of MARIPOSA later this year. Does that mean the interim has passed at this point? And maybe just put some context of what you think you need to show in that study to dislodge share from TAGRISSO.

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Thanks, Chris. I appreciate the questions. So first, with respect the $57 billion, I wanted to make sure that I was clear on the record since I had the opportunity to do that about a month ago that everybody understood the message around the math component of it.

We feel very good about our pipeline. We continue to work towards some really good data that came out this quarter around multiple myeloma, MARIPOSA, which we'll talk about in a minute. We continue to see some uptake of some of our newer products. And the goal is still that for us. But you'll have a much better and much more informed and probably timely update once we hit the December 5th meeting at the New York Stock Exchange. So stay posted on that.

What I do feel comfortable though is that we're moving certainly in the right direction. I wanted to take out the unclarity that maybe was created by currency and the dramatic movements that occurred over the last 18 months.

So for MARIPOSA, I would say the study of RYBREVANT and lazertinib in frontline non-small cell lung cancer versus TAGRISSO remains very much on track. It's an event-driven trial. So there's the potential for final analysis later this year, which is actually 2 quarters ahead than what we had originally expected, was originally expected to be second quarter of 2024.

The accrual to the study we can say is very rapid as there was tremendous interest. And the interim analysis was specified in the protocol with a significantly limited follow-up and supported the continuation of the study.

We were blinded to that interim analysis. And as far as what we need to show, I think we're just going to let the science dictate, let the trial results come out. But we feel pretty comfortable where we're at now and pleased with how quickly the trial enrolled.

Operator

Next question is coming from Matt Miksic from Barclays.

Matthew Stephan Miksic ***Barclays Bank PLC, Research Division - Research Analyst***

I have, if I could, just one question on Knees and a quick follow-up, kind of a general strategy question on STELARA pharma if I could. So on Knees in the U.S., obviously, very strong growth. And just wondering if you could -- and I think expectations have been strong throughout Q1.

I just was wondering if you could maybe give a little bit of color as to what's driving that strength? How much of that is maybe the robot? How much of that is other product launches? And then one quick follow-up on pharma if I may.

Ashley A. McEvoy ***Johnson & Johnson - Executive VP & Worldwide Chairman of MedTech***

Matt, thank you for the question. And before I turn it to Joe on STELARA, it's really nice to see 12% growth in the U.S. for Knees. We haven't seen that in a while. But before I get into specifically Knees, maybe just a quick frame on like the quarter.

Obviously, first, the industry I think continues to remain strong and growing. Procedures are well in recovery mode. It's awesome to see an 11% operational performance and 6.4 adjusted ops for the first quarter.

It was our first quarter with Abiomed. So if you look at them on like-for-like periods, as a standalone of 22% growth. But I think when I look at all of the math, if you will, for the quarter, what I'm most pleased about is really the balanced growth.

And we had our BWI business up 13%. Our global Vision, up 8%. And our U.S. business, our largest market, growing north of 8% really fueled by Ortho performance, up 6% as well as Surgery up 6. And you hear us talk about these 12 $1 billion platform, but 6 of those grew double digit in the United States in the quarter.

EMEA was strong, and Asia was a little bit softer again by China. Obviously, Jan and Feb was a bit softer. We were encouraged with March procedures recovered in March. But I would call it 3 specific innovations, and then I'll go deeper into Knees.

One is our pulse field ablation. So we're very pleased with the data in AFib that it's promising. We have 4 clinical trials ongoing. 2 out of the 4, we've completed enrollment, and we shared the data from the inspiRE trial where we met the primary endpoint for both safety and efficacy.

Our Abiomed, as we've talked about, we're about 90 days in. They continue to advance the innovation pipeline. They're in clinic in 4 clinical trials to expand new products and to expand indications to get Class 1 designation.

And last, I would say, Matt, we are in all things robotics. So let's talk about VELYS. We just received CE Mark positioning it for expansion to more global markets. Right now, we're in 5. But I'm pleased to say that it's now the fastest-growing knee robotic system in the United States.

We've completed over 20,000 procedures. And we're taking a systems approach to our business in hips to shoulders and the spine. Our Monarch platform is the first and only multispecialty flexible robotics solution with FDA clearance in bronchoscopy as well as endo-urology.

We've completed 25,000 procedures and are in clinic right now combining the Monarch endoluminal navigation with ablation treatment technology of NeuWave. And just recently, in February, we were -- the first patient received robotic-assisted removal of kidney stone. We're trying to get a higher kidney stone clearance rate than the standard of care.

And last, as we talked about our team in OTTAVA is really progressing significantly, really looking forward to a back half of the year update with the team. So VELYS is really a combination of having access to cementless, both on fixed bearing and rotating platform,

revision, our new introduction of the medial stabilized knees and most importantly, not just coupled with the robotic system of VELYS, but coupled with the most modern knee implant in the world.

Matthew Stephan Miksic ***Barclays Bank PLC, Research Division - Research Analyst***

Well, that was a fantastic overview. Congrats on all the innovation and the significant change and momentum across all those businesses. Just a quick question, I guess, I had on pharma was -- I mean, it's a big question, and I think it's on a lot of investors' minds is if we turn into the end of the year and you think about STELARA, and you think about sort of the actions that you expect to take whether organic, the pipeline that you have and as it comes through, and some of these new products launch and get bigger. And then strategic, if you could maybe give a sense of what are your goals over the next 12, 18 months as you sort of weather that LOE, and what sort of mix of action should we expect you to take to kind of manage through that?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Sure. Thanks, Matt, for the question. A lot to maybe unpack possibly there. But let me first start with our base assumption, the guidance, which has the underlying assumption that in the U.S., STELARA will lose exclusivity in the late third quarter, early fourth quarter of this year. And that's kind of the assumption that we're going on.

What I would say is that's somewhat fluid. At this point, there are currently no biosimilars approved. In terms of our planning, we are expecting -- despite learning a lot over the last few years with REMICADE, we're expecting a steeper erosion curve than what was experienced there because this is a self-administered subcutaneous product.

There will be multiple competitors on the market at some point, and they may have the affordability of interchangeability. But we may remain committed to growing through the patent expiration. One of the great things about our portfolio, whether we're talking within Pharmaceuticals or across the broader businesses, is we've got 30 products or platforms that generate over $1 billion in annual revenue. So we're not dependent on one product the way others may have.

In terms of unpacking your question maybe a little bit further, I got the sense you were heading towards M&A. Certainly, we always remain vigilant and look at a number of opportunities, making sure there's a strategic fit before we act. If there's strategic fit, then we're going to look to deploy capital in the way that returns to shareholders to compensate them, quite frankly, for the risk that we're bearing on their behalf.

But we're not going to do anything out of desperation based on the breadth of our product portfolio. We are lucky in that we've got a strong balance sheet to do whatever we'd like, but we want to make sure it makes good strategic and financial sense. So that's probably the best way to answer that.

I know Jennifer and the team are very committed to growing through STELARA whenever that may occur. And the pipeline data that we're generating now as well as really the early success we're having in some of these newer products, I think, positions us well to meet those goals.

Operator

Your next question today is coming from Terence Flynn from Morgan Stanley.

Terence C. Flynn ***Morgan Stanley, Research Division - Equity Analyst***

Great. Maybe a 2-part one for me as well. Thanks for the update on the talc litigation, Joe. I was just wondering if you could comment at all about any additional progress towards that 75% threshold, specifically the denominator and kind of where that's shaking out?

And then on the oral IL-23 program there, just wondering if you can confirm if you're going to advance into Phase III and where that drug might be positioned ultimately in the treatment paradigm based on the data you guys have seen thus far?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Great. Thanks for the question, Terence. Let me start with the second one first with respect to the oral IL-23, where our partners at Protagonist announced some very encouraging data out of the Phase II FRONTIER-1 study. So we do plan to present data from various preclinical and clinical studies on this compound at medical conferences beginning in the second quarter of this year.

We believe this could be very much an important and underappreciated asset within our Immunology portfolio. With respect to the litigation, we thought that this could come up as a question. So we're very pleased to have Andrew White, our Assistant General Counsel, here with us today.

But let me say a little maybe a couple of qualitative things, from my seat, and then we can have Andrew either clean it up or give you some more specifics. But it is important to note that these cases and we stand by the safety of the product, there's decades of independent research conducted by reputable government agencies, patient advocacy groups as well as academic institutions that support the safety of cosmetic talc.

Furthermore, it was only 2 years ago at a Daubert hearing where the judge really restricted the use of many of the claims, supposedly scientific claims that were being made by the plaintiffs attorneys in this case and many pundits even classified it as junk science at that point. Here, we have the support of 60,000 to 70,000 claimants that would vote for the proposal as it's currently presented.

But curiously, we've got a small number of plaintiff's attorneys who don't even want to give their claimants the right to vote. So we're simply asking that they get the right to vote.

Now from my chair as CFO, it is unfortunate that we've got to put dollars towards, quite frankly, baseless scientific claims. However, litigation is inherently costly when it's protracted. And it's also inherently uncertain. And our proposal really aims to bring certainty in a very efficient manner for all really involved, something that would otherwise take probably decades to resolve. So let me turn it over to Andrew in terms of maybe any of the specifics that you can add.

Andrew White ***Johnson & Johnson - Assistant General Counsel***

Thanks, Joe. As Joe mentioned, we are very confident in the position that we stand today in terms of support for the plan. We have well over 60,000 that have expressed a desire to vote for this plan. And the expectation is that we will move forward with a reorganization plan to present to the court within the next 30 days and hope to quickly move to a vote.

And we believe once we put that plan out for a vote, we'll gain even more support from a small, but I would say, vocal minority of attorneys. So we believe we're going to reach that 75% threshold and look forward to getting that plan out to a vote.

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Thank you, Andrew.

Operator

Next question today is coming from Larry Biegelsen from Wells Fargo.

Lawrence H. Biegelsen ***Wells Fargo Securities, LLC, Research Division - Senior Medical Device Equity Research Analyst***

Joe, 2 for you on the guidance. I heard you on CNBC this morning, and you said you turned from cautious in January to optimistic now about 2023. So I was curious about 2 things. One, on the guidance you previously expected second half to be better than the first half in MedTech and Pharma because of the growth drivers you outlined -- on the Q4 call. So what changed there? Why do you expect growth to be more stable through the year?

And second, Joe, on the margins. Q1 was up about 60 basis points year-over-year in Q1 on the operating margin but you expect -- and you expect gross margins to improve through 2023 as inflation wanes. So why would the operating margin be flat for the full year?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Yes. Thanks, Larry. Well, first, I do want to correct the record a little bit on you. Responsibly was in front of both cautious as well as optimistic. So we've moved from responsibly cautious to responsibly optimistic.

Why do I say that? It's because we did see some dynamics within our P&L, the team's great ability to really manage our resources effectively with the backdrop of really a company separation that could lend itself to some stranded costs. We're managing those extremely well.

There is still inflation within the P&L. I don't think we should say that it's now behind us. We have a good data point with respect to where we landed Q1. We're very pleased with the first quarter results and the strength of that and why we've maybe moved from a little bit more of a consistent approach throughout the year versus a stronger second half from the first half is really around the first quarter results.

So in terms of Pharmaceutical pricing, it was still unfavorable as you might expect with respect to Pharmaceutical, but not as unfavorable as we anticipated. And then maybe Ashley can talk here, too. When we came out in January, there was -- the pandemic was kind of full-blown in the Asia Pacific region. And we did see a very positive data point in March with respect to China specifically. I don't know, Ashley, anything to add there?

Ashley A. McEvoy ***Johnson & Johnson - Executive VP & Worldwide Chairman of MedTech***

Yes. No, Larry, what I would share is I would say that procedures are trending well above all pre-COVID levels. It was up until December with the exception of China. China in December, January and February were well below pre-COVID levels. In January trending net down 50%.

So I am encouraged to see in March that they're back up. They're back up a little bit ahead of pre-COVID levels. And so that's why we're kind of rebalancing the year. I think that we're going to have more stability throughout the balance to go year versus earlier thinking that we would be having a stronger second half versus first half.

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Yes. And Larry, with respect to operating margins, it's still very early in the year. It's still only April. If we have the opportunity to manage these macroeconomic headwinds that we ended the year with and then maybe provide the flexibility for further investment for great opportunities down the road that fortify the future, we'll certainly look to do that.

You guys know us well enough that if we don't find those meaningful opportunities, we'll probably have the opportunity to take up guidance down the road. But my first preference would be to deploy that in investment opportunities that secure both MedTech and Pharmaceuticals for the future.

Operator

Next question today is coming from Louise Chen from Cantor Fitzgerald.

Louise Alesandra Chen ***Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD***

So I had a Pharmaceutical question for you. You've built a really strong Oncology franchise. And what are some unique approaches you think you can take to create combos and regimens that might not be available to other companies? And are there any additional areas in Oncology that you would like to be involved in that you are not now currently involved in?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Yes. Thanks for the question, Louise. So I think we're always looking at combinations. The one that's most prolific at this point now is certainly the one for non-small cell lung cancer, which really impacts about 20% of -- lung cancer that's diagnosed today with a certain mutation.

We're very much looking forward to the data that may read out later this year with respect to that. In terms of new areas, I know that the teams are looking very much. I would say some of the new areas that we're coming into now would be some of the bispecific antibodies

with respect to multiple myeloma rounding out that portfolio.

We know how, I want to say, almost personalized that disease is and having multiple options for treatments and maybe even someday potentially cures certainly lends itself with the multiple options that we have. We're going to be focused on multiple myeloma, obviously, prostate cancer, lung cancer. We're very excited about some of the data that could read out on what I'll call the MedTech pharma combo of -- for bladder cancer and with the TARIS device with the drug eluting BALVERSA. So there's multiple plays within Oncology, which is now our biggest franchise with Immunology in terms of sales contribution to the pharmaceutical success.

Jessica Moore ***Johnson & Johnson - VP of IR***

The only aspect that I'd add, Louise, is as you know, our multiple myeloma platform is extremely strong. And we're looking at some multiple clinical trials about not cannibalizing those products, but rather looking at combination treatments as well as sequences of those products between TECVAYLI, DARZALEX, CARVYKTI and then hopefully our soon to be approved talquetamab.

Operator

Next question is coming from Josh Jennings from TD Cowen.

Joshua Thomas Jennings ***TD Cowen, Research Division - MD & Senior Research Analyst***

Had a question for Ashley just on the VARIPULSE PFA platform. I was hoping that just get an update on commercial time lines. Anything you can share just in terms of CE Mark and then FDA approvals.

And then maybe digging a little bit deeper, just helping us understand. I mean, our expectation is that VARIPULSE will be third to market in the United States, but what percentage of Biosense Webster's revenues are levered to the ablation catheter segment within the EP industry? And what drives your optimism that VARIPULSE will maintain -- be able to maintain license leadership position in the ablation catheter segment?

Ashley A. McEvoy ***Johnson & Johnson - Executive VP & Worldwide Chairman of MedTech***

Thank you, Josh. Listen, it's a really important space. And we always say at J&J, we're always trying to intercept disease before it advances. And this is one example of managing atrial fibrillation, which is the leading cause of cardiac arrhythmia and unmanaged, that could lead to a stroke.

So what gives us confidence that we can lead and compete and have a source of differentiation, I would say kind of the following. I'd say, one, we have a 20-year track record of being a world leader in cardiac ablation. We have 5,000-plus installed base.

We do see the promise of PFA. We are actively engaged in 4 clinical trials. 2 of those trials have completed enrollment, the European inspire as well as the U.S. We've shared data in February at the International AFib symposium that we met the primary endpoint.

And I would tell you, our approach is really what's differentiated, Josh. So we're kind of leveraging a deep expertise and the insights into the various ablation strategies. So we have a portfolio of PFA catheters, which are fully integrated into their CARTO 3 system and it's powered by our TRUEPULSE generator.

So we really underscore the importance of how important mapping is and vision to know where operators are and what they're doing in the heart anatomy. And kind of the bottom line for us is we actually think access to radio frequency, which has like 20-plus years of safety and efficacy coupled with the newer generation of PFA is really going to be the winning combo for electrophysiologists.

It's really why we are in clinic right now with the dual energy solution because we think it could offer the relative safety of the PFA and really the proven durability of radio frequency. So we're not issuing specific timelines, but you can know that we've completed enrollment in 2 of those 4 clinical trials.

Operator

Your next question is coming from Geoff Meacham from Bank of America.

Geoffrey Christopher Meacham ***BofA Securities, Research Division - Research Analyst***

I have 2 related ones in Pharma. So on IMBRUVICA, how do you guys view the impact from the indication withdrawal? And is there a risk of other non-CLL indications like follicular being pulled? And then related to your hematology business, do you guys have a status update on CARVYKTI supply after or was this quarter a really good quarter?

Joseph J. Wolk ***Johnson & Johnson - Executive VP & CFO***

Yes. Thanks for the question, Geoff. So with respect to IMBRUVICA, I would say that we're not expecting any more withdrawals at this point. It is obviously based on our performance encountering competitive pressures. But it's really the competition that's been the biggest driver in terms of the performance that we're not seeing there, quite frankly. But it's -- the withdrawal was a very small part of our business to begin with, but we don't anticipate other withdrawals at this point.

With respect to your second question and supply on CARVYKTI, I would say that you probably did read the announcement recently that we did sign on for additional capacity to scale up some production and increase availability moving forward. The manufacturing is ramping up to supply markets.

We have really tremendous demand given some of the data that supports this -- the CARVYKTI, the CAR-T for Johnson & Johnson. And we're committed to doing everything we can to accelerate our manufacturing abilities to meet that demand. We work in our facility and again continues to progress. And it will serve as an important part of our supply chain network for not just this but other cell therapies in the future.

Operator

Our final question today is coming from Danielle Antalffy from UBS.

Danielle Joy Antalffy ***UBS Investment Bank, Research Division - Analyst***

It's good to be back talking to you all. Ashley, just a quick question for you on the Orthopaedics number. A very good quarter. I was just wondering, I know this is really hard to parse out, but what is -- from your sense, what does backlog work down versus real underlying growth and/or more specific to J&J share gain? Anything you can say on how to think about what's happening in the Orthopaedics market right now in the U.S. Thanks so much.

Ashley A. McEvoy ***Johnson & Johnson - Executive VP & Worldwide Chairman of MedTech***

Thank you, Danielle. It's great to hear your voice. Listen, it's really a combination of both. Procedures are accelerating, particularly like even as recently as March in China, as an example, U.S. working through some of the backlog. So I do think that the market is in our favor.

But at the same time, I have to give huge acknowledgment to the Orthopaedics team, who has really built a very differentiated portfolio. And they are now participating in the fastest-growing segments within the Orthopaedics category.

So if the category is going 3 to 4, they're competing in areas that are high single digit. And what are those areas? It's all things robotics. It's around new sites of care like ASCs. It's around extremities.

I'm very pleased with our recent acquisition of CrossRoads, a foot and ankle. It's what we talked about around revision Knees and cementless Knees. Those are really the faster-growing segments in Orthopaedics, and we are well positioned to take advantage of that demand. Thank you for the question.

Jessica Moore ***Johnson & Johnson - VP of IR***

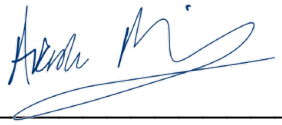
Thank you, Danielle, and thanks to everyone for your questions and your continued interest in our company. We apologize to those that we couldn't get to because of time, but don't hesitate to reach out to the Investor Relations team with any remaining questions that you may have. Enjoy the rest of your day.

Operator

Thank you. This concludes today's Johnson & Johnson's First Quarter 2023 Earnings Conference Call. You may now disconnect.

Exhibit "F9"

This is Exhibit “F9” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.



A Commissioner for Taking Affidavits, etc.

Arash Rouhi

REDACTED

Exhibit "F10"

This is Exhibit “F10” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

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A Commissioner for Taking Affidavits, etc.

Arash Rouhi

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Exhibit "F11"

This is Exhibit “F11” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

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Arash Rouhi

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Exhibit "F12"

This is Exhibit “F12” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

JANSSEN BIO ADVANCE®

Bioadvance Canada
19 Green Belt Drive
Toronto, ON M3C 1L9
Tel: 855-544-5487 Fax: --

Fax

To: [redacted] **From:** [redacted]

Fax: [redacted] **Date:** May [redacted]/24 [redacted]

Subject: Sterala update

Hello Dr. [redacted]

This is an update regarding ODB formulary changes for Stelara for Dermatology patients.

Do not hesitate to contact me if you have any questions.

Regards

[redacted]

[redacted]*RN*

BioAdvance Coordinator

Coordonnatrice BioAdvance

Tel: [redacted]

Tel:

Fax:

Email: [redacted]*@bioadvancemail.ca*

BIOADVANCE

May [redacted] 2024

Dear Dr [redacted]

In response to the ODB's formulary changes effective April 30th, 2024, I wish to update you as follows:

- As of April 30th, 2024, ODB no longer reimburses STELARA® for new patients.
- Coverage for STELARA® will continue for patients previously approved for ODB coverage.
- Patients who have private reimbursement coverage or are currently receiving STELARA® at no cost through Janssen's patient access and affordability program are not impacted by this provincial update. However, some private insurers may choose to update their plans.
- Janssen will be offering patients who are prescribed STELARA® and are impacted by the Ontario biosimilar initiative an opportunity to remain or be enrolled in BioAdvance®.
    - Newly prescribed STELARA® patients who do not have public or private STELARA® coverage will have the option to receive a ustekinumab biosimilar in the BioAdvance® program.
    - More information will be made available in the coming weeks.

I will reach out to you when this option is available or notify you if there are any immediate changes that need to be made for your patients and will work with you to ensure a seamless transition if a switch is required."

Regards

[redacted]

Exhibit "F13"

This is Exhibit “F13” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

From: Sébastien Levesque
To: Amélie Faubert
Subject: TR: Ontario Biosimilar Introduction and STELARA
Date: Friday, June 14, 2024 2:04:54 PM
Attachments: image001.jpg

FYI Pour tes dossiers,
Vieux e-mail que je viens de trouver si tu ne l'avais pas déjà
seb

Sébastien Lévesque
Chef de Produit Senior / Sr Product Manager
JAMP Corporation / BIOJAMP division
Mobile. (438)-303-9895
slevesque@biojamp.com
1310 Nobel, Boucherville, QC J4B 5H3
jamppharma.com

De : Lesley Mason <lmason@biojamp.com>
Envoyé : 15 mai 2024 13:08
À : Jeff Verreault <jverreault@biojamp.com>; Amélie Faubert <afaubert@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Objet : FW: Ontario Biosimilar Introduction and STELARA

Hello,

As previously mentioned, customers are getting confused on the letter below which Janssen has been distributing for a couple weeks now. This letter is believed to be the most up to date version which is signed by Andy (VP). The obvious issue is that the doctors don't want to switch if their patients can stay on brand. Do we have a rebuttal for this?

Thank-you!

Lesley

Janssen Inc.

19 Green Belt Drive
Toronto, ON M3C 1L9
1-800-387-8781 toll free
416-449-9444 tel
416-449-2658 fax

www.janssen.com/canada

Janssen Logo

May 7, 2024

Re: Ontario Biosimilar Introduction and STELARA®

Dear Healthcare Professional,

In response to the Ontario Government's recent biosimilar reimbursement announcement, we wish to provide you with information on how this may impact patients prescribed STELARA®.

1. Patients prescribed STELARA® who have **private reimbursement coverage will not be impacted** by this biosimilar policy. However, some private insurers may choose to update their plans.
2. Patients currently receiving STELARA® at no cost through Janssen's patient assistance program **(BioAdvance®) will not be impacted** by the introduction of biosimilars.
3. Patients **currently prescribed STELARA®** who rely on **public reimbursement coverage for PsO WILL NOT** be required to switch to a biosimilar.
4. As of April 30, 2024, the Ontario Drug Benefit plan is no longer covering new STELARA® PsO patients.

To preserve continuity of care and support physician choice, Janssen will be offering **new patients who are prescribed STELARA® and do not have public or private STELARA® coverage** an opportunity to be enrolled in BioAdvance® and receive a ustekinumab option.

There is nothing you need to do at this time, your BioAdvance® Coordinator will reach out and notify you if there are any changes that need to be made for your patients. If you have any questions or concerns, please contact your BioAdvance® Coordinator or Janssen Representative and they will be able to assist you.

Sincerely,
signature

Andy Williams
Vice President, Immunology
Janssen Canada

Exhibit "F14"

This is Exhibit “F14” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

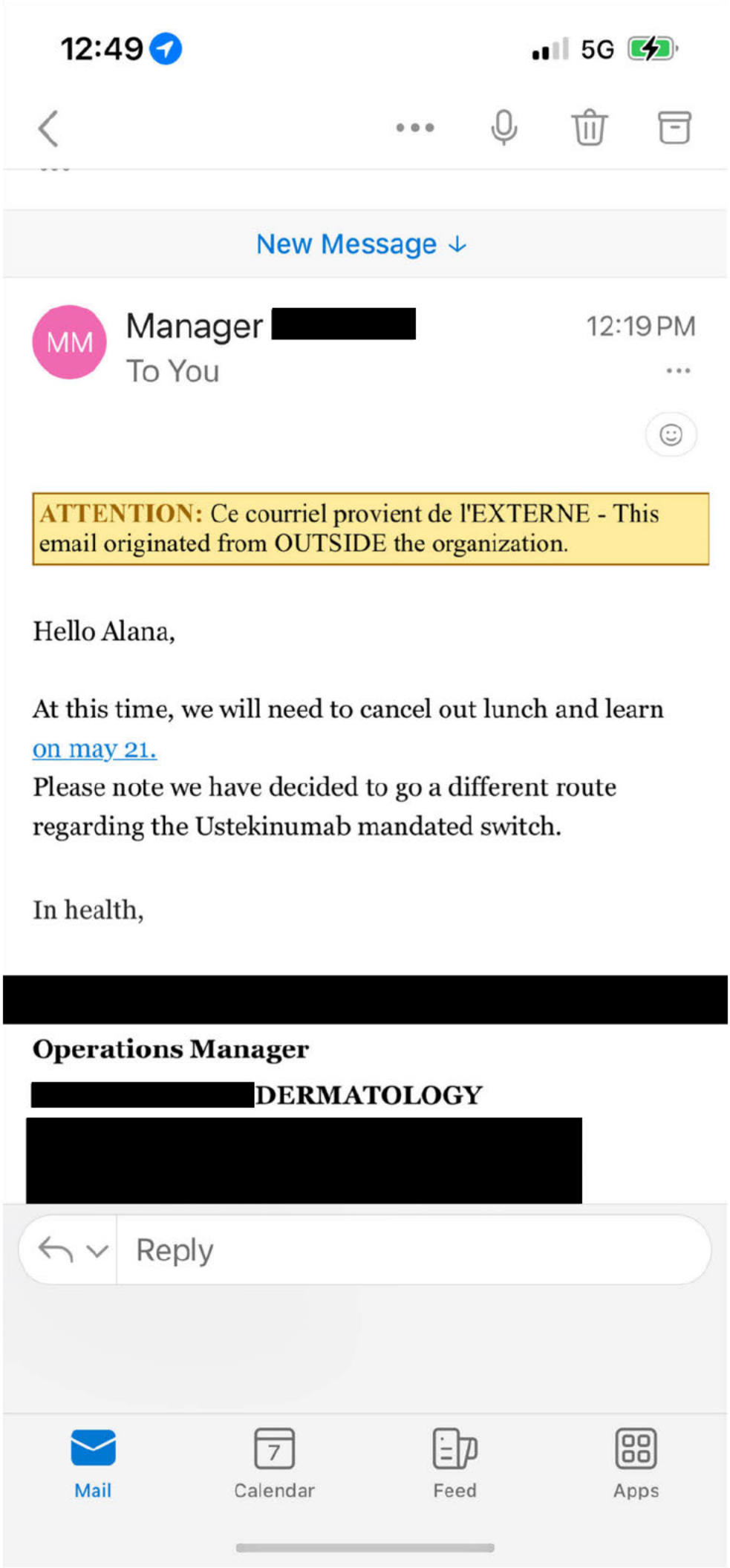
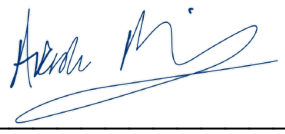

12:49
5G
New Message
MM
Manager [redacted]
12:19 PM
To You
ATTENTION: Ce courriel provient de l'EXTERNE - This email originated from OUTSIDE the organization.
Hello Alana,
At this time, we will need to cancel out lunch and learn on may 21.
Please note we have decided to go a different route regarding the Ustekinumab mandated switch.
In health,
[redacted]
Operations Manager
[redacted] DERMATOLOGY
[redacted]
Reply
Mail
Calendar
Feed
Apps

Exhibit "F15"

This is Exhibit “F15” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.



A Commissioner for Taking Affidavits, etc.
Arash Rouhi

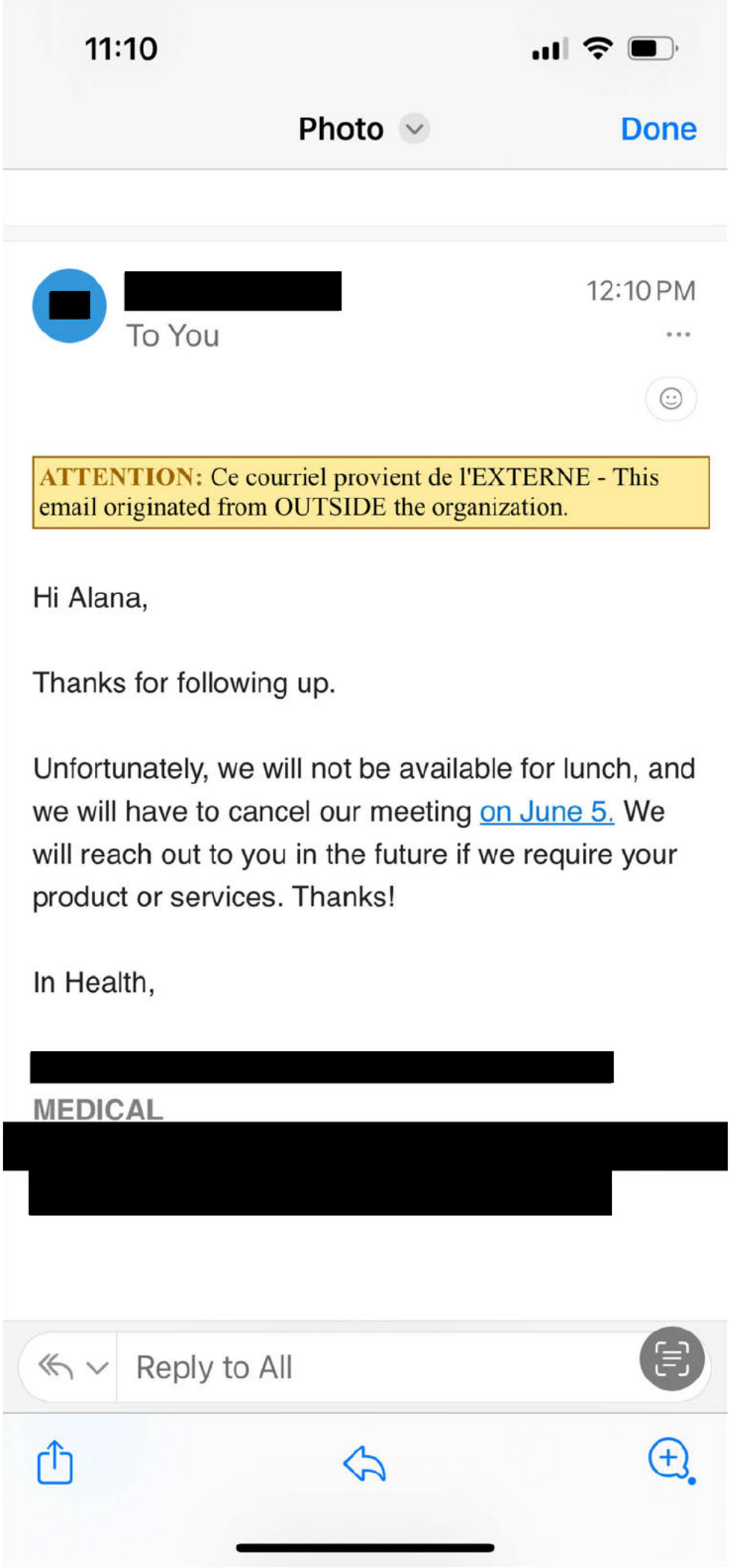

11:10
Photo
Done
[redacted]
12:10 PM
To You
ATTENTION: Ce courriel provient de l'EXTERNE - This email originated from OUTSIDE the organization.
Hi Alana,
Thanks for following up.
Unfortunately, we will not be available for lunch, and we will have to cancel our meeting on June 5. We will reach out to you in the future if we require your product or services. Thanks!
In Health,
[redacted]
MEDICAL
[redacted]
Reply to All

Exhibit "F16"

This is Exhibit “F16” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

From: Nova Bais
To: Sébastien Levesque; Jeff Verreault; Amélie Faubert; Josyanne Bourget
Subject: Fwd: Jamp Care
Date: Monday, June 17, 2024 3:35:34 PM
Attachments: image001.png
image002.png
image003.jpg

FYI

Nova Bais RN, BScN
Manager, Patient Support Programs
Mobile : (587)338-1757
1310 Nobel, Boucherville, QC J4B 5H3
jamppharma.com

From: [redacted]@gmail.com>
Sent: Monday, June 17, 2024 1:16 PM
To: Nova Bais <nbais@jamppharma.com>
Subject: Re: Jamp Care

Good Afternoon Nova,

Bioadvance says we can hold off on making any switches until October. No switches need to make at this time,

If you could email the updates that would be great, i dont think we need a lunch at this time.

Thank you

On Mon, Jun 17, 2024 at 9:53 AM Nova Bais <nbais@jamppharma.com> wrote:

> Good morning,
>
> I am just checking in to see how your Stelara switches are going?
>
> Did you want to meet to review the updates from the GoA at all? I could bring in lunch if you would like?
>
> Kind regards,
>
> **Nova Bais RN, BScN**
>
> **Manager, Patient Support Programs**
>
> Mobile : (587)338-1757

1310 Nobel, Boucherville, QC J4B 5H3

jamppharma.com

Exhibit "F17"

This is Exhibit “F17” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

_____

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

From: Andrew Trites
To: Amélie Faubert; Jonathan Blanchard
Cc: Jeff Verreault; Sébastien Levesque
Subject: Janssen Field Intel
Date: Wednesday, June 5, 2024 4:06:06 PM

Good afternoon.

I had lunch with [redacted] from Dr. [redacted] office today and she informed me Janssen is telling the physicians NOT to switch their Ustekinumab patients and that worst case they'll provide free goods until they find a solution.

I shared this with Jonathan and he wanted me to share by email.
Thanks,
Andrew

Get Outlook for iOS

Exhibit "F18"

This is Exhibit “F18” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

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A Commissioner for Taking Affidavits, etc.
Arash Rouhi

Drug Prior Authorization Form
Ustekinumab

226

The purpose of this form is to obtain information required to assess your drug claim.

IMPORTANT: Please answer all questions. Your claim assessment will be delayed if this form is incomplete or contains errors.

Any costs incurred for the completion of this form are the responsibility of the plan member/patient.

Canada Life recognizes and respects the importance of privacy. Personal information collected is used for the purposes of assessing eligibility for this drug and for administering the group benefits plan. For a copy of our Privacy Guidelines, or if you have questions about Canada Life's personal information policies and practices (including with respect to service providers), refer to www.canadalife.com or write to Canada Life's Chief Compliance Officer.

I authorize Canada Life, any healthcare provider, my plan administrator, any insurance or reinsurance company, administrators of government benefits or patient support programs or other benefits programs, other organizations, or service providers working with Canada Life or any of the above, located inside or outside Canada, to exchange personal information when relevant and necessary for these purposes. I understand that personal information may be subject to disclosure to those authorized under applicable law within or outside Canada.

I acknowledge that the personal information is needed to assess eligibility for this drug and to administer the group benefits plan. I acknowledge that providing consent will help Canada Life to assess my claim and that refusing to consent may result in delay or denial of my claim. Canada Life reserves the right to audit the information provided on this form at any time and this consent extends to any audit of my claim. This consent may be revoked by me at any time by sending written instruction to that effect.

I also consent to the use of my personal information for Canada Life and its affiliates' internal data management and analytics purposes.

If the patient is a person other than myself, I confirm that the patient has given their consent to provide their personal information and for Canada Life to use and disclose it as set out above.

I certify that the information given below is true, correct, and complete to the best of my knowledge. Failure to provide true, correct and complete information on this form could result in revocation of any approval decision, a requirement to repay paid claims or other appropriate action.

Plan Member's signature: _____ Date: _____

Form Completion Instructions:

1. **Complete "Patient Information" sections.**
2. **Have the prescribing physician complete the "Physician Information" sections.**
3. **Send all pages of the completed form to us by mail, fax or email as noted below.**

Note: As email is not a secure medium, any person with concerns about their prior authorization form/medical information being intercepted by an unauthorized party is encouraged to submit their form by other means.

Mail to: **The Canada Life Assurance Company**
Drug Claims Management
PO Box 6000
Winnipeg MB R3C 3A5

Fax to: **The Canada Life Assurance Company**
Fax 1-204-946-7664
Attention: Drug Claims Management

Email to: **cldrug.services@canadalife.com**
Attention: Drug Claims Management

For additional information regarding Prior Authorization and Health Case Management, please visit our Canada Life website at www.canadalife.com or contact Group Customer Contact Services at 1-800-957-9777. Deaf or hard of hearing and require access to a telecommunications relay service? Please contact us at 711 for TTY to Voice or 1-800-855-0511 for Voice to TTY.

(Continued on next page)

M6453(USTEKINU)-03/24

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Patient Information
Ustekinumab

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Plan Member Information – Complete all sections of this page (please print)

Plan Member:	Patient Name:	
Plan Name:	Plan Number:	Plan Member ID Number:
Patient Date of Birth (DD/MM/YYYY):	Address (number, street, city, province, postal code):	

Please indicate preferred contact number and if there are any times when telephone contact with you about your claim would be most convenient.

May we contact you by email? (Note that some correspondence may still need to be sent by regular mail).

☐ Yes ☐ No If yes, please provide email address: _____

Tell us if you have been on this drug before

Is the patient currently on, or previously been on this drug? ☐ Yes ☐ No

If Yes, a) indicate start date (DD/MM/YYYY): _____

b) coverage provided by: _____

(if coverage is not provided by Canada Life please provide pharmacy print-out showing purchase of this drug)

Tell us if you have coverage with any other benefits plan

Does the patient have drug coverage under any other group benefits plan? ☐ Yes ☐ No

If Yes, name of other Insurance Company: _____

If other plan is with Canada Life, tell us the plan and ID number: _____

Name of plan member: _____

Relationship to patient: _____

Provide details and attach documentation of acceptance or decline:

_____

_____

Tell us about any Provincial or other coverage you may have

Does the patient have coverage under a provincial program or from any other source? ☐ Yes ☐ No

If Yes, name of program or other source: _____

Provide details and attach documentation of acceptance or decline: _____

Is the patient currently receiving disability benefits for the condition for which this drug has been prescribed? ☐ Yes ☐ No

Tell us about any Patient Support Program you might be enrolled in

Has the patient enrolled in the patient support program for this drug? ☐ Yes ☐ No

If Yes, please provide the following information:

1. Patient support program patient ID Number: _____
2. Patient support program contact person name and phone number:

   Contact Name: _____ Phone Number: _____

(Continued on next page)

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Physician Information
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Note to Physician: In order to assess a patient's claim for this drug, we require detailed information on the patient's prescription drug history as requested below.

Attach extra information if necessary. *GENETIC TEST RESULTS ARE NOT REQUIRED*

Physician's Information (please print)

Name of prescribing physician:

Specialty:

Address (number, street, city, province, postal code):

Telephone Number (including area code):	Fax Number (including area code):

1. Prescribed drug (in alphabetical order):
   - ☐ Finlius
   - ☐ Jamteki
   - ☐ Stelara
   - ☐ Wezlana
   - ☐ Other: _____
2. Health Canada indication (include date of initial diagnosis) (MM/YYYY): _____

☐ **Plaque Psoriosis**

Adult

Patient's current weight: _____ kg	Induction Dose weeks 0 and 4	Maintenance Dose
☐ ≤ 100kg	☐ 45mg	☐ 45mg every 12 weeks
☐ > 100kg	☐ 90mg	☐ 90mg every 12 weeks

☐ Other (please specify): _____

Provide rationale: _____

Pediatric (12 to 17 years of age)

Patient's current weight: _____ kg	Induction Dose weeks 0 and 4	Maintenance Dose	Delivery Method
☐ < 60kg	☐ (0.75mg/kg)	Indicate mg every 12 weeks _____	☐ 45mg vial
☐ ≥ 60kg to ≤ 100kg	☐ 45mg	☐ 45mg every 12 weeks	☐ vial ☐ prefilled syringe
☐ > 100kg	☐ 90mg	☐ 90mg every 12 weeks	☐ prefilled syringe

☐ Other (please specify): _____

Provide rationale: _____

☐ **Psoriatic Arthritis**

Patient's current weight: _____ kg	Induction Dose weeks 0 and 4	Maintenance Dose
☐ ≤ 100kg	☐ 45mg	☐ 45mg every 12 weeks
☐ > 100kg	☐ 90mg	☐ 90mg every 12 weeks

☐ Other (please specify): _____

Provide rationale: _____

(Continued on next page)

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Physician Information
Ustekinumab

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Physician's Information *(continued)* (please print)

☐ **Crohn's Disease** ☐ **Ulcerative Colitis**

Patient's current weight: _____ kg	Single IV Induction Dose (130mg vial)	Subcutaneous Maintenance Dose
☐ ≤ 55kg	☐ 260mg (2 vials)	☐ 90mg every 8 weeks
☐ 55kg to ≤ 85kg	☐ 390mg (3 vials)	☐ 90mg every 8 weeks
☐ ≥ 85kg	☐ 520mg (4 vials)	☐ 90mg every 8 weeks

☐ Other (please specify): _____

Provide rationale: _____

Complete questions 1 – 6 and Physician's information

☐ Other (approved by Health Canada): _____

Dosage and Regimen: _____

Complete questions 1 – 6 and Other condition (Health Canada approved)

☐ Other (prescribed use is not approved by Health Canada): _____

Dosage and Regimen: _____

Complete questions 1 – 6 and Off-label use

3. What is the anticipated duration of treatment with this drug? _____

4. Where will treatment be administered? ☐ Home ☐ Physician's Office ☐ Private clinic ☐ Hospital in-patient ☐ Hospital out-patient

5. Please provide medical rationale why this drug has been prescribed instead of an alternate drug in the same therapeutic class:

_____

_____

6. Drug and Treatment History – **must be completed for every request.** If coverage for these drugs was not provided by Canada Life, please submit a pharmacy printout for the last 12 months.

Drug(s) and Treatment(s) past and present	Dosing Regimen	Start Date (DD/MM/YYYY)	End Date (DD/MM/YYYY)	Clinical Results/Outcome
				☐ Failure ☐ Intolerance ☐ Other Clinical details:
				☐ Failure ☐ Intolerance ☐ Other Clinical details:
				☐ Failure ☐ Intolerance ☐ Other Clinical details:
				☐ Failure ☐ Intolerance ☐ Other Clinical details:

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Physician Information
Ustekinumab

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Physician's Information *(continued)* (please print)

Crohn's Disease

Does the patient have a diagnosis of moderate or severe Crohn's Disease? ☐ Yes ☐ No

Site of disease and complications: _____

Has the patient had a trial of at least one of the following drugs for a minimum of 12 weeks? ☐ Yes ☐ No

Select the drugs:

☐ 6-mercaptopurine ☐ azathioprine ☐ methotrexate ☐ prednisone ☐ other: _____

* Patients who experience gastrointestinal intolerance to PO methotrexate must have a trial of parenteral methotrexate (IM or SC) to be considered an adequate trial

If no, please provide medical rationale as to why these medications have not been tried

_____

_____

_____

Was ustekinumab started in hospital? ☐ Yes ☐ No

If yes, provide one of the following scores prior to ustekinumab start:

HBI: _____ Date determined (DD/MM/YYYY): _____

CDAI:_____ Date determined (DD/MM/YYYY): _____

Did patient receive a trial of IV steroids for a minimum of 3 days while hospitalized? ☐ Yes ☐ No

Please ensure the Drug and Treatment History chart is completed (include daily steroid dose).

Plaque Psoriasis

% BSA: _____

Areas of body involved: _____

Current result and date of the following scores (DD/MM/YYYY): _____

DLQI: _____ PASI: _____

Has the patient had an adequate trial of one of the following for a minimum of 12 weeks? ☐ Yes ☐ No:

Select one:

☐ acitretin ☐ cyclosporine ☐ methotrexate ☐ other: _____

* Patients who experience gastrointestinal intolerance to PO methotrexate must have a trial of parenteral methotrexate (IM or SC) to be considered an adequate trial

If no, please provide medical rationale as to why these medications have not been tried

_____

_____

_____

Please ensure Drug and Treatment History chart is completed

Psoriatic Arthritis

Swollen and tender joint count: _____

Current result and date of one of the following scores (DD/MM/YYYY): _____

HAQ: _____ BASDAI: _____

Has the patient had a trial of two of the following DMARDs for 12 weeks each? ☐ Yes ☐ No

Select the drugs:

☐ hydroxychloroquine ☐ leflunomide ☐ methotrexate ☐ sulfasalazine ☐ other: _____

* Patients who experience gastrointestinal intolerance to PO methotrexate must have a trial of parenteral methotrexate (IM or SC) to be considered an adequate trial

If no, please provide medical rationale as to why these medications have not been tried

_____

_____

_____

Please ensure Drug and Treatment History chart is completed

Ulcerative Colitis

Diagnosis of moderate or severe ulcerative colitis? ☐ Yes ☐ No

Was ustekinumab started in hospital? ☐ Yes ☐ No

Results and dates of the Partial Mayo score:

Partial Mayo score components:

Mayo rectal bleeding score (0 to 3 points):_____ Date (DD/MM/YYYY): _____

Mayo bowel frequency score (0 to 3 points): _____ Date (DD/MM/YYYY): _____

Mayo clinician's global assessment score (0 to 3 points):____ Date (DD/MM/YYYY): _____

The patient had a trial of at least one of the following (select all that apply):

☐ Azathioprine for 3 months

☐ 6-mercaptopurine for 3 months

☐ Budesonide 9mg orally for 3 months

☐ Prednisone ≥40mg orally for 7 days

☐ IV steroids for 7 days

☐ IV steroids for 3 days

☐ Other: _____

Will ustekinumab be used concurrently with other UC therapies? ☐ Yes ☐ No

If yes, please specify:_____

Please ensure the Drug and Treatment History chart is completed for previous and concurrent UC therapies (include daily steroid use)

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Physician Information
Ustekinumab

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Other condition (Health Canada approved)

Please provide any relevant information related to the disease and attach supporting documentation.

Off-label use

Question 1 – 6 must be completed.

Date of initial diagnosis (DD/MM/YYYY): _____

Is there clinical evidence supporting the off-label use of this drug? ☐ Yes ☐ No

Provide clinical literature/studies to support the request for off-label use, such as:

- At least two Phase II or two Phase III clinical trials showing consistent results of efficacy; and
- Published recommendations in evidence-based guidelines supporting its use.

Provide medical rationale why this drug has been prescribed off-label instead of an alternate drug with an approved indication for this condition.

Provide any pertinent medical history or information to support this off-label request.

If this is a renewal request, provide documentation showing treatment efficacy since previous request.

Note for Physician: To be eligible for reimbursement, Canada Life may require your patient to purchase a drug requiring prior authorization from a pharmacy designated by Canada Life. If applicable, a health case manager will contact you with further information.

I certify that the information provided is true, correct, and complete.

Physician's Signature: _____ Date: _____

License Number: _____

It is important to provide the requested information in detail to help avoid delay in assessing claims for the above drug. This form may be subject to audit. The completed form can be returned to Canada Life by mail, fax, or email.

Note: As email is not a secure medium, any person with concerns about their prior authorization form/medical information being intercepted by an unauthorized party is encouraged to submit their form by other means.

Mail to: **The Canada Life Assurance Company**
Drug Claims Management
PO Box 6000
Winnipeg MB R3C 3A5

Fax to: **The Canada Life Assurance Company**
Fax 1-204-946-7664
Attention: Drug Claims Management

Email to: **cldrug.services@canadalife.com**
Attention: Drug Claims Management

Clear

Exhibit "F19"

This is Exhibit “F19” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

MARCH 2024

Drug pipeline

What's on the horizon for diabetes, weight loss, generics, biosimilars and more in employer plans.

ALBERTA BLUE CROSS®

CONTENTS

EXECUTIVE SUMMARY

Drug coverage is a core and valued component of benefit plans. In 2023, drug claims accounted for over a third of the benefits costs for Alberta Blue Cross® private health and dental benefit plans. With this in mind, it is critically important to have insights into new drug therapies to support the health and wellness of our plan members, while also having a strong understanding of the associated costs to ensure the future sustainability of benefit plan offerings.

Alberta Blue Cross continuously monitors the Canadian drug pipeline, assessing more than 300 drugs currently under Health Canada review, to understand the major therapeutic areas and specific drug therapies that are likely to impact private drug plans. This report will provide an update on some of the notable developments, providing plan sponsors with insight into what's to come.

DRUG PIPELINE AT A GLANCE

Diabetes and weight loss

Diabetes continues to have an impact on private drug plans, typically ranking within the top 3 health conditions by spend. People with insulin dependent diabetes typically require daily insulin injections. Recently approved by Health Canada, the first once-weekly injectable basal insulin could improve adherence and convenience for these people.

It is anticipated that manufacturers of existing diabetes medications will continue to seek regulatory approval to use their drugs for health conditions beyond diabetes. Mounjaro (tirzepatide), which has been approved for diabetes in Canada, has received approval in the United States for weight loss. It is also being studied for other health conditions that benefit from weight loss (for example, for chronic heart failure and obstructive sleep apnea). Other new molecules are being studied for both diabetes and weight loss where early-stage clinical trials are showing greater weight loss effects than currently available therapies.

Migraines

In recent years, we have seen new injectable medications for migraine treatment and prevention, such as Aimovig, Emgality, Ajovy and Vyepti. In addition to these new injectable medications, new oral medications such as Qulipta, Ubrelvy and Nurtec ODT, now offer options for individuals averse to injectable therapies or unable to use conventional therapies like triptans.

Dermatology

The number of treatments for various dermatological conditions continue to increase with the introduction of two new biologics as well as 2 novel topical medications. The first and only treatment available for alopecia areata was recently approved by Health Canada in December 2023. Additionally, 2 innovative topical therapies are currently under review by Health Canada—1 for the treatment of plaque psoriasis and the other for both vitiligo and mild-moderate atopic dermatitis. These new topical treatment alternatives are expected to come with a higher price tag compared to other conventional topical therapies.

Neurology

A breakthrough treatment for Alzheimer's disease, which slows disease progression and improves symptoms in individuals diagnosed early on, is currently under review in Canada. Newly targeted therapies for the treatment of generalized myasthenia gravis will make their way to the Canadian market. While these novel therapies may provide symptom improvement for those not effectively managed with conventional therapies, they will come with high price tags, placing pressure on private drug plans.

COVID treatments

Paxlovid, a 5-day treatment for mild to moderate COVID-19 infections, no longer has universal government funding and is now covered by private payers in the United States. We are closely monitoring Canadian developments to see if government funding will also stop in Canada.

Rare disease drugs

Advancements in drug treatments for rare diseases continue to expand, with many therapies currently undergoing review or receiving recent approval in Canada. While these drugs provide crucial therapeutic options for patients with rare conditions, they are accompanied by extremely high costs. The National Strategy for Drugs for Rare Diseases was announced by the federal government in March 2023; however, considering the number of rare disease drugs in the pipeline and the ultra-high cost of these therapies, newly allocated federal funding won't be sufficient to provide universal coverage for rare disease drugs.

Generics and biosimilars

Generics and biosimilars continue to enter the market providing more affordable treatment options, and savings for benefit plans, which helps with drug plan sustainability. Biosimilars have recently been marketed for Stelara, a high-cost drug commonly utilized for various autoimmune disorders. The biosimilar pipeline is expanding to new therapeutic areas including bone health, infertility and asthma.

There are notable first entry generics coming to the Canadian market for a number of highly utilized diabetes medications and for Vyvanse, which is used for Attention-Deficit Hyperactivity Disorder (ADHD). Also, a generic for the specialty drug Mavenclad, an oral treatment for Relapsing Remitting Multiple Sclerosis (RRMS), is under review by Health Canada.

BACKGROUND

There are currently more than 300 new drugs and generic drugs under review with Health Canada. This list has been reviewed and only the drugs most likely to have an impact on private drug plans are included in this report. A summary of the drugs included and excluded from this review is outlined below.

INCLUDED	EXCLUDED
• New drugs most likely to have an impact on private plans that are - under review with Health Canada as of December 2023, - recently approved (authorized for sale in Canada but not yet marketed), or - recently marketed (currently being sold in Canada). • Notable first-entry generic drugs and biosimilar drugs.	• Drugs for use in cancer or HIV as government programs may provide funding for medications with these indications.

The pricing of new drugs in Canada is subject to approval by the Patented Medicine Prices Review Board (PMPRB) and not known until the drug is marketed. Any prices provided in this publication for drugs not yet marketed are meant as reference points only as they reflect the list prices in other countries where the drug is available. As most of these drug prices are the list price in the United States, the Canadian list price, once marketed, will most likely be lower than the referenced United States price.

NOTABLE DRUGS

DIABETES AND WEIGHT LOSS

DRUG NAME	MEDICINAL INGREDIENT	INDICATION	HEALTH CANADA STATUS	ESTIMATED PRICING
Awiqli	Insulin icodec	Diabetes	Approved (March 2023)	$1,085 to $1,357 per year[1]

Insulin icodec

Health Canada has approved the first basal insulin designed for once-weekly administration. This dosing is unique as basal insulins on the market today require daily administration. A reduction in the frequency of basal insulin injections has the potential to enhance treatment acceptance and adherence, particularly among patients managing Type 2 diabetes.

Diabetes drugs with expanding uses

Based on recent developments in the United States, it is anticipated that there will continue to be the expansion of indications for existing diabetes medications. Numerous pharmaceutical companies are studying diabetes drugs for weight loss, as well as for health conditions that benefit from weight loss (for example, tirzepatide for chronic heart failure and obstructive sleep apnea). Although not currently submitted to Health Canada for review, we will take a deeper dive into some of the products we may soon see come down the Canadian pipeline.

- As mentioned in last year's pipeline, Mounjaro (tirzepatide) has been approved in the United States and Canada for use in Type 2 diabetes. In November 2023, the Food and Drug Administration (FDA) approved tirzepatide's use for chronic weight management in adults under the name Zepbound. Zepbound has not been submitted to Health Canada.
- In addition to Mounjaro, pharmaceutical company, Eli Lilly, has several other medications in their development pipeline being studied for obesity and diabetes. These include orforglipron and retatrutide. Retatrutide will be the first triple agonist targeting 3 hunger-regulating hormones, Glucose-dependent Insulinotropic Polypeptide (GIP) receptor, Glucagon-like Peptide-1 (GLP-1) receptor and glucagon receptor. Although there have not been any head-to-head studies conducted to date with other drugs, promising phase 2 results for retatrutide have demonstrated an average body weight loss of 24 per cent, representing the highest percentage of weight loss for any drug.
- Pharmaceutical company, Novo Nordisk, currently markets Wegovy, Ozempic, Rybelsus and Saxenda. Their new pipeline drug, CagriSema, is being studied for use in Type 2 diabetes and obesity. It is a new drug combination of an amylin analogue and semaglutide, which is the active ingredient of Ozempic and Wegovy. Anticipation builds for the clinical trial results as the study compares the efficacy and safety of CagriSema to Zepbound (Eli Lilly's weight loss drug).

Weight loss drugs and diabetic drugs that promote weight loss will continue to have an impact on private drug plans considering the prevalence of obesity and diabetes in Canada. Approximately 30 per cent of adults in Canada are considered obese and 35 per cent are overweight, and according to recent findings from Diabetes Canada[2] the prevalence of diabetes in 2022 stands at 10.2 per cent, affecting more than 4 million Canadians[3]. The relationship between obesity and diabetes remains strong as an estimated 80 to 90 per cent[4] of people with Type 2 diabetes are either overweight or obese. Prescribers are following evolving treatment guidelines suggesting treatment based on patient comorbidities.

Costly second- or third-line therapies that positively impact weight loss are being initiated earlier, which contribute to the growth in diabetes claim expenditure, and we expect this trend to continue. Strong drug management will be imperative to control off-label use of these medications and maintain drug plan sustainability.

MIGRAINE

DRUG NAME	MEDICINAL INGREDIENT	INDICATION	HEALTH CANADA STATUS	ESTIMATED PRICING
Ubrelvy	Ubrgepant	Treatment of acute migraine	Marketed (May 2023)	$740 to $2,900 per year[5]
Nurtec ODT	Rimegepant	Prevention and treatment of acute migraine	Approved (December 2023)	$131 USD per pill, $2,200 to $3,200 USD per year[6]

Ubrelvy and Nurtec ODT

In recent years, there have been new injectable medications for migraine treatment and prevention, such as Aimovig, Emgality, Ajovy and Vyepti, with costs from $6,400 to $20,000 annually. In the past year, additional new oral therapies have been coming to market for those who are averse to using injectable therapies to treat their migraines. These oral treatments can also be an option for patients who have developed medication overuse headaches with other treatments, or are unable to use triptans, such as those with heart disease or stroke risk.

Qulipta was the first oral Calcitonin Gene-Related Peptide Receptor (CGRP) antagonist that entered the Canadian market for migraine prevention with an annual cost of $6,700. This was followed with the launch of Ubrelvy, which is another oral therapy used for migraine treatment, in May 2023. Ubrelvy's Canadian pricing aligns closely with that of branded triptans like Axert and Imitrex; however, is considerably more expensive than generic triptans. For those treating a minimum of 4 migraines monthly, meeting the criteria for episodic migraine diagnosis, the estimated annual cost of Ubrelvy would be around $740. However, individuals experiencing 15 or more migraines monthly may face an annual cost just under $3,000.

Nurtec ODT, the third oral CGRP antagonist, was recently approved by Health Canada. Nurtec ODT differs from Ubrelvy in that it is an oral disintegrating tablet that is seeking approval for both acute migraine treatment, as well as migraine prevention. We anticipate the pricing for Nurtec ODT to be similar or slightly higher, reflecting its use for both prevention and treatment of migraines.

With an estimated migraine prevalence of 12 per cent in Canada, affecting almost 4.5 million Canadians[7], we expect continued growth in both plan spend and claimants for migraine therapies.

DERMATOLOGY

DRUG NAME	MEDICINAL INGREDIENT	INDICATION	HEALTH CANADA STATUS	ESTIMATED PRICING
Litfulo	Ritlecitinib	Alopecia areata	Marketed (February 2024)	$18,100 per year[8]
Unknown	Lebrikizumab	Atopic dermatitis	Under review	Unknown
Vtama	Tapinarof	Plaque psoriasis	Under review	$1,400 USD per tube[9]
Opzelura	Ruxolitinib	Nonsegmental vitiligo and mild to moderate atopic dermatitis	Under review	$2,008 USD per tube[10]

Litfulo

A once-daily oral treatment, Litfulo is the first and only treatment approved by Health Canada for individuals 12 years of age and older with severe alopecia areata. Approximately 2 per cent[11] of the global population and an estimated 775,000 Canadians are affected by alopecia areata[12]. Alopecia areata is an autoimmune disease where the immune system attacks the body's hair follicles causing patchy to complete hair loss on the scalp, face and/or body. Litfulo is also being studied for the treatment of vitiligo, rheumatoid arthritis, Crohn's disease and ulcerative colitis.

Lebrikizumab

Lebrikizumab is currently under review by Health Canada and if approved, will be the third, targeted biologic therapy for the treatment of moderate-to-severe atopic dermatitis. An extended study[13] showed promising long-term results of sustained skin clearance, itch relief and reduced disease severity. The main competitors currently on the market will be Dupixent and Adtralza; however, lebrikizumab could have a dosing advantage of only once monthly compared to every 2 weeks.

Vtama

Vtama is a new chemical entity and first-in-class non-steroidal cream to be developed in the psoriasis space in 25 years. It has been marketed in the United States since June 2022. Recent phase 3 trials demonstrated a significant improvement in itch, which is the most prevalent symptom of atopic dermatitis. Vtama's manufacturer, Dermavant Sciences, plans to submit the new indication for FDA approval in early 2024, and we can anticipate similar plans for Health Canada.

Opzelura

Opzelura has been approved in the United States to treat mild to moderate atopic dermatitis and nonsegmental vitiligo. Opzelura is currently the first and only Janus Kinase (JAK) inhibitor cream, and the first and only treatment to address repigmentation in patients with vitiligo. Patients with vitiligo suffer from the loss of skin colour affecting the skin on any part of the body.

These topical treatments offer new therapies for individuals whose condition is not effectively managed with current therapies, or where treatments did not exist previously; however, the annual expenses associated with these treatments will be significantly higher than currently available topical medications.

NEUROLOGY

DRUG NAME	MEDICINAL INGREDIENT	INDICATION	HEALTH CANADA STATUS	ESTIMATED PRICING
Leqembi	Lecanemab	Alzheimer's disease	Under review	$26,500 USD per year[14]
Vyvgart	Efgartigimod	Generalized Myasthenia Gravis (gMG)	Marketed (November 2023)	$316,000 -$474,000[15]
Zilbrysq	Zilucoplan	Generalized Myasthenia Gravis (gMG)	Under review	Unknown
Rystiggo	Rozanolixizum-ab-noli	Generalized Myasthenia Gravis (gMG)	Under Review	$6,050 USD per vial[16]

Leqembi

Leqembi was approved by the FDA in January 2023 and is currently under review by Health Canada for the treatment of Alzheimer's disease. The drug is not a cure for Alzheimer's but has been shown to reduce cognitive decline in people living with early-stage disease, often still managing symptoms enough for patients to continue working. Leqembi is administered intravenously once every 2 weeks. The annual cost in the United States is approximately $26,000 USD; which is significantly higher than conventional oral Alzheimer's disease therapies currently available in Canada ranging from $200 to $2,100 annually.

Vyvgart, Zilbrysq and Rystiggo

New targeted therapies for the treatment of Generalized Myasthenia Gravis (gMG) are making their way to the Canadian market. Vyvgart was recently marketed and 2 others are currently under review. gMG is a chronic, autoimmune disease characterized by unpredictable and debilitating symptoms that weaken the skeletal muscles, potentially leading to challenges in walking, swallowing and breathing.

Targeted therapies, referred to as complement inhibitors, will provide add-on treatment options for the estimated 15 per cent of patients who are inadequately managed with conventional therapies due to suboptimal effectiveness and/or safety concerns. These treatments not only improve symptom management, but also target the disease process without the broad immune suppression characteristic of conventional treatments. We can expect the pricing of Zilbrysq and Rystiggo to be in line with other complement inhibitors like Vyvgart, Ultomiris, and Soliris, costing hundreds of thousands annually.

COVID-19 TREATMENT

Paxlovid was approved in 2022 by Health Canada to treat mild to moderate COVID-19 infections. Since coming to market, the 5-day treatment course has been publicly funded and available to eligible Canadians free of charge. In our April 2022 COVID-19 vaccine and drug pipeline report, we highlighted the possible shift towards private plans being asked to cover the expenses of COVID-19 outpatient treatments. This is the scenario currently happening in the United States.

In the United States, Paxlovid has been provided to the public free of charge since December 2021 when the FDA first authorized the treatment. However, beginning in 2024, Pfizer is now selling Paxlovid directly to health insurers, with a price of $1,390 per course, more than double what the United States government paid.

Private payors may soon see a similar development in Canada. Pfizer submitted Paxlovid for Canadian Agency for Drugs and Technologies in Health (CADTH) review in September 2023, which is likely a sign that universal provincial coverage will cease. At time of writing, the provinces are still providing the publicly funded Paxlovid supply. Alberta Blue Cross® is monitoring this development closely.

RARE DISEASE

The number of rare disease drugs in development and under Health Canada review continues to grow exponentially. As there are still many rare diseases without treatment, this trend is anticipated to persist. Due to the limited patient population and complex research involved, the development of rare disease treatments continues to present unique challenges including extremely high costs.

In March 2023, Canada's federal government announced its first-ever National Strategy for Drugs for Rare Diseases, including an investment of up to $1.5 billion over 3 years to help increase drug access and affordability. However, given the number of rare disease drugs in the pipeline and the ultra-high cost of these therapies, newly allocated federal funding most likely won't be sufficient to provide universal coverage for rare disease drugs.

The table below outlines some of the rare disease drugs currently under review or recently approved in Canada. Alberta Blue Cross actively monitors these drugs for potential alternative funding or inclusion in government programs, aiming to ensure publicly funded programs are accessed first in the event that a member requires 1 of these high-cost therapies. Given the growing availability and significant costs of rare disease drugs, plan sponsors are advised to conduct a comprehensive review of drug benefit plan designs and financial management strategies to ensure the ongoing sustainability of their drug plan. Alberta Blue Cross is available to aid in conducting this review.

DRUG NAME	MEDICINAL INGREDIENT	INDICATION	HEALTH CANADA STATUS	ESTIMATED PRICING
Joenja	Leniolisib	Activated Phospho-inositide 3-Kinase Delta Syndrome (APDS)	Under review	$547,000 per year[17]
Hemgenix	Etranacogene dezaparvovec	Treatment of haemophilia B (factor IX deficiency) in adults	Approved (October 2023)	$3.5 million USD per dose only 1 time administration[18]
Beqvez	Fidanacogene elaparvovec	Treatment of haemophilia B (factor IX deficiency) in adults	Approved (January 2024)	Unknown
Livmarli	Maralixibat	Cholestatic pruritis in patients with Alagille syndrome	Marketed (August 2023)	$457,000 to $1,469,000 per year depending on patient weight[19]
Isturisa	Osilodrostat phos-phate	Cushing's syndrome	Under review	$421,000 USD per year[20]
Evkeeza	Evinacumab	Homozygous Familial Hypercholesterolaemia (HoFH)	Marketed (November 2023)	Unknown
Myalepta	Metreleptin	Leptin deficiency in lipodystrophy	Approved (January 2024)	$1.26 Million USD per year[21]
Bylvay	Odevixibat	Progressive Familial Intrahepatic Cholestasis (PFIC)	Marketed (February 2024)	$193,000 to $2,312,000 per year[22]
Xenpozyme	Olipudase alfa	Chronic Acid Sphingomye-linase Deficiency (ASMD)	Approved (February 2024)	$780,000 USD per year[23]
TBD	Eplontersen	Hereditary Transthyretin Amyloidosis (hATTR)	Under review	$500,000 USD per year[24]

BIOSIMILARS

Biosimilars continue to enter the market providing more affordable treatment options, and savings for benefit plans, which helps with drug plan sustainability. Biosimilar transitioning policies by provincial governments have been implemented in 11 out of the 13 jurisdictions, with Manitoba and Nunavut remaining as the only jurisdictions in Canada without a biosimilar switch policy. The growing influence of emerging public payer biosimilar policies is shaping prescribing decisions and subsequently driving greater adoption of biosimilar drugs.

Biosimilars of Stelara are entering the Canadian market with 2 products currently under review, 1 approved, and 2 recently marketed. Stelara is used for several autoimmune disorders and is ranked within the top 10 drugs by spend on the Alberta Blue Cross book of business. Some of the biosimilars will have Health Canada approval for all Stelara indications including plaque psoriasis, psoriatic arthritis, Crohn's disease and ulcerative colitis. Finlius, was approved by Health Canada in April 2023 and if marketed, will be a first of a kind biosimilar launch as this biosimilar is manufactured by the same company that makes the innovator product, Stelara.

The biosimilar pipeline is expanding to new therapeutic areas including bone health, infertility and asthma. The first biosimilars have been approved for Prolia and Xgeva, and biosimilars for Xolair (omalizumab) and Gonal-F (follitropin alfa) are in phase 3 clinical trials but have not been submitted to Health Canada. There are other notable biosimilars currently in phase 3 clinical trials for Simponi (golimumab), indicated for numerous autoimmune disorders, and Ocrevus (ocrelizumab), a treatment for multiple sclerosis.

A summary of the notable biosimilars currently under review with Health Canada or recently approved are outlined below.

			BIOSIMILAR STATUS		
INNOVATOR BIOLOGIC	**MOLECULE**	**THERAPEUTIC USE**	**UNDER HEALTH CANADA REVIEW**	**APPROVED (NOT YET MARKETED)**	**MARKETED**
Stelara	Ustekinumab	Numerous autoimmune disorders, such as plaque psoriasis, ulcerative colitis and psoriatic arthritis	CT-P43 (Celltrion Healthcare), SB17 (Samsung Bioepis)	Finlius	Jamteki, Wezlana
Eylea	Aflibercept	Wet age-related macular degeneration and Diabetic Macular Edema (DME)	CT-P42 (Celltrion Healthcare), ABP 938 (Amgen)		
Prolia Xgeva	Denosumab	Osteoporosis in postmeno-pausal women, preventing skeletal-related compli-cations in cancer that has spread to the bone		Jubbonti, Wyost	
Soliris	Eculizumab	Paroxysmal Nocturnal Hemoglobinuria (PNH)	Bekemv Epysqli		

FIRST-ENTRY GENERICS

A new agreement was reached between the pan-Canadian Pharmaceutical Alliance (pCPA) and the Canadian Generic Pharmaceutical Association (CGPA) that will maintain savings achieved from previous negotiated agreements and also provide additional savings on new generic products entering the market. The new framework increases the level of savings on new single source generics that have entered the Canadian market after October 1, 2023. Previously listed at 75 per cent or 85 per cent of brand name price under the old framework, new single source generic products will see their pricing drop to 55 per cent of brand name price after 3 months for products that are listed by provincial drug plans.

There are notable first entry generics coming to the Canadian market for diabetes and ADHD. These health conditions consistently ranked among the top 5 by spend on Alberta Blue Cross private drug plans. Generic alternatives for several highly utilized drugs for diabetes and Vyvanse for ADHD will contribute to mitigating the expenditure growth within both of these health condition categories. Vyvanse is the last ADHD medication without a generic alternative and continues to rank among top 10 drug lists for private drug plans.

Generic products have recently made their way to the Canadian market for Dexilant. Dexilant is the most expensive Proton Pump Inhibitor (PPI) on the Canadian market and also the last PPI to have a generic alternative. Plan sponsors with generic pricing policies can expect to see savings from this newly available generic.

An area where we will see continued sizeable savings for plan members and plan sponsors is specialty generics. A generic for Mavenclad, an oral treatment for RRMS, is under review by Health Canada. Mavenclad is the most expensive and last oral therapy for RRMS without a generic alternative with an average annual cost ranging from $25,700 to $64,200. With non-biologic specialty drug treatments, generic substitution can result in thousands of dollars in annual savings per plan member given the high cost of these products.

The table below outlines notable first-entry generic drugs that are currently under review, approved or recently marketed by Health Canada.

			GENERICS' STATUS		
BRAND NAME DRUG	THERAPEUTIC USE	NUMBER OF GENERIC PRODUCTS	UNDER HEALTH CANADA REVIEW	APPROVED (NOT YET MARKETED)	MARKETED
Vyvanse*	ADHD	7	✓		
Victoza*	Diabetes	2	✓		
Trajenta*	Diabetes	9	✓		
Jentadueto*	Diabetes	3	✓		
Synjardy*	Diabetes	1	✓		
Jardiance*	Diabetes	10	✓		
Invokana*	Diabetes	4	✓		
Dexilant	Gastroesophageal Reflux Disease (GERD)	3		✓ (1)	✓ (2)
Mavenclad	RRMS	2	✓		
Myrbetriq	Overactive bladder	2	✓		
Blexten	Antihistamine	8	✓		
Rupall	Antihistamine	1	✓		
Entresto	Heart failure	2	✓		
Emend	Antiemetic	1	✓		
Rexulti	Depression and schizophrenia	6	✓		
Viibryd	Depression	1	✓		
Movantik	Drugs for constipation	1	✓		

*__Included in Alberta Blue Cross 2023 pipeline document.__ *Generic products are still under review by Health Canada.*

ALBERTA BLUE CROSS DRUG MANAGEMENT STRATEGY

Drug plan management at Alberta Blue Cross starts with a solid unique foundation built on systems and management processes that benefit all our drug plans. In addition, we offer numerous optional plan management features that mitigate rising drug costs and ensure plan sustainability.

Foundational drug plan management

MANAGEMENT STRATEGY	DESCRIPTION
Comprehensive drug review process	New drugs are thoroughly reviewed by our in-house pharmacists and drug review committee who critically assess the scientific, therapeutic and economic value of each drug before a listing decision is rendered.
Drug price management	We have extensive management of drug prices to ensure our plans are not paying excessive drug costs.
Product listing agreements	On behalf of plan sponsors, we negotiate product listing agreements with drug manufacturers for various drugs to maintain drug plan affordability and sustainability.
Opioid management	We promote proactive narcotic management based on current guidelines and best practice prescribing through use of the following: • Step therapy (standard on our managed formulary)—ensuring use of short-acting low potency narcotics before use of long-acting or high potency narcotics. • Special authorization (standard on our managed formulary)—requiring special authorization approval on high potency, high-risk narcotics. • Drug Utilization Review (DUR) at pharmacy point of sale. • Collaborative work with professional colleges.
Responsive management strategies	We continue to monitor the drug environment as utilization and government policies evolve and will continue to adapt our listing strategies to ensure continued optimal management and savings for our drug plans.

Optional drug plan management strategies

MANAGEMENT STRATEGY	DESCRIPTION
Managed formulary	This formulary includes special authorization and step therapy as standard strategies. Our managed formulary protects plan sponsors as the market for high-cost therapies continues to expand.
Special authorization	A standard feature on our managed formulary that is applied to high-cost drugs where there is opportunity to ensure those therapies are covered only for plan members meeting clinical criteria. Additionally, special authorization ensures members are accessing any publicly funded drug programs first before coverage is granted on their private plan.
Step therapy	Another standard feature on our managed formulary used to manage lower-cost traditional drugs. It is a clinical management feature that requires the use of one or more "first-line" drugs before a "second-line" drug is approved for coverage through the automated real-time claims adjudication system.
Biologic strategy	With our managed formulary we are not limited to using just one strategy. We currently use a biosimilar first strategy for some biologics and maintain member or prescriber choice for others by using manufacturer agreements to ensure costs of the innovator biologic and biosimilar are comparable. We also offer a biosimilar first formulary and a provincial government-mirror formulary.
Other strategies for traditional drugs • **Generic pricing** • **Mandatory Generic Substitution** • **Maintenance Medication Program (MMP)** • **Maximum Allowable Cost (MAC) pricing**	We have several management strategies available for lower-cost traditional drugs. The savings realized from these management strategies ensure plan sponsors can continue to offer access to higher-cost therapies while keeping their drug plan sustainable.

WHAT'S NEXT

Alberta Blue Cross continues to closely monitor the growing pipeline of new medicines, assessing and managing the impact on drug benefit plans. We are committed to helping our customers navigate the drug landscape while always prioritizing the health of plan members and the sustainability of drug plans.

REFERENCES

1 British Columbia Ministry of Health (2024). "B.C. PharmaCare Drug Information Sheet for insulin icodec (Awiqli)." Available at: **https://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/your-voice-drug-info/insulin_icodec_awiqli_3966_dis.pdf**

2 Diabetes Canada (2022). "Diabetes in Canada 2022 Backgrounder." Available at: **2022_Backgrounder_Canada_English_1.pdf (diabetes.ca)**

3 Elflein, John. "Percentage of Canadian adults that are overweight or obese based on BMI from 2015 to 2022." Available at: **Overweight and obesity rate Canada 2015-2022 | Statista**

4 Diabetes Canada. "Weight management." Available at: **Weight management - Diabetes Canada**

5 Canadian list price

6 Government of Canada (2022). Meds Entry Watch, 6th Edition. Available at: **Meds Entry Watch, 6th Edition - Canada.ca**

7 Migraine Canada. "Canadian Language Guide." Available at: **languageguide-onepager-EN-finalweb.pdf (migrainecanada.org)**

8 Canadian list price.

9 Drugs.com. "Vtama Prices, Coupon and Patient Assistance Programs." Available at: **Vtama Prices, Coupons, Copay & Patient Assistance – Drugs.com**

10 Opzelura.com (2023). "Opzelura Cost." Available at: **https://www.opzelura.com/vitiligo/cost**

11 Pfizer. "Alopecia Areata." Available at: **Alopecia Areata Overview: Types, Causes, Symptoms, and Treatment | Pfizer**

[12] Pfizer (2023). "Litfulo Receives Health Canada Approval…" Available at: **LITFULO™ Receives Health Canada Approval, Becoming the First Approved Treatment for Severe Alopecia Areata in Canada | Pfizer Canada**

[13] Lilly Investors (2023). News Release. Available at: **Nearly 80% of patients with moderate-to-severe atopic dermatitis maintained clear or almost clear skin with Lilly's lebrikizumab monthly maintenance dosing at two years | Eli Lilly and Company**

[14] Eisai Global (2023). "Eisai's Approach to U.S. Pricing for Leqembi…" Available at: **EISAI'S APPROACH TO U.S. PRICING FOR LEQEMBI™ (LECANEMAB), A TREATMENT FOR EARLY ALZHEIMER'S DISEASE, SETS FORTH OUR CONCEPT OF "SOCIETAL VALUE OF MEDICINE" IN RELATION TO "PRICE OF MEDICINE" | News Release : 2023 | Eisai Co., Ltd.**

[15] Canada list price

[16] Formulary Watch (2023). "FDA Approves Rystigoo for Generalized Myasthenia Gravies." Available at: **FDA Approves Rystiggo for Generalized Myasthenia Gravis (formularywatch.com)**

[17] Formulary Watch (2023). "FDA Approves First Treatment for Rare Immunodeficiency Disease." Available at: **https://www.formularywatch.com/view/fda-approves-first-treatment-for-rare-immunodeficiency-disease**

[18] Fierce Pharma (2022). "Sporting a $3.5M price tag, CSL and uniQure's hemophilia B gene therapy crosses FDA finish line." Available at: **https://www.fiercepharma.com/pharma/csl-and-uniqures-hemophilia-b-gene-therapy-scores-approval-35-million-price-tag**

[19] CADTH (2023). ""CADTH Reimbursement Recommendation Report."(Draft): Maralixibat (Livmarli)". Available at: **https://www.cadth.ca/sites/default/files/DRR/2023/SR0780%20Livmarli%20-%20Confidential%20Draft%20CADTH%20Recommendation%20October%2019%2C%202023_Posting%20.pdf**

[20] National Library of Medicine (2023). Disentangling the Cost of Orphan Drugs Marketed in the Unite States. Available at: **Disentangling the Cost of Orphan Drugs Marketed in the United States - PMC (nih.gov)**

[21] Rxbenefits.com. "10 Most Expensive Drugs in the US." Available at: **https://www.rxbenefits.com/ebooks/10-most-expensive-drugs-2023/**

[22] Canadian list price.

[23] Pharmaphorum (2022). "Xenpozyme is first FDA-approved drug for rare disease ASMD." Available at: **https://pharmaphorum.com/news/xenpozyme-is-first-fda-approved-drug-for-rare-disease-asmd#:~:text=The%20company%20has%20set%20a%20US%20list%20price,%24780%2C000%20per%20year%2C%20before%20any%20discounts%20or%20rebates**

[24] BioSpace (2023). "Ionis and AstraZeneca Seek to Challenge Alnylam with New ATTR Data." Available at: **https://www.biospace.com/article/ionis-and-astrazeneca-seek-to-challenge-alnylam-in-attr-with-phase-iii-data/**

APPENDIX

Atopic dermatitis: A condition that causes dry, itchy and inflamed skin; also known as, eczema.

Biologic drugs: Drugs that are produced using a living system, such as a microorganism, plant cell, or animal cell. They are often made using biotechnology and are generally larger and more complex (administered by injection) than chemically produced pharmaceutical drugs.

Biosimilar drugs: Biologic drugs that are highly similar to an innovator biologic drug (reference biologic). Biosimilars are clinically similar in efficacy and safety compared to the reference biologic, and enter the market after the the reference biologic.

Brand name drug: The first version of a drug to be sold in Canada. The drug manufacturer that first developed and patented the drug sells the brand name drug.

Generic drug: A drug that contains the same amount of active ingredient as a brand name drug. A generic drug is equivalent in efficacy and safety as the brand name drug but the non-medicinal ingredients may vary.

Canadian drug pipeline: Drugs that are currently being developed by a Canadian pharmaceutical company or are under review/ awaiting market approval by Health Canada.

Myasthenia gravis: A chronic autoimmune disorder that causes muscles to feel weak and get tired quickly. Antibodies destroy the communication between nerves and muscle, resulting in muscle weakness. Symptoms can include weakness of arm or leg muscles, drooping eyelids, and problems speaking, chewing, swallowing and breathing.

Nonsegmental vitiligo: A disease that causes areas of skin to lose color, resulting in spots and patches of lighter skin. A person with nonsegmental vitiligo will have area of affected skin on both sides of the body, like both knees or both hands; this is the most common type of vitiligo. Segmental vitiligo patients tend to see affected skin on one side or part of the body.

QUESTIONS?

If you have any questions about this topic, please don't hesitate to contact your Alberta Blue Cross representative.

Exhibit "F20"

This is Exhibit “F20” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.

Arash Rouhi

REDACTED

Exhibit "F21"

This is Exhibit “F21” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

Wall, Jonathan

From: Olga Dupuis <odupuis@jamppharma.com>
Sent: Friday, July 19, 2024 12:09 PM
To: Joelle Bibeau
Cc: Amélie Faubert; Genia Radeva; Sébastien Levesque
Subject: Re: Finlius disponibilité grossiste

191480 FINLIUS IV FIO 130MG 26ML 2537311

Statistiques

Fournisseur
Fournisseur: JANSSEN INC
Produit Fournisseur: 471632

Info Produit
GTIN/CUP: U-00069502624091
Narcotique: Non
Forme: SOLUTION
Teneur: 5MG/ML
Format: 26
Classe du produit: PHARMACEUTIQUE

Date eff.:
Unité de Vente: U
Quantité/Caisses: 1
MQE: 1
CD: MONTREAL

Prix
Prix: 1,342.42 **C/E:** **Min/$ spec:**

191476 FINLIUS SERINGUE PRE REMPLIE 90MG/ML 1 2537257

Statistiques

Fournisseur
Fournisseur: JANSSEN INC
Produit Fournisseur: 471629

Info Produit
GTIN/CUP: U-00069502624060
Narcotique: Non
Forme: SOLUTION
Teneur: 90MG/ML
Format: 1
Classe du produit: PHARMACEUTIQUE

Date eff.:
Unité de Vente: U
Quantité/Caisses: 1
MQE: 1
CD: MONTREAL

Prix
Prix: 2,964.37 **C/E:** **Min/$ spec:**

191479 FINLIUS FIOLE 45MG/0.5ML 1 2537303

Statistiques

Fournisseur	Info Produit	
Fournisseur: JANSSEN INC	**GTIN/CUP:** U-00069502624084	**Date eff.:**
Produit Fournisseur: 471621	**Narcotique:** Non	**Unité de Vente:** U
	Forme: SOLUTION	**Quantité/Caisses:** 1
	Teneur: 45MG/0.5ML	**MQE:** 1
	Format: 1	**CD:** MONTREAL
	Classe du produit: PHARMACEUTIQUE	

Prix		
Prix: 2,964.37	**C/E:**	**Min/$ spec:**

191477 FINLIUS SERINGUE PRE REMPLIE 45MG/0.5ML 1 2537303

Statistiques

Fournisseur	Info Produit	
Fournisseur: JANSSEN INC	**GTIN/CUP:** U-00069502624077	**Date eff.:**
Produit Fournisseur: 471628	**Narcotique:** Non	**Unité de Vente:** U
	Forme: SOLUTION	**Quantité/Caisses:** 1
	Teneur: 45MG/0.5ML	**MQE:** 1
	Format: 1	**CD:** MONTREAL
	Classe du produit: PHARMACEUTIQUE	

Prix		
Prix: 2,964.37	**C/E:**	**Min/$ spec:**

Olga Dupuis
Chef, Relations commerciales
odupuis@jamppharma.com
514-703-6362
1310 Nobel, Boucherville, QC, J4B 5H3

From: Joelle Bibeau <jbibeau@jamppharma.com>
Sent: July 19, 2024 12:07 PM
To: Olga Dupuis <odupuis@jamppharma.com>
Cc: Amélie Faubert <afaubert@jamppharma.com>; Genia Radeva <gradeva@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Subject: RE: Finlius disponibilité grossiste

Merci Olga,
Est-ce que c'est possible d'avoir le prix ?

Joëlle

From: Olga Dupuis <odupuis@jamppharma.com>
Sent: Friday, July 19, 2024 11:49 AM
To: Joelle Bibeau <jbibeau@jamppharma.com>
Cc: Amélie Faubert <afaubert@jamppharma.com>; Genia Radeva <gradeva@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Subject: Re: Finlius disponibilité grossiste

Bonjour Joelle,

En stock

# Item	Description	DIN/NPN	C/E	Statut	Inventaire
191480	FINLIUS IV FIO 130MG 26ML	2537311			✔
191476	FINLIUS SERINGUE PRE REMPLIE 90MG/ML 1	2537257			✔
191479	FINLIUS FIOLE 45MG/0.5ML 1	2537303			✔
191477	FINLIUS SERINGUE PRE REMPLIE 45MG/0.5ML 1	2537303			✔

Merci,

Olga Dupuis
Chef, Relations commerciales
odupuis@jamppharma.com
514-703-6362
1310 Nobel, Boucherville, QC, J4B 5H3

From: Joelle Bibeau <jbibeau@jamppharma.com>
Sent: July 19, 2024 10:09 AM
To: Olga Dupuis <odupuis@jamppharma.com>
Cc: Amélie Faubert <afaubert@jamppharma.com>; Genia Radeva <gradeva@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Subject: RE: Finlius disponibilité grossiste

Bonjour Olga,

Est-ce qu'il serait possible de revérifier le statut de Finlius (ustekinumab) svp ?

Merci,
Joëlle

From: Olga Dupuis <odupuis@jamppharma.com>
Sent: Tuesday, July 9, 2024 11:09 AM
To: Joelle Bibeau <jbibeau@jamppharma.com>
Cc: Amélie Faubert <afaubert@jamppharma.com>; Genia Radeva <gradeva@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Subject: Re: Finlius disponibilité grossiste

Bonjour Joelle,

Listé mais non-disponible:

# Item	Description	DIN/NPN	C/E	Statut	Inv
191480	FINLIUS IV FIO 130MG 26ML	2537311			
191476	FINLIUS SERINGUE PRE REMPLIE 90MG/ML 1	2537257			
191479	FINLIUS FIOLE 45MG/0.5ML 1	2537303			
191477	FINLIUS SERINGUE PRE REMPLIE 45MG/0.5ML 1	2537303			

Olga Dupuis
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514-703-6362
1310 Nobel, Boucherville, QC, J4B 5H3

From: Joelle Bibeau <jbibeau@jamppharma.com>
Sent: July 9, 2024 11:07 AM
To: Olga Dupuis <odupuis@jamppharma.com>
Cc: Amélie Faubert <afaubert@jamppharma.com>; Genia Radeva <gradeva@jamppharma.com>; Sébastien Levesque <slevesque@biojamp.com>
Subject: Finlius disponibilité grossiste

Bonjour Olga,

Est-ce que tu peux regarder si Finlius (ustekinumab) est disponible chez les grossistes ?

Merci,
Joëlle

Joëlle Bibeau, MSc, LLM
Directrice, Accès au marché, Biosimilaires et médicaments de marque
Director, Market Access, Biosimilars and Brand Products
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1310 Nobel, Boucherville, QC J4B 5H3

www.jamppharma.com

Exhibit "F22"

This is Exhibit “F22” referred to in the Affidavit of Amélie Faubert, sworn before me this 25th day of July, 2024.

A Commissioner for Taking Affidavits, etc.
Arash Rouhi

REDACTED

The document that is being electronically submitted to the Tribunal is an electronic version of a document that has been signed by the affiant. The signed document in paper copy is available and will be produced if requested by the Tribunal.

Jonathan Wall
Goodmans LLP

File No. CT-2024-006

COMPETITION TRIBUNAL

IN THE MATTER OF the *Competition Act*, R.S.C. 1985, c. C-34 (the "**Act**");

AND IN THE MATTER OF an application by JAMP Pharma Corporation for an order pursuant to section 103.1 of the Act granting leave to bring an application under section 79 of the Act;

AND IN THE MATTER OF an application by JAMP Pharma Corporation for an order pursuant to sections 79 of the Act;

BETWEEN:

JAMP PHARMA CORPORATION

Applicant

– and –

JANSSEN INC.

Respondent

AFFIDAVIT OF AMÉLIE FAUBERT
(Pursuant to section 103.1 of the *Competition Act*)

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