Meds PIPELINE MONITOR 2023

NPDUIS
National Prescription Drug Utilization Information System

Patented Medicine Prices Review Board
Conseil d'examen du prix des médicaments brevetés

Canada

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Patented Medicine Prices Review Board
Standard Life Centre
Box L40
333 Laurier Avenue West
Suite 1400
Ottawa, ON K1P 1C1

Tel.: 1-877-861-2350
TTY 613-288-9654

Email: PMPRB.Information-Renseignements.CEPMB@pmprb-cepmb.gc.ca
Web: www.pmprb-cepmb.gc.ca

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About the PMPRB

The Patented Medicine Prices Review Board (PMPRB) is an independent quasi-judicial body established by Parliament in 1987. The PMPRB has a dual regulatory and reporting mandate: to ensure that prices at which patentees sell their patented medicines in Canada are not excessive; and to report on pharmaceutical trends of all medicines and on research and development spending by patentees.

The NPDUIS Initiative

The National Prescription Drug Utilization Information System (NPDUIS) research initiative was established by federal, provincial, and territorial Ministers of Health in September 2001. It is a partnership between the PMPRB and the Canadian Institute for Health Information (CIHI).

Pursuant to section 90 of the *Patent Act*, the PMPRB has the mandate to conduct analysis that provides decision makers with critical information and intelligence on price, utilization, and cost trends so that Canada's healthcare system has more comprehensive and accurate information on how medicines are being used and on sources of cost pressures.

The specific research priorities and methodologies for NPDUIS are established with the guidance of the NPDUIS Advisory Committee and reflect the priorities of the participating jurisdictions, as identified in the NPDUIS Research Agenda. The Advisory Committee is composed of representatives from public drug plans in British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Yukon, the Non-Insured Health Benefits Program (NIHB), and Health Canada. It also includes observers from CIHI, Canada's Drug Agency (CDA), the Ministère de la Santé et des Services sociaux du Québec (MSSS), and the pan-Canadian Pharmaceutical Alliance (pCPA) Office.

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Disclaimer

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EXECUTIVE SUMMARY

Meds Pipeline Monitor (MPM) is a horizon scanning report that features a selection of new medicines undergoing clinical evaluation or in pre-registration that may have an impact on future clinical practice and drug spending in Canada.

This edition expands the review for the selected medicine candidates in Phase III clinical trials or pre-registration to include information on other drugs in Phase II that share the same mechanism of action or indication. Having insight into other drugs under investigation (i.e., in Phase II) may provide additional information on the potential place in therapy for these pipeline candidates. Medicines in Phase III clinical trials or pre-registration are selected as candidates for the 'new medicines' list if they have the potential to address an unmet therapeutic need, offer a novel mechanism of action or therapeutic benefit over existing therapies, or treat a serious condition. The medicines in Phase II are also examined to identify other drugs that are in earlier phases of the pipeline that contain the same indication or mechanism of action as the selected medicine candidates.

The report collects data from two main sources: GlobalData's Healthcare database, which identifies medicines currently undergoing clinical evaluation, and Health Canada's Drug and Health Product Submissions Under Review Lists, which provide information on new medicines under review in Canada.

Highlights of the *Meds Pipeline Monitor 2023*

- As of April 2024, the pipeline contained over 12,000 new medicines in various stages of clinical development, compared to just over 9,000 the year before. The number of drugs in the pipeline is increasing by an average of 19% per year since 2019.
- Oncology continues to dominate the therapeutic mix in 2023, with cancer treatments representing one third (33%) of medicines in all phases of clinical trials. Treatments for infectious diseases and central nervous system diseases held the second and third largest share of the pipeline, at 13% and 12%, respectively.
- On average, 20% of medicines in Phase III clinical trials and pre-registration in 2023 had an early orphan designation approved through the U.S. FDA or the EMA, which is roughly a 33% decrease from previous years.
- Twenty new medicines were selected for the 2023 new medicines list (Table 4) based on their potential to impact the Canadian healthcare system. Fourteen of the medicines listed in this year's report (Tables 4 through 7) have forecasted global annual revenues over US $1 billion by 2029.
- Of the 51 new and retained medicines listed in the previous edition (*MPM 2022*), 15 received market authorization, 23 were retained on this year's list as they continued to satisfy the selection criteria, and 13 were removed as their clinical trials were discontinued or they no longer meet the selection criteria.
- Six new medicines under review by Health Canada were selected for this report as they have a novel mechanism of action or have demonstrated improved efficacy and/or safety in clinical trials.

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LIST OF TERMS

For the purpose of this report, the following terms and associated definitions apply.

Cell therapy:
The transplantation of human cells to replace or repair damaged tissue and/or cells.

Clinical efficacy:
The maximum response achievable from a medicine in research settings and the capacity for sufficient therapeutic effect in clinical settings.[i]

Gene therapy:
A technique for the treatment of genetic disease in which a gene that is absent or defective is replaced by a healthy gene, as defined by Health Canada.[ii]

Market authorization:
The process of approval for a medicine to be marketed in a given country. In Canada, market approval is granted following a substantive scientific evaluation of a product's safety, efficacy, and quality, as required by the Food and Drugs Act and Regulations.[iii]

Medicinal ingredient:
A chemical or biological substance responsible for the claimed pharmacologic effect of a drug product. Sometimes referred to as a molecule, active substance, or active ingredient.[iv]

Medicine:
A broad term encompassing both the final drug product and medicinal ingredient(s); this encompasses chemically manufactured active substances and biologics, including gene therapies. Medicines are reported at the medicinal ingredient level and can refer to a single ingredient or a unique combination of ingredients.

New medicine:
A medicinal ingredient that has not previously received market authorization by a regulator.[iv]

Orphan medicine:
A medicine used to treat a rare disease. For the purposes of this study, orphan medicines are defined as having an orphan designation granted by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA) for the relevant indication.

Patent evergreening:
The acquisition of additional patents for minor modifications to an existing pharmaceutical product in order to extend the patent life of the medicine (e.g., new delivery systems, new dosages, new uses, new combinations or new forms).[v]

PHASES OF CLINICAL TRIALS

Phase I:
These trials test an experimental medicine on a small group of people for the first time. The purpose is to look at the medicine's safety, determine a safe dosage range, and monitor if there are any side effects.

Phase II:
In this phase, the medicine is given to a larger group of people (usually 100 or more) to gather data on how well the medicine works to treat a disease or condition, check its safety on a wider range of people, and determine the best dose.[vi]

Phase III:
These controlled or uncontrolled trials are conducted after preliminary evidence suggesting efficacy of the medicine has been demonstrated. They are intended to gather additional and confirmatory information about the clinical efficacy and safety of the medicine under the proposed conditions of use.[ii] Phase III trials are usually randomized with double-blind testing in several hundred to several thousand patients.

Pre-registration:
A medicine is in the pre-registration phase once all the necessary clinical trials have been completed and it is waiting for registration or approval for use by a governing body.[vii]

i Holford NHG, Sheiner LB. 1981. Understanding the dose-effect relationship: Clinical application of pharmacokinetic-pharmacodynamic models. Clin. Pharmacokinet. 6 (6): 429–453. doi: 10.2165/00003088-198106060-00002.

ii https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/health-canada-clinical-trials-database/glossary.html

iii https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products.html

iv https://www.canada.ca/en/patented-medicine-prices-review/services/npduis/analytical-studies/resources/glossary-npduis.html

v https://academic.oup.com/jlb/article/5/3/590/5232981, https://pubmed.ncbi.nlm.nih.gov/35543377/

vi https://www.canada.ca/en/health-canada/services/clinical-trials.html

vii http://www.appliedclinicaltrialsonline.com/are-phase-labels-still-relevant

INTRODUCTION

This edition of the *Meds Pipeline Monitor* (MPM) features a selection of new medicines in Phase III clinical trials or pre-registration that have the potential to impact clinical practice and drug spending in Canada.

The methodology, which is detailed in the next section, uses a specific set of criteria to identify a list of new medicines in the pipeline from the GlobalData Healthcare database, as well as a list of medicines currently under review from Health Canada's Drug and Health Product Submissions Under Review (SUR) Lists. The new medicines listed in this report are selected based on a scientific review of the literature and clinical trial outcomes to determine if the medicine may impact the Canadian healthcare system by: addressing an unmet therapeutic need; offering a novel mechanism of action or therapeutic benefit over existing therapies; or treating a serious condition. Medicines reported in previous editions of the MPM are also reviewed and updated in this report. This report also provides an update on the medicines in last year's edition that have since received market authorization by either the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), or Health Canada. Likewise, the new medicines featured in this report will be monitored in future editions of the MPM to identify candidates that successfully enter the market.

To provide context for the selection of medicines, the MPM includes a snapshot of the number of drugs in each clinical phase of the pipeline year over year (2019-2023), and a breakdown of the various therapeutic areas for each phase of clinical development.

Meds Pipeline Monitor is a companion publication to *Meds Entry Watch*, which analyzes the market launch patterns of newly approved medicines in Canada and internationally. Together, these two PMPRB reports monitor the market continuum of late-stage pipeline medicines and new approvals, providing decision makers, researchers, patients, clinicians, and other stakeholders with information on the emerging medicines and evolving cost pressures.

METHODOLOGY

Snapshot of the Pipeline

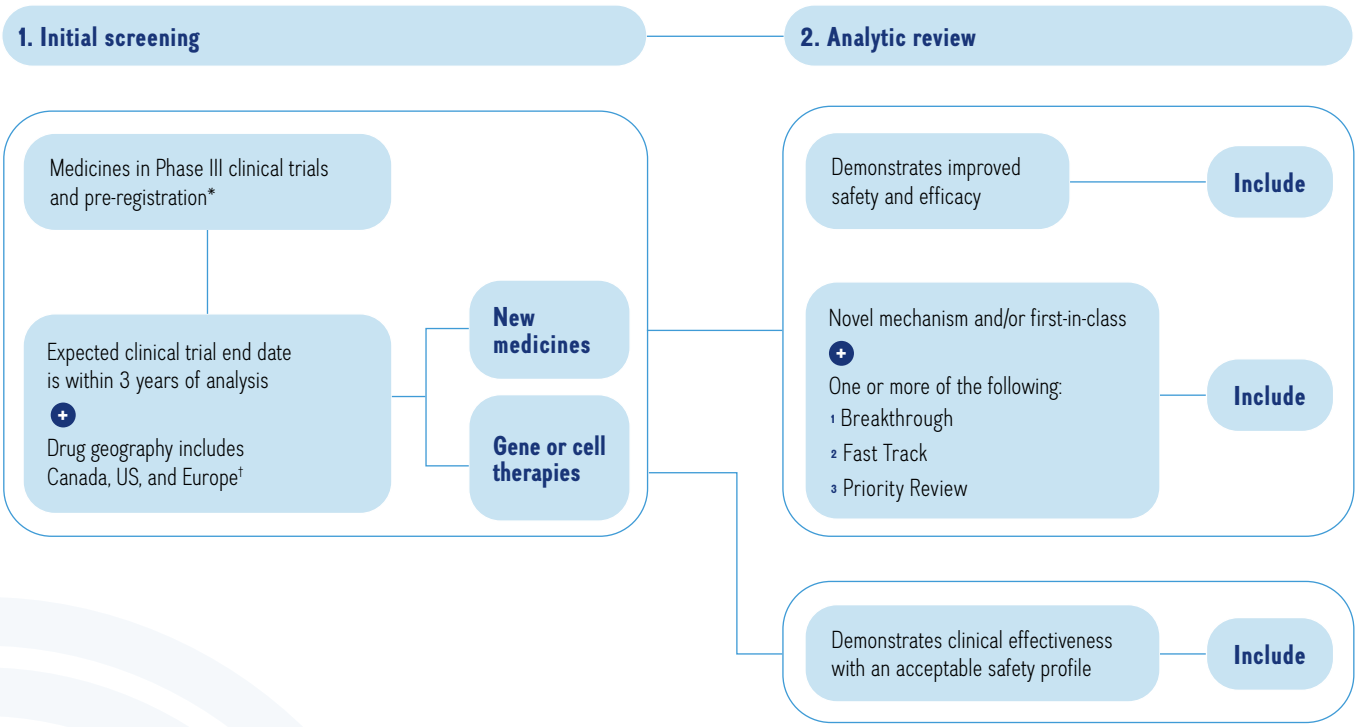
The snapshot of the 2023 pipeline identifies the composition of medicines in various phases of clinical development. For the purpose of this analysis, a full list of pipeline medicines was retrieved from GlobalData's Healthcare database in April 2024 and the selected medicine candidates for this year's report have been validated as of August 30, 2024.

New medicinal ingredients are identified as those with no prior approvals through the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), or Health Canada. The distribution of new medicines by therapeutic area corresponds to the indication under evaluation, as reported by GlobalData. Note that a single new medicine may be undergoing multiple clinical studies for separate indications.

Meds Pipeline Monitor

The MPM selects new medicines in Phase III clinical trials or pre-registration in Canada, the United States, and Europe. Many of the pipeline candidates are first-in-class or represent novel mechanisms for treatment in a specific therapeutic area. For this reason, this report includes additional review on other drugs undergoing Phase II clinical evaluation that share the same indication or mechanism of action in earlier stages of the pipeline (i.e., Phase II). Pipeline medicines are selected for inclusion using a two-stage process (Figure 1). The initial screening stage selects medicines in the late phases of clinical evaluation, while the analytic review stage involves a more rigorous appraisal of each potential candidate to identify medicines that may have a significant clinical and budgetary impact.

FIGURE 1.
Selection process for medicines featured in the Meds Pipeline Monitor



* In pre-registration with the US Food and Drug Administration (FDA).

† Has Phase III clinical trials in Canada, the United States, or geographic Europe (excluding Russia and Türkiye).

Stage 1. Initial screening

GlobalData's Healthcare database is used to identify a list of medicines undergoing Phase III clinical trials or in pre-registration. These medicines serve as the basis for the initial screening stage.

The drug geography, defined as the geographical region or country in which the medicine is either marketed or in pipeline development, is restricted to Canada and other countries with similar regulatory and approval processes: the US and geographic Europe (excluding Russia and Türkiye). Only new medicinal ingredients that have adequate data that supports increased efficacy and safety from clinical trials are considered as candidates for inclusion.

Medicines approved or sold in Canada, the US, or Europe for any other indication or in any other strength or formulation are excluded during the selection process, as are medicines whose clinical trials are inactive, suspended, withdrawn, or terminated.

Stage 2: Analytic screening

Selection criteria

Following the initial screening, the second stage of the process considers a number of selection criteria to determine the final list of pipeline candidates. These criteria are detailed in Table 1.

Earlier phases of the pipeline (i.e., Phase II) are also examined to determine if there are other medicines with the same indication or mechanism of action as the selected candidates in Phase III and pre-registration. This provides additional information on the number of novel, first-in-class medicines that are undergoing clinical evaluation in Phase II that may influence the therapeutic significance of the selected candidates in Phase III and pre-registration.

TABLE 1.
Selection criteria for the Meds Pipeline Monitor

Selection Criteria	
	**Improved safety and efficacy shown in clinical trials:** a medicine that demonstrates increased safety, new outcome measures, or increased life expectancy or quality of life
	**Novel mechanism / First-in-class:** a medicine that uses a new mechanism of biochemical interaction to produce a medical effect, or a medicine that is the first in its therapeutic class In addition, **the medicine must fall into one or more of the three following FDA designations** for expedited development and review:
	**Breakthrough:** medicines intended to treat a serious condition and for which preliminary clinical evidence indicates that they may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)
	**Fast Track:** medicines used to treat serious conditions and fill an unmet medical need
	**Priority Review:** medicines that would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications
	**Gene or cell therapy:** a technique for the treatment of genetic disease in which a gene that is absent or defective is replaced by a healthy gene; or the transplantation of human cells to replace or repair damaged tissue and/or cells

Additional descriptive information

A profile of each successful pipeline candidate is provided, including the indication and mechanism of action, as well as a summary of the applicable published outcomes from clinical trials. Specific attributes that may influence the potential uptake or cost of each medicine are also identified. Table 2 provides a detailed description of these key attributes.

TABLE 2.
Key attributes of new medicines selected for the Meds Pipeline Monitor

Attribute		Relevance	Data sources
	**Phase III clinical trials in Canada**	Medicines tested in Canada are likely to be of interest to Canadians	GlobalData Healthcare; Health Canada Clinical Trials Database; Health Canada Drug and Health Product Submissions Under Review; National Institutes of Health (NIH) Clinical Trial Registry
	**Rare or orphan designation**	Medicines used to treat rare diseases or conditions that generally have high treatment costs and may result in substantial spending	GlobalData Healthcare
	**Biologic medicine**	These complex molecules produced by living organisms are expected to have high costs, resulting in substantial spending	
	**Add-on therapy**	Medicines designed to be used in conjunction with existing medicines may increase the treatment cost and contribute to higher spending	
	**Potential evergreening**	Modified forms of the same product in order to extend the patent life. (e.g., new delivery systems, new dosages, new uses, new combinations or new forms)	GlobalData Healthcare

The profile also provides details of potential cost implications, if available, which includes the forecasted global revenues reported by GlobalData.

The indications and therapeutic areas of the featured medicines correspond to their Phase III clinical trial or pre-registration stage. A single clinical trial may assess multiple indications within the same therapeutic area. These medicines may also have additional indications at various phases of clinical evaluation that are not mentioned in this report. The scientific description and key attributes provided are focused on the specified indication(s) for the selected medicines.

Medicines reported for a given year are reassessed for each following edition of the MPM. They may be retained on the MPM list if they continue to meet the selection criteria. Medicines for which clinical trials have been discontinued or for which the selection criteria is no longer met are not reported in subsequent editions.

Spotlight on Canada

Health Canada's Drug and Health Product Submissions Under Review (SUR) Lists are assessed using a modified approach to the selection criteria to establish a list of medicines that may have the potential to impact Canadian drug spending or clinical practice.

Medicines listed in the SUR include new drug submissions containing medicinal ingredients that have not been approved in Canada for any indication, in any strength or form. Unlike the selection of medicines identified in the pipeline lists, these medicines may have previously received market authorization through the U.S. FDA or the EMA.

Selection Criteria

Following this initial screening, the medicine must demonstrate at least one of three selection criteria to qualify for inclusion in the report. These criteria are listed in Table 3.

TABLE 3.
Selection criteria for the list of medicines currently under review by Health Canada

Selection Criteria	
	**Improved safety and efficacy shown in clinical trials:** a medicine that demonstrates increased safety, new outcome measures, or increased life expectancy or quality of life
	**Novel mechanism or First-in-class:** a medicine that uses a new mechanism of biochemical interaction to produce a medical effect, or a medicine that is the first in its therapeutic class
	**Gene or cell therapy:** a technique for the treatment of genetic disease in which a gene that is absent or defective is replaced by a healthy gene; or the transplantation of human cells to replace or repair damaged tissue and/or cells

Additional descriptive information

The profile of each medicine under review includes the key attributes listed in Table 2, as well as the indication and mechanism of action, and a summary of the applicable published outcomes from clinical trials. Specific attributes that may influence the potential uptake or cost of each medicine are also identified, as well as potential cost implications, if available, which includes the forecasted global revenues reported by GlobalData.

Although FDA designations for expedited development or review are not a selection criteria for this list, relevant Breakthrough, Fast Track, and Priority Review designations are indicated where available. For a description of these designations, see Table 1.

Indications and therapeutic areas correspond to the information provided by GlobalData. The scientific description and key attributes provided are focused on the specified indication(s) for the selected medicine. For medicines under review for multiple indications, the primary indication is used.

Data Sources

The GlobalData Healthcare database is the primary data source for the identification of pipeline medicines and their corresponding clinical information. GlobalData Healthcare tracks medicines from pre-clinical discovery, through clinical trials, to market launch and subsequent sales. The database is a comprehensive resource of medicines under various stages of clinical development. Search capabilities allow for controlled selection of specific attributes, including but not limited to the following: phase of clinical development, therapeutic area, molecule type, indication, drug geography, mechanism of action, and regulatory designations.

Health Canada's Drug and Health Product Submissions Under Review (SUR) Lists are used to determine the featured selection of new medicines currently undergoing review by Health Canada. The SUR is a publicly available set of lists that identify pharmaceutical and biologic drug submissions containing new medicinal ingredients not previously approved in Canada that have been accepted for review. This applies to submissions accepted on or after April 1, 2015.

As this selection is restricted to new medicines, additional sources of information are cross-referenced to confirm that the candidates have not previously been approved or sold. These include recorded sales data from the IQVIA MIDAS® Database (all rights reserved); regulatory approval records from the National Institutes of Health (NIH), U.S. FDA, the EMA, and Health Canada; and information in Health Canada's Clinical Trials database and ClinicalTrials.org.

LIMITATIONS

This analysis captures a snapshot of the pipeline over a specific time period. Although it is assumed to be representative of the composition of medicines over the entire year, the pipeline is fairly dynamic and the share of medicines in any particular therapeutic area will vary.

This assessment is restricted to medicines under development for market in Canada and other countries with similar regulatory and approval processes: the US and Europe (excluding Russia and Türkiye). Medicines that have not yet received market authorization in these countries were considered as potential pipeline candidates, even if they have been approved elsewhere in the world.

Some of the selected medicines may be undergoing clinical trials for additional indications; this analysis only reports on indications in the late stages of development—that is, in Phase III clinical trials or pre-registration with the U.S. FDA—that satisfy the selection criteria set out in the methodology.

For each selected pipeline medicine, the primary manufacturer(s) and trade name, if available, are given along with the indication. In some cases, additional manufacturers, including subsidiaries, may also be involved in the development of the medicine with the primary companies, or other manufacturers may be developing the same medicine for other indications.

Although this report attempts to identify the most important pipeline medicines, the selection is not exhaustive and some medicines that are not included in this selection may have a significant impact on future clinical practice and drug spending in Canada.

Unless otherwise specified, the featured lists capture the composition of the pipeline as of April 2024 and are validated as of the end of August 2024. Due to the unpredictability and fast-moving nature of pipeline medicines entering the market, some of the medicines listed in this edition may have been approved or marketed in Canada, the US, or Europe following this date. Pipeline medicines that have not been included in this report due to the timing of the selection may presently meet the selection criteria; these, along with the rest of the drug pipeline, will be considered for the next edition of the report.

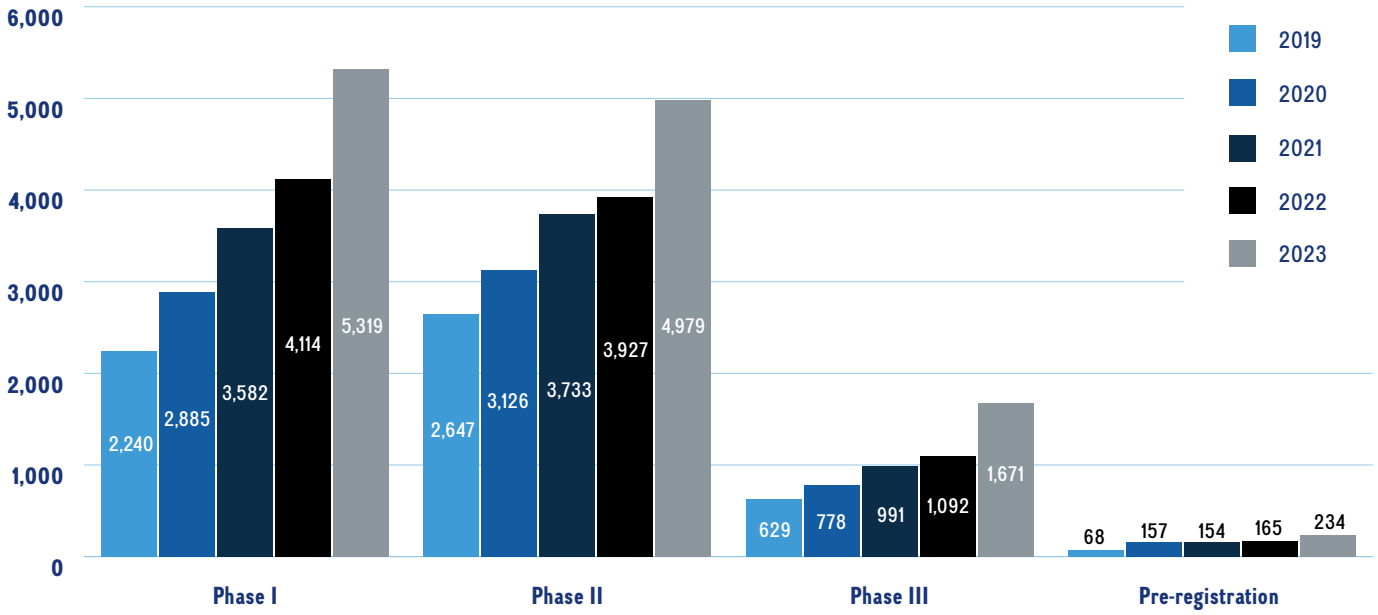
SNAPSHOT OF THE 2023 PIPELINE

The number of new pharmaceutical developments in the pipeline is increasing year over year. In 2023, over 12,000 new medicines were undergoing clinical evaluation, which has been increasing by an average of 19% per year since 2019.

Figure 2 provides a snapshot of the pipeline including the number of new medicinal ingredients in each phase of clinical development over the last 5 years.

FIGURE 2.

Number of new medicines in each phase of clinical evaluation, 2019–2023

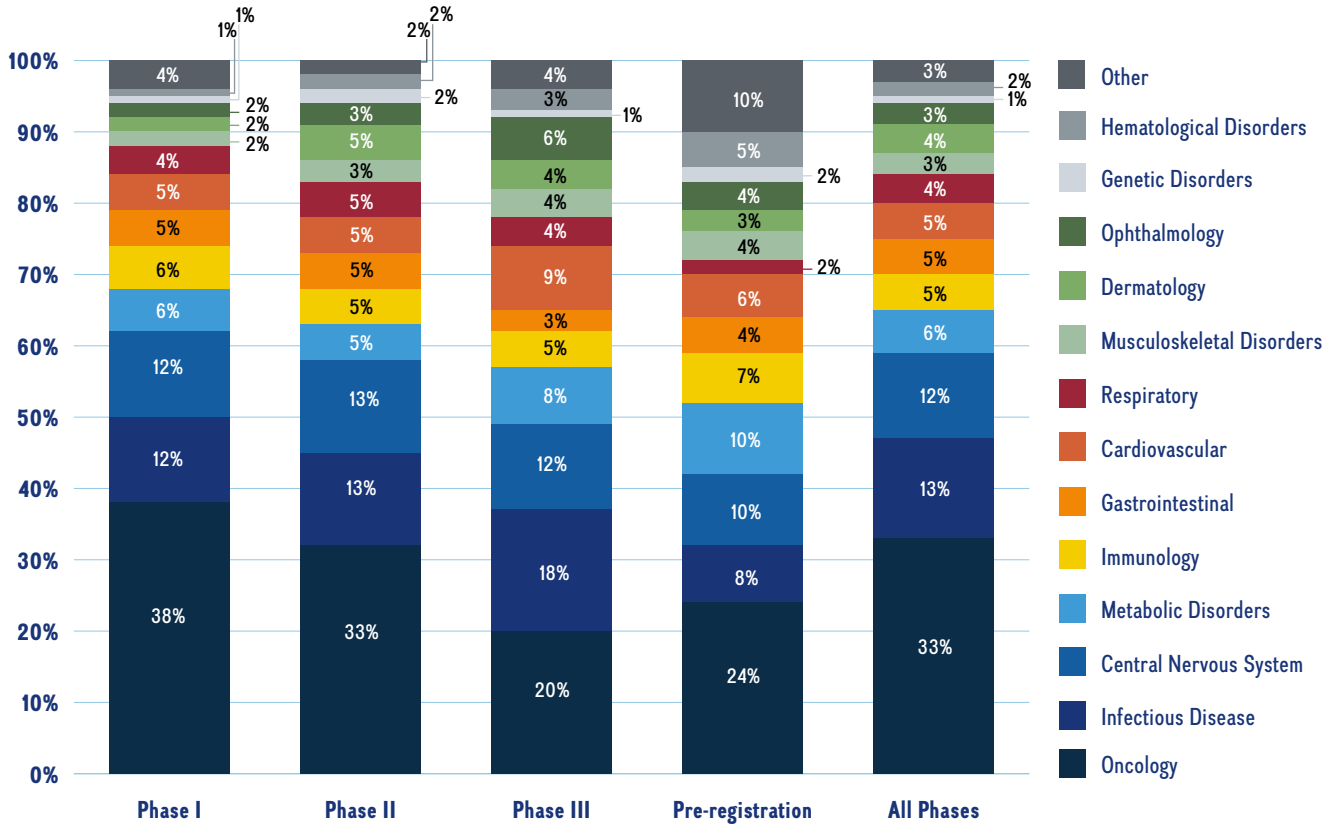


Data source: GlobalData Healthcare database (accessed April 2024); IQVIA MIDAS© Database.

Figure 3a illustrates the distribution of new medicines by therapeutic area from Phase I through to pre-registration. Although the findings show that pipeline medicines represented a wide range of therapeutic areas in 2023, cancer treatments dominated the therapeutic mix in each phase of the pipeline, accounting for one third (33%) of medicines in all phases of clinical evaluation. Other important pipeline therapies include those for infectious diseases (13%) and central nervous system therapies (12%).

FIGURE 3A.

Therapeutic class distribution of pipeline medicines by phase of clinical evaluation, 2023

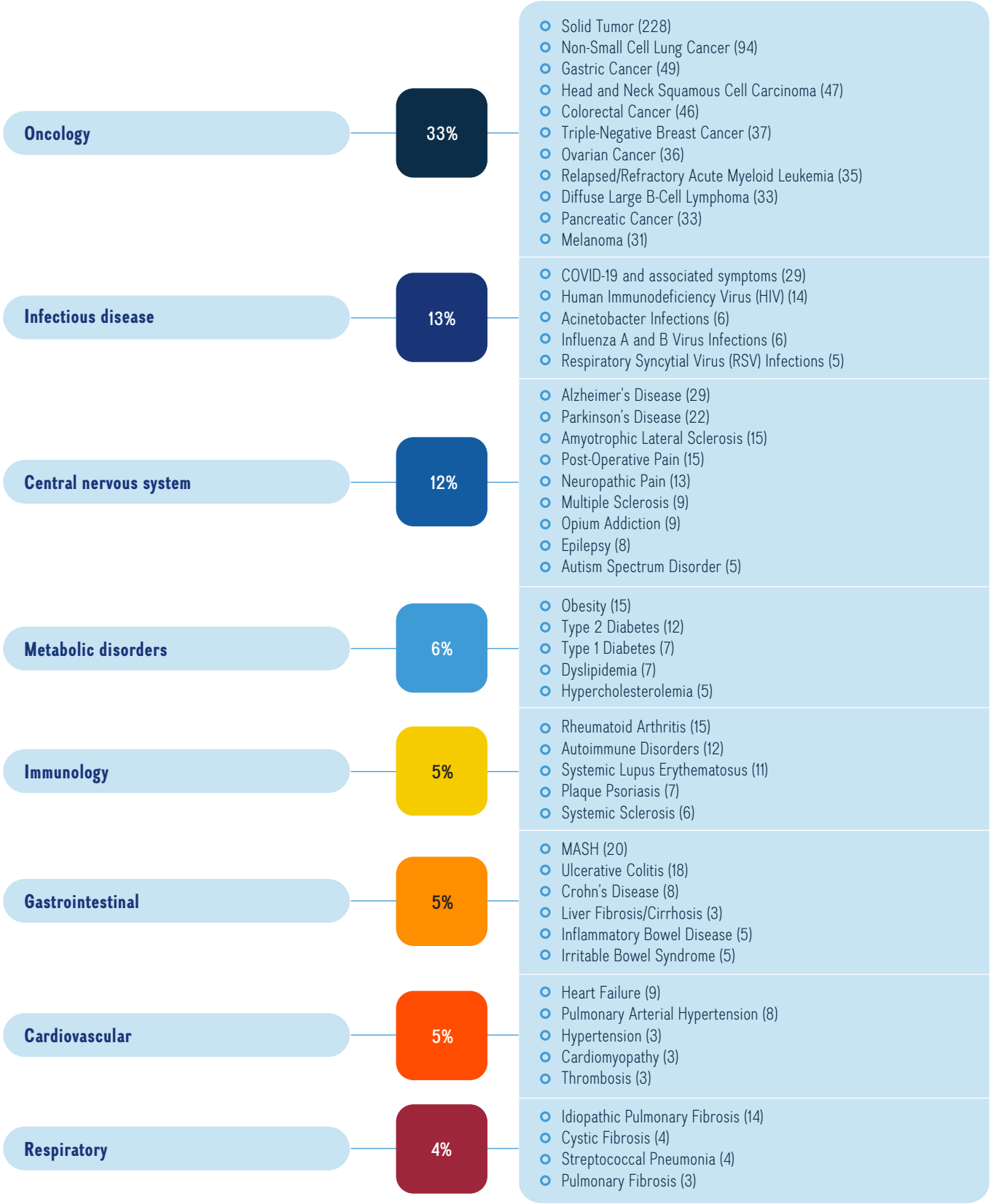


Data source: GlobalData Healthcare database (accessed April 2024).

Figure 3b illustrates the top indications and number of medicines undergoing Phase II, Phase III or pre-registration in the major therapeutic areas in the pipeline in 2023.

FIGURE 3B.

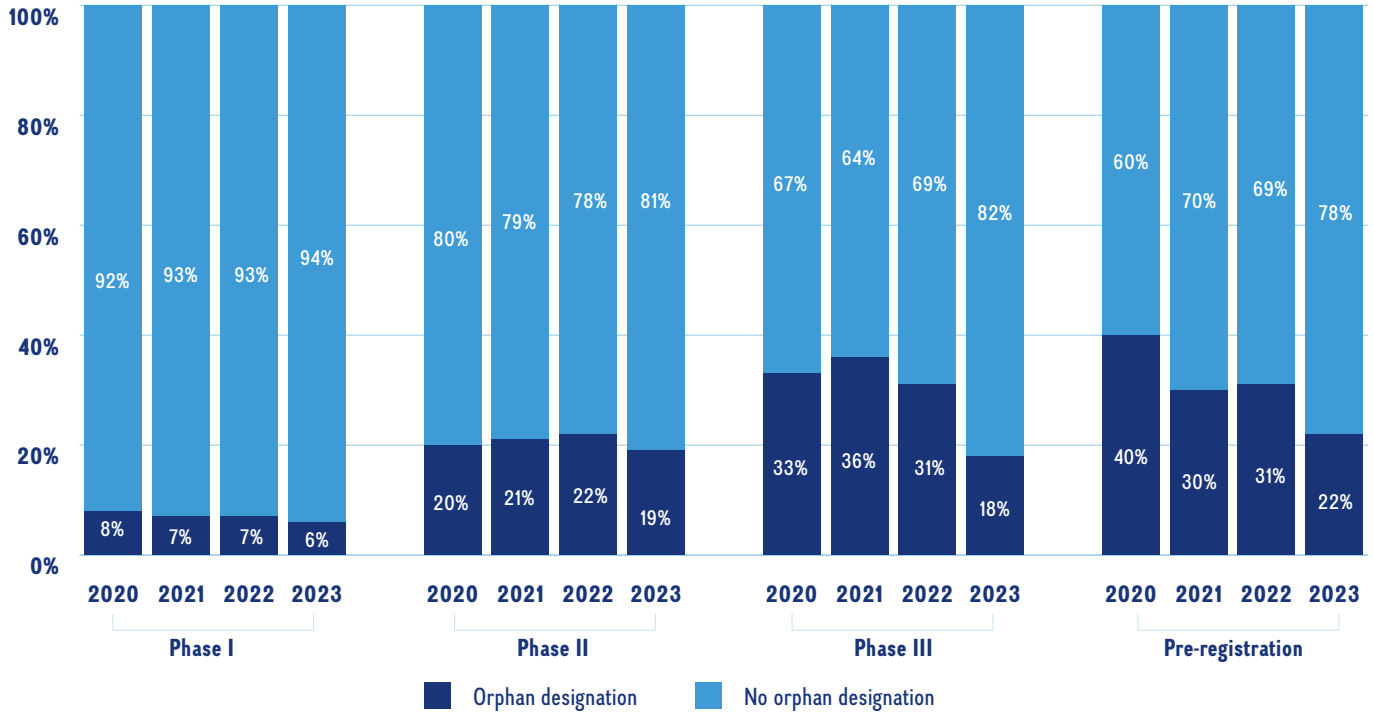
Top indications for major therapeutic areas in the pipeline, 2023



Orphan medicines, as designated by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA), accounted for a notable proportion of medicines in the 2023 pipeline. Figure 4 provides the shares of orphan designated medicines for all phases in the pipeline from 2020–2023. Orphan designated medicines make up a greater share in the later stages of the pipeline, increasing from 6% in Phase I to 22% in pre-registration in 2023.

FIGURE 4.

Share of orphan medicines in the pipeline by highest phase of clinical evaluation, 2020–2023



Note: Includes all pipeline medicines with a highest development stage of Phase I to pre-registration that are being developed for market in Canada, the United States, or geographic Europe (excluding Russia and Türkiye). Orphan medicines were defined as pipeline medicines that have been granted an orphan designation by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA).

Data source: GlobalData Healthcare database (accessed April 2024).

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The following tables include selected new medicine candidates for 2023 (Table 4), retained medicines from previous editions of the *Meds Pipeline Monitor* (Table 5), and medicines from previous editions that have gained market authorization (Table 6).

Medicines in Phase III clinical trials or pre-registration are considered as candidates for the Meds Pipeline Monitor (MPM) if they have the potential to impact future clinical practice and drug spending in Canada (e.g., address an unmet therapeutic need, offer a novel mechanism of action or therapeutic benefit over existing therapies, or treat a serious condition).

Screening new medicine candidates

Of the 1,905 pipeline medicines in Phase III and pre-registration in 2023, twenty (20) new medicines were selected for inclusion in the new medicines list (Table 4). Many of the pipeline candidates are first-in-class or represent novel mechanisms for the treatment of specific therapeutic areas. Having insight into other drugs under investigation (i.e., in Phase II) may provide additional information on the potential place in therapy of these pipeline candidates. The medicines in Phase II were examined to identify other drugs in the pipeline that have the same indication or mechanism of action as those listed in the 2023 new medicines list. The description for each new medicine listed in the 2023 new medicines list includes a statement indicating if there are any other drugs in Phase II development with the same indication or mechanism of action. Appendix A (Table A2) provides some further insights into the other drugs identified in Phase II for the indications targeted by the pipeline candidates. It is important to keep in mind that not all drugs in Phase II development will progress to Phase III. According to an industry analysis, Phase II clinical programs experience the lowest success rate of the development phases, with only 28.9% of developmental candidates advancing to Phase III.[1]

Of the new medicines featured in previous reports, 23 were retained as recent evidence continues to support promising clinical benefit and satisfies the selection criteria (Table 5). Fifteen of the 2022 pipeline medicines have received market authorization in the US, Europe, or Canada as of August 30, 2024 (Table 6), while 13 were removed from the list as their clinical trials were discontinued or they no longer fulfill the selection criteria.

Screening biosimilars

The availability of biosimilars could significantly impact costs in a wide range of therapeutic areas. Appendix A (Table A1) provides a list of the identified biosimilars in Phase III clinical trials and indicates whether a biosimilar currently exists for the originator biologic.

TABLE 4.
Selected new medicines for 2023

Selection criteria		
Increased safety and efficacy	Novel mechanism	Gene or cell therapy
Breakthrough	Fast Track	Priority Review

Key attributes		
Clinical trials in Canada	Rare or orphan designation	Potential evergreening
Biologic medicine	Add-on therapy	

Medicine (Trade name) Company	Indication(s)	Description and key attributes
CARDIOVASCULAR		
Aficamten Cytokinetics Inc.	Hypertrophic cardiomyopathy	○ It is a selective cardiac myosin inhibitor that reduces left ventricular outflow tract gradients by mitigating cardiac hypercontractility. ○ Administered orally. **Clinical trials** ○ It has similar efficacy to mavacamten (Camzyos), also a cardiac myosin inhibitor, but it has a shorter half-life (t1/2) and fewer drug-drug interactions,[2] suggesting improved safety. The shorter half-life allows for the dose to be uptitrated quickly, resulting in earlier symptomatic relief.[3] ○ One Phase III trial has been completed;[4] others are ongoing.[5, 6, 7, 8] ○ No other drug for this indication was identified in Phase II development at this time.[9] **Forecasted revenue** ○ Total global annual revenue forecasted to be $2.3 billion by 2029.*
Nerinetide NoNO Inc.	Acute ischemic stroke	○ It acts as a neuroprotective eicosapeptide by inhibiting the post-synaptic density protein 95 (PSD-95). ○ Administered as an intravenous infusion. **Clinical trials** ○ There is promising evidence for improving the outcomes of patients with acute ischemic stroke.[10] ○ The Phase III trials have been completed.[11, 12, 13] ○ There are other drugs in Phase II development (n=10), but none with the same mechanism of action as nerinetide.[14] See Appendix A for additional information. **Forecasted revenue** ○ Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Description and key attributes
Pelacarsen sodium Novartis AG	Cardiovascular disease; Hyperlipidemia	 • It is a first in class ligand-conjugated antisense (LICA) medicine designed to inhibit the production of apolipoprotein(a), or apo(a), in the liver to offer a direct approach for reducing Lp(a). Elevated Lp(a) is recognized as an independent, genetic cause of cardiovascular disease (CVD). It inhibits elevated levels of apolipoprotein(Lp)(a). There are no approved drug therapies that are designed to target Lp(a) with the goal of lowering the Lp(a) level in patients who have increased risk. • Administered as a monthly subcutaneous injection. **Clinical trials** • Evidence to date shows that a single dose of pelacarsen yields optimal results with persisting substantial reductions in Lp(a) levels, potentially enhancing CVD risk reduction.[15] • There are ongoing Phase III trials.[16, 17, 18, 19] • There are other drugs in Phase II development (n=5), but none with the same mechanism of action as pelacarsen. See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $625 million by 2029.*
CENTRAL NERVOUS SYSTEM		
Fosigotifator (ABBVCLS-7262) Calico Life Sciences LLC	Amyotrophic lateral sclerosis (ALS)	 • It is a eukaryotic translation initiation factor 2 subunit beta (EIF2B) activator. • Administered orally once a day. **Clinical trials** • In Phase II trials, ABBV-CLS-7262 increased eIF2B activity and inhibited the Integrated Stress Response (ISR) in blood cells collected from trial participants.[20] The ISR is activated in people with ALS causing a reduction in normal protein synthesis, an increase in production of stress proteins, and formation of stress granules containing TDP-43. • There is an ongoing Phase II/III trial (enrolling by invitation)[21]; 300 patients to participate. • There are other drugs in Phase II development (n>10), but none with the same mechanism of action as ABBVCLS-7262.[22] See Appendix A for additional information. **Forecasted revenue** • Forecasted annual global revenue unknown.
Iclepertin Boehringer Ingelheim International GmbH	Cognitive impairment associated with schizophrenia (CIAS)	 • It is a glycine transporter 1 (GlyT1) inhibitor. • Administered orally. **Clinical trials** • A Phase II study has demonstrated that iclepertin is safe and well tolerated in patients with schizophrenia and improves cognition.[23] • It has the potential to become the first treatment option for cognitive impairment associated with schizophrenia.[24] • Phase III trials are ongoing.[25, 26, 27, 28, 29, 30] • There are other drugs in Phase II development (n=5) but none with the same mechanism of action as iclepertin.[31] See Appendix A for additional information. **Forecasted revenue** • Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Description and key attributes
Resiniferatoxin Grunenthal GmbH	Osteoarthritis pain	 • It is an ultrapotent capsaicin analog that acts as a transient receptor potential vanilloid subtype 1 (TRPV1) agonist. Its administration can reversibly defunctionalise TRPV1-expressing nociceptors. This may result in long-lasting pain relief. • Administered by intraarticular injection. **Clinical trials** • The therapeutic window of resiniferatoxin is broad, allowing for the full desensitization of pain perception and neurogenic inflammation without causing unacceptable side effects.[32] • If approved, it has the potential to become a meaningful non-opioid treatment option providing long-lasting pain relief and functional improvement of the affected joint, combined with a favourable safety profile.[33] • Phase III trials are undergoing a protocol change. • There are other drugs in Phase II development (n>10) with one having the same mechanism of action as resiniferatoxin.[34] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $24 million by 2029.*
Xanomeline-trospium (KarXT) Karuna Therapeutics Inc.	Schizophrenia; Psychosis	 • It is a dual M1/M4 muscarinic acetylcholine receptor agonist that does not block D2 dopamine receptors. KarXT combines xanomeline with the peripherally restricted muscarinic receptor antagonist trospium chloride with the goal of ameliorating xanomeline-related adverse events associated with peripheral muscarinic receptors. • Administered orally. **Clinical trials** • In the EMERGENT-2 Phase III trial, KarXT was effective in reducing positive and negative symptoms in schizophrenia and was generally well tolerated.[35] A meaningful response was defined as a 30% or greater reduction in total PANSS score by week 5. Using this definition, 55% of persons on KarXT responded versus 28% on placebo. This difference was both statistically significant and clinically meaningful.[36] • Some Phase III trials for schizophrenia have been completed,[37, 38, 39] others are ongoing.[40, 41, 42, 43] One was terminated (company's business decision).[44] There are ongoing Phase III trials for psychosis associated with Alzheimer's disease.[45, 46, 47] • It is currently under review by the U.S. FDA. • There are other drugs in Phase II development (n=4) with several having the same mechanism of action as xanomeline-trospium.[48] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $3.3 billion by 2029.*

Medicine (Trade name) Company	Indication(s)	Description and key attributes
DERMATOLOGY		
Prademagene zamikeracel Abeona Therapeutics Inc. 	Epidermolysis bullosa	 • It is designed to incorporate the functional collagen-producing COL7A1 gene into a patient's own skin cells and enable long-term gene expression by using a retroviral vector to stably integrate into the dividing target cell genome.[49] • Applied topically, as engineered autologous epidermal sheets. **Clinical trials** • Findings from the Phase III trial50 showed 81.4% of prademagene-treated wounds achieved 50% or greater wound healing compared with 16.3% of untreated control wounds (p<.001). Additionally, a statistically significant improvement in pain reduction associated with wound dressing changes was observed with the prademagene when compared with untreated control wounds (p=.0002).[51, 52] • Another Phase III trial is ongoing.[53] • Although FDA issued a complete response letter in April 2024, specifying chemistry, manufacturing and controls issues that must be addressed, the company has since met with the FDA and is planning to resubmit.[54] • There are other drugs in Phase II development (n=4) with one having the same mechanism of action as prademagene zamikeracel.[55] See Appendix A for additional information. **Forecasted revenue** • Forecasted annual global revenue unknown.
GASTROINTESTINAL DISORDERS		
Efruxifermin Akero Therapeutics Inc. 	Metabolic dysfunction-associated steatohepatitis (MASH)	 • It is a bivalent, long-acting fibroblast growth factor 21 (FGF21) analog that is designed to reduce liver fat and inflammation, reverse fibrosis, increase insulin sensitivity and improve lipids. • Administered subcutaneously. **Clinical trials** • In Phase II studies, treatment with efruxifermin significantly reduced hepatic fat fraction (HFF) in patients with F1-F3 stage NASH (now referred to as MASH), with an acceptable safety profile.[56, 57] • When added to glucagon-like peptide-1 receptor agonists (GLP-1RAs), its tolerability appeared comparable to that of either drug alone, while also significantly reducing HFF and noninvasive markers of fibrosis in patients with MASH and type 2 diabetes (T2D). Liver health in patients already on a GLP-1RA may be further improved by addition of efruxifermin.[58] • Phase III trials are ongoing.[59, 60] • There are other drugs in Phase II development (n>10) with one having the same mechanism of action as efruxifermin.[61] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $546 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Description and key attributes
Obefazimod Abivax SA	Ulcerative colitis	○ It is a small molecule with anti-inflammatory properties through the specific and selective upregulation of miR-124 expression. ○ Administered orally. **Clinical trials** ○ Findings from the maintenance phases of Phase II trials showed that long-term obefazimod treatment provides continued improvement in clinical symptoms of disease, with a substantial proportion of patients in clinical remission, and an overall good safety profile.[62] ○ Phase III trials are ongoing.[63, 64, 65] ○ There are other drugs in Phase II development (n>10), but none with the same mechanism of action as obefazimod.[66] See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $715 million by 2029.*
GENETIC DISORDERS		
Fazirsiran sodium Arrowhead Pharmaceuticals Inc.	Alpha-1 antitrypsin deficiency (A1AD)	○ It is a small, interfering RNA (siRNA) that inhibits the mutant alpha-1 antitrypsin (Z-AAT) protein. ○ Administered subcutaneously. **Clinical trials** ○ In a Phase II trial, fazirsiran was associated with a strong reduction of Z-AAT (the Z allele of alpha1-antitrypsin protein) concentrations in the serum and liver and concurrent improvements in liver enzyme concentrations. ○ Phase III trials are ongoing.[67, 68, 69] ○ There are other drugs in Phase II development (n=3) with two having the same mechanism of action as fazirsiran. See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $495 million by 2029.*
GENITO URINARY SYSTEM AND SEX HORMONES		
Inaxaplin (VX19-147) Vertex Pharmaceuticals Inc.	Focal segmental glomerulosclerosis (FSGS); Chronic kidney disease (chronic renal failure)	○ It is an inhibitor of Apolipoprotein L1 (APOL1) channel activity that reduces proteinuria in patients with APOL1-mediated kidney disease (AMKD). ○ Administered orally. **Clinical trials** ○ In a Phase II trial, inaxaplin reduced proteinuria in participants with two APOL1 variants and focal segmental glomerulosclerosis.[70] If this is confirmed in Phase III trials, it would a major advance in the therapy of proteinuric CKD.[71] ○ A Phase III trial is ongoing.[72] ○ There are other drugs in Phase II development (n=2), but none with the same mechanism of action as inaxaplin.[73] See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $539 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Description and key attributes
METABOLIC DISORDERS		
RGX-121 RegenxBio Inc. 	Mucopolysaccharidosis II (MPS II) (Hunter syndrome)	 • It is a gene therapy designed to deliver a functional copy of the iduronate-2-sulfatase gene, using the NAV® AAV9 vector, to cells in the central nervous system (CNS). • Administered directly to the CNS using intracisternal or intracerebroventricular delivery, as a one-time dose. **Clinical trials** • Interim data from the CAMPSIITE® trial supports that RGX-121 changes the course of disease by restoring the gene missing in boys with Hunter syndrome and has the potential to significantly improve vital brain function for patients living with this debilitating disease.[74] • The CAMPSIITE® trial is ongoing.[75] • There are other drugs in Phase II development (n=5) with one having the same mechanism of action as RGX-121.[76] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $406 million by 2029.*
ONCOLOGY		
Datopotamab deruxtecan Daiichi Sankyo Co Ltd. 	Breast cancer, both HR-positive/HER2-negative and triple-negative	 • It is a TROP2-targeted antibody-drug conjugate. TROP2 is a transmembrane protein sporadically expressed in healthy tissue, but broadly expressed and associated with poor prognosis in HR-positive/HER2-negative and triple negative breast cancer.[77] **Clinical trials** • In a Phase III trial, it demonstrated a statistically significant and clinically meaningful improvement for the dual primary endpoint of progression-free survival compared to investigator's choice of chemotherapy in patients with unresectable or metastatic HR-positive, HER2-negative breast cancer previously treated with endocrine-based therapy and at least one systemic therapy. For the dual primary endpoint of overall survival (OS), interim results numerically favoured datopotamab deruxtecan over chemotherapy but were not mature at the time of data cut-off. The trial is ongoing and OS will be assessed at future analyses.[78] • If approved, datopotamab deruxtecan has the potential to provide patients an efficacious and better tolerated alternative to conventional chemotherapy.[79] • The selective payload delivery of datopotamab deruxtecan, which is enabled by the selectively cleavable plasma-stable linker that releases deruxtecan after proteolytic processing by tumour cell–enriched lysosomal enzymes, reduces systemic exposure while achieving a sustained response, resulting in an improved benefit-risk profile. This may account for the comparatively low incidences of neutropenia and diarrhea in this study compared with sacituzumab govitecan, another TROP2-targeted antibody-drug conjugate marketed, as Trodelvy, in Canada since 2021.[80] • Phase III trials in breast cancer are ongoing.[81, 82, 83, 84, 85] • Under review by the U.S. FDA.[86] • While there are other drugs for breast cancer in Phase II development, there are no other drugs for all types of breast cancer targeted by datopotamab.[87] **Forecasted revenue** • Total global annual revenue forecasted to be $4.4 billion by 2029.*

Medicine (Trade name) Company	Indication(s)	Description and key attributes
Gemcitabine (GemRIS) Johnson & Johnson	Non-muscle invasive bladder cancer (NMIBC) (superficial bladder cancer); Muscle invasive bladder cancer (MIBC)	 • It acts as a ribonucleoside diphosphate reductase subunit M1 inhibitor. It is a drug-device combination product designed to deliver a targeted, sustained release of gemcitabine into the bladder for weeks at a time. • Administered intravesically. It is installed in a physician's office setting during a 3- to 5-minute procedure with no anesthesia. **Clinical trials** • In a Phase II study, treatment with gemcitabine produced complete responses (CR) and was well tolerated in patients with Bacillus Calmette-Guérin–unresponsive, high-risk non–muscle-invasive bladder cancer (NMIBC).[88] Additional data from the study show rapid achievement of CR with 98% achieving a CR within 12 weeks.[89] • Phase III trials are ongoing.[90, 91, 92] • There are other drugs in Phase II development (n=1), but none with the same mechanism of action as Gemcitabine.[93] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $1 billion by 2029.*
Patidegib hydrochloride Sol-Gel Technologies Ltd.	Gorlin syndrome (basal cell nevus syndrome/nevoid basal cell carcinoma syndrome)	 • It is a hedgehog signaling pathway blocker. • Applied topically, as a gel. **Clinical trials** • Patidegib is able to decrease tumour burden, reducing the adverse effects induced by systemic targeted therapies.[94] • A Phase III trial has been completed[95] and one is ongoing.[96] One trial was terminated early due to low blinded event rate; termination was not related to safety of the drug.[97] • There are other drugs in Phase II development (n=1), but none with the same mechanism of action as patidegib.[98] See Appendix A for additional information. **Forecasted revenue** • Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Description and key attributes
Revumenib citrate (SNDX-5613) Syndax Pharmaceuticals Inc.	Acute lymphocytic leukemia (ALL); Acute lympho-blastic leukemia; Refractory acute myeloid leukemia; Relapsed acute myeloid leukemia	• It is a selective, menin-mixed lineage leukemia inhibitor. • Administered orally. **Clinical trials** • The breakthrough therapy designation (by U.S. FDA) underscores its potential as a first- and best-in-class therapy to meaningfully change the treatment paradigm for patients with R/R KMT2Ar acute leukemia, whether it presents clinically as acute myeloid leukemia or acute lymphocytic leukemia, in adults or children.[99] • Phase III trials have not been listed in clinicaltrials.gov. • It is under review by the U.S. FDA. • There are other drugs in Phase II development (n=8) with several having the same mechanism of action as revumenib.[100] See Appendix A for additional information. **Forecasted revenue** • Total global annual revenue forecasted to be $583 million by 2029.*
Vorasidenib citrate Les Laboratoires Servier SAS	Astrocytoma; Low-grade glioma; Oligodendroglioma	• It inhibits the activity of isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2). • Administered orally. **Clinical trials** • In the Phase III INDIGO trial, it significantly improved progression-free survival and delayed the time to the next intervention such as surgery, radiation, or chemotherapy, with a manageable safety profile.[101] At 2 years follow-up, over 83% per cent of patients on vorasidenib did not require further treatment compared to only 27% on the placebo medication. • It is under review by the U.S. FDA and the EMA. If the Phase III study confirms these results, "relacorilant plus nab-paclitaxel has the potential to become a new standard of care."[102] • The Phase III trial is ongoing.[103] • No other drug for all indications was identified in Phase II development at this time.[104] **Forecasted revenue** • Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Description and key attributes
RESPIRATORY		
AD-109 (atomoxetine + R-oxybutynin) Apnimed, Inc.	Obstructive sleep apnea (OSA)	○ It is a combination of R-oxybutynin, a selective antimuscarinic, and atomoxetine, a selective norepinephrine reuptake inhibitor. ○ It has the potential to be the first oral pharmacologic that could both treat the underlying night-time airway obstruction and hypoxia that characterize OSA, as well as improve the daytime consequences of OSA, such as fatigue. ○ Administered orally, once daily at bedtime. **Clinical trials** ○ Phase II studies showed that AD109, at the doses tested, achieved a statistically significant reduction of the Apnea-Hypopnea Index (AHI4, 4% desaturation definition for hypopneas) compared to placebo ($p<0.001$ vs. placebo). Dosing with AD109 led to clinically important reductions in AHI in most patients with mild, moderate and severe OSA.[105, 106, 107] ○ Currently, fewer than half of the people using PAP therapy are compliant long-term, leaving many people at risk from the consequences of untreated OSA, including a higher risk for stroke and heart attack.[108] ○ Phase III trials are ongoing.[109, 110] ○ No other drug for this indication was identified in Phase II development at this time.[111] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
Brensocatib Insmed Inc.	Bronchiectasis	○ It is a selective, reversible dipeptidyl peptidase 1 (cathepsin C) inhibitor that exhibits anti-inflammatory action through suppressing the activity of neutrophil serine proteases. ○ Administered orally. **Clinical trials** ○ In a Phase II trial in patients with bronchiectasis, Brensocatib prolonged the time to the first exacerbation and led to fewer exacerbations than placebo.[112, 113] ○ It is under review by the U.S. FDA. ○ A Phase III trial in bronchiectasis is ongoing.[114] ○ A Phase III trial in COVID-19 has been completed.[115] ○ There are other drugs in Phase II development (n=3), but none with the same mechanism of action as brensocatib.[116] See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $1.3 billion by 2029.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q2-2024, and are given in US dollars.

Data source: GlobalData Healthcare database.

TABLE 5.

Update on pipeline medicines retained from the 2022 *Meds Pipeline Monitor*

Selection criteria		
Increased safety and efficacy	Novel mechanism	Gene or cell therapy
Breakthrough	Fast Track	Priority Review

Key attributes	
Clinical trials in Canada	Rare or orphan designation
Biologic medicine	Add-on therapy

Medicine (Trade name) Company	Indication(s)	Update
CARDIOVASCULAR		
Abelacimab (Anthos Therapeutics Inc.)	Deep vein thrombosis (DVT); Pulmonary embolism; Atrial fibrillation	**Clinical trials** ○ According to a cost-effectiveness study, abelacimab could offer a potential cost-savings of $50,000 USD and improvements of 1.5 quality-adjusted life years (QALY's) per person over a lifetime horizon as compared to rivaroxaban, a direct oral anticoagulant.[117] ○ Two Phase III trials in cancer-associated thrombosis are ongoing; targeted to be completed in September 2025.[118, 119] ○ A Phase III trial in high-risk atrial fibrillation is ongoing; targeted to be completed in March 2025.[120] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
Etripamil (Milestone Pharmaceuticals Inc.)	Supraventricular tachycardia	**Clinical trials** ○ Positive results from the phase 3 RAPID clinical trial of etripamil nasal spray in patients with PSVT have been published.[121] ○ Two Phase III trials have been completed[122, 123] and others are still ongoing,[124] including an open extension study by invitation.[125] ○ It has been submitted to the U.S. FDA for review.[126] **Forecasted revenue** ○ Total global annual revenue forecasted to be $237 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Update
Obicetrapib NewAmsterdam Pharma Company	Dyslipidemia; Heterozygous familial hypercholesterolemia (HeFH); Atherosclerosis	**Clinical trials** ○ According to a meta-analysis of trials, cholesteryl-ester transfer-protein inhibitors—including obicetrapib—are associated with reduced cardiovascular disease-related mortality and myocardial infarction.[127] ○ Phase III trials are still ongoing.[128, 129, 130, 131, 132] **Forecasted revenue** ○ Total global annual revenue forecasted to be $582 million by 2029.*
CENTRAL NERVOUS SYSTEM		
Soticlestat Takeda Pharmaceutical Co Ltd.	Lennox-Gastaut syndrome; Dravet syndrome (severe myoclonic epilepsy of infancy)	**Clinical trials** ○ Two Phase III trials have been completed[133, 134] and others are still ongoing.[135, 136] **Forecasted revenue** ○ Total global annual revenue forecasted to be $204 million by 2029.*
Latozinemab (previously AL-001) Alector Inc.	Frontotemporal dementia (FTD)	**Clinical trials** ○ In a Phase II study, latozinemab treatment for frontotemporal dementia showed no significant impact on disease progression, although the treatment was generally safe and well-tolerated.[137] ○ The Phase III trial is still ongoing; targeted to be completed in October 2027.[138] A Phase III continuation study has been initiated.[139] ○ The U.S. FDA has granted breakthrough designation.[140] **Forecasted revenue** ○ Total global annual revenue forecasted to be $9 million by 2029.*
Valiltramiprosate (previously ALZ-801) Alzheon Inc.	Alzheimer's disease (AD)	**Clinical trials** ○ The Phase III trial completed in July 2024.[141] A long-term extension study hasbeen added.[142] **Forecasted revenue** ○ Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Update
Midomafetamine (MDMA) Lykos Therapeutics (formerly Multidisciplinary Association for Psychedelic Studies Public Benefit Corporation)	Post-traumatic stress disorder (PTSD)	**Clinical trials** ○ Another Phase III trial has been completed.[143] Two Phase III trials have been initiated in 2024.[144, 145] ○ Phase III trials to date suggest that MDMA is superior to antidepressant medications for treating PTSD.[146] ○ Lykos Therapeutics has submitted an NDA (priority review) to the U.S. FDA.[147] The FDA is convening a meeting of the Psychopharmacologic Drugs Advisory Committee on June 4, 2024, to review data.[148] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
ND-0612 (levodopa/ carbidopa for subcutaneous infusion) Neuroderm, a Mitsubishi Tanabe Pharma Corp subsidiary	Parkinson's disease (PD)	**Clinical trials** ○ Positive results from the Phase III trial have been reported[149] and published.[150] ○ The Phase III trial is ongoing (has been extended to collect long-term safety data); targeted to be completed in February 2027.[151] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
GASTROINTESTINAL DISORDERS		
Seladelpar lysine CymaBay Therapeutics Inc.	Primary biliary cholangitis (primary biliary cirrhosis)	**Clinical trials** ○ Phase III results have been published. The percentage of patients who had a biochemical response and alkaline phosphatase normalization was significantly greater with seladelpar than with placebo. It also significantly reduced pruritus among patients who had moderate-to-severe pruritus at baseline.[152] ○ Two Phase III trials were completed[153, 154] and another is ongoing.[155] ○ The U.S. FDA accepted an NDA (priority review) in February 2024; a decision is expected by August 2024.[156] **Forecasted revenue** ○ Total global annual revenue forecasted to be $478 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Update
GENETIC DISORDERS		
REC-2282 Recursion Pharmaceuticals Inc.	Neurofibromatosis type II (NF2)	**Clinical trials** ○ A Phase II/III trial is ongoing.[157] **Forecasted revenue** ○ Total global annual revenue forecasted to be $163 million by 2029.*
GENITO URINARY SYSTEM AND SEX HORMONES		
Gepotidacin mesylate GlaxoSmithKline plc	Cystitis; Urinary tract infections (UTI)	**Clinical trials** ○ It had been reported that the company expected to submit regulatory filings to the U.S. FDA in the first half of 2023.[158] It now expects to file in the second half of 2024.[159] **Forecasted revenue** ○ Total global annual revenue forecasted to be $434 million by 2029.*
HEMATOLOGICAL DISORDERS		
Bentracimab SFJ Pharmaceuticals Inc.	Bleeding and clotting disorders	**Clinical trials** ○ The company filed a BLA in August 2024. The FDA has granted a priority review.[160] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
Fitusiran Sanofi	Hemophilia A; Hemophilia B	**Clinical trials** ○ Positive results from Phase III trials, that were previously reported in press releases, have now been published.[161, 162] ○ The Phase III long-term study is ongoing, until November 2026.[163] ○ Another Phase III trial has been completed; no information on results is available at this time.[164] ○ A Phase III trial in pediatric patients is ongoing.[165] **Forecasted revenue** ○ Total global annual revenue forecasted to be $459 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Update
HORMONAL DISORDERS		
Palopegteriparatide Ascendis Pharma AS	Hypoparathyroidism	**Clinical trials** ○ The U.S. FDA review time has been extended until August 2024.[166] **Forecasted revenue** ○ Total global annual revenue forecasted to be $1.8 billion by 2029.*
IMMUNOLOGICAL DISORDERS		
Garadacimab CSL Ltd.	Hereditary angioedema (HAE) (C1 esterase inhibitor [C1-INH] deficiency)	**Clinical trials** ○ Results of the Phase III trial have been published. Results show that monthly garadacimab administration significantly reduced hereditary angioedema attacks in patients aged 12 years and older compared with placebo and had a favourable safety profile.[167] ○ One Phase III trial was completed[168] and another one is ongoing.[169] ○ The U.S. FDA accepted a BLA in December 2023; so has the EMA.[170] ○ Under review by Health Canada.[171] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
INFECTIOUS DISEASES		
Zoliflodacin Innoviva Inc.	Uncomplicated cervical and urethral gonorrhea	**Clinical trials** ○ Results of the Phase III trial have been positive.[172] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
METABOLIC DISORDERS		
Birtamimab Prothena Corp plc	Primary systemic amyloidosis	**Clinical trials** ○ Post hoc analyses from the Phase 3 VITAL trial has suggested that birtamimab plus standard of care confers a survival benefit in patients with advanced (Mayo Stage IV) AL amyloidosis.[173] ○ The Phase III confirmatory trial (AFFIRM-AL) is ongoing; targeted to be completed in June 2025.[174] **Forecasted revenue** ○ Total global annual revenue forecasted to be $283 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Update
ONCOLOGY		
Bemarituzumab Amgen Inc. 	Adenocarcinoma of the gastroesophageal junction; Gastric cancer; Bladder cancer; Gastroesophageal (GE) junction carcinomas	 **Clinical trials** o Final analysis of Phase II trial showed that the combination of bemarituzumab-mFOLFOX6 led to numerically longer median progression-free survival and overall survival compared with mFOLFOX6 alone.[175] o Phase III trials are ongoing.[176, 177] **Forecasted revenue** o Total annual global revenue forecasted to be $559 million by 2029.*
Navitoclax dihydrochloride AbbVie Inc. 	Myelofibrosis	 **Clinical trials** o Phase III trials are ongoing.[178, 179] **Forecasted revenue** o Total annual global revenue forecasted to be $496 million by 2029.*
Rusfertide acetate Protagonist Therapeutics Inc. 	Polycythemia vera (PV)	 **Clinical trials** o Results from the Phase II trial have been published. Rusfertide treatment was associated with a mean hematocrit of less than 45% during the 28-week dose-finding period, and the percentage of patients with a response during the 12-week randomized withdrawal period was greater with rusfertide than with placebo.[180] o A Phase III trial is ongoing.[181] **Forecasted revenue** o Forecasted annual global revenue unknown.
SGX-301 Hypericin sodium (synthetic hypericin) Soligenix Inc. 	Cutaneous T-cell lymphoma (CTCL)	 **Clinical trials** o The company filed an NDA in December 2022 with the U.S. FDA. Upon preliminary review, the FDA determined that the NDA was not sufficiently complete to permit substantive review.[182] After discussion with the FDA, a confirmatory Phase III trial is being undertaken.[183, 184] **Forecasted revenue** o Forecasted annual global revenue unknown.

Medicine (Trade name) Company	Indication(s)	Update
Zolbetuximab Astellas Pharma Inc.	Adenocarcinoma of the gastroesophageal junction; Gastric cancer	**Clinical trials** ○ Approved in Japan (Vyloy; March 26, 2024).[185] ○ FDA reviewed (priority review) but did not approve due to insufficiencies pertaining to a pre-license inspection at a third-party manufacturing site for the agent.[186] **Forecasted revenue** ○ Total annual global revenue forecasted to be $716 million by 2029.*
OPHTHALMOLOGY		
Lenadogene nolparvovec GenSight Biologics SA	Leber's hereditary optic neuropathy (Leber optic atrophy)	**Clinical trials** ○ The efficacy of lenadogene nolparvovec in improving visual acuity in MT-ND4 Leber hereditary optic neuropathy (LHON) was confirmed in a large cohort of patients, compared to the spontaneous natural history decline.[187] ○ Phase III trials have been completed[188, 189, 190] and one is ongoing.[191] **Forecasted revenue** ○ Forecasted annual global revenue unknown.

* Consensus forecasts for global revenue data were collected from GlobalData, Q2-2024, and are given in US dollars.

Data source: GlobalData Healthcare database.

TABLE 6.

Pipeline medicines from the 2022 Meds Pipeline Monitor that have gained market authorization

Selection criteria		
Increased safety and efficacy	Novel mechanism	Gene or cell therapy
Breakthrough	Fast Track	Priority Review

Key attributes		
Clinical trials in Canada	Rare or orphan designation	Potential evergreening
Biologic medicine	Add-on therapy	

Medicine (Trade name) Company	Indication(s)	Approval status and key attributes
CARDIOVASCULAR		
Aprocitentan (Tryvio) Idorsia Pharmaceutical Ltd.	Resistant hypertension	**Approval** ○ Approved by the U.S. FDA (Tryvio; March 19, 2024).[192] **Forecasted revenue** ○ Total global annual revenue forecasted to be $165 million by 2029.*
Sotatercept (Winrevair) Acceleron Pharma Inc.	Pulmonary arterial hypertension (PAH)	**Approval** ○ Approved by the U.S. FDA (Winrevair; March 26, 2024).[193] **Forecasted revenue** ○ Total global annual revenue forecasted to be $5.6 billion by 2029.*
DERMATOLOGY		
Beremagene geperpavec (Vyjuvek) Krystal Biotech Inc.	Epidermolysis bullosa	**Approval** ○ Approved by the U.S. FDA (Vyjuvek; May 19, 2023).[194] **Forecasted revenue** ○ Total global annual revenue forecasted to be $895 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Approval status and key attributes
GASTROINTESTINAL DISORDERS		
RBX-2660 (Rebyota) Ferring Pharmaceuticals Inc.	*Clostridium difficile* infections (*C. difficile* associated disease)	**Approval** ○ Approved by the U.S. FDA (Rebyota; November 30, 2023).[195] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
Resmetirom (Rezdiffra) Madrigal Pharmaceuticals Inc.	Metabolic dysfunction-associated steatohepatitis (MASH)	**Approval** ○ Approved by the U.S. FDA (Rezdiffra; March 14, 2024).[196] **Forecasted revenue** ○ Total global annual revenue forecasted to be $3.9 billion by 2029.*
GENETIC DISORDERS		
Delandistrogene moxeparvovec (Elevidys) Sarepta Therapeutics Inc.	Duchenne muscular dystrophy	**Approval** ○ Approved by the U.S. FDA (Elevidys; June 22, 2023).[197] **Forecasted revenue** ○ Total global annual revenue forecasted to be $3 billion by 2029.*
HEMATOLOGICAL DISORDERS		
Danicopan (Voydeya) Alexion Pharmaceuticals Inc.	Paroxysmal nocturnal hemoglobinuria (PNH)	**Approval** ○ Approved by the U.S. FDA (Voydeya; March 29, 2024).[198] ○ Under review by Health Canada.[199] **Forecasted revenue** ○ Total global annual revenue forecasted to be $302 million by 2029.*
Fidanacogene elaparvovec (Beqvez) Pfizer Inc.	Hemophilia B (factor IX deficiency)	**Approval** ○ Approved by the U.S. FDA (Beqvez; April 25, 2024).[200] **Forecasted revenue** ○ Total global annual revenue forecasted to be $516 million by 2029.*

Medicine (Trade name) Company	Indication(s)	Approval status and key attributes
IMMUNOLOGICAL DISORDERS		
Omidubicel (Omisirge) Gamida Cell Ltd.	Hematopoietic stem cell transplantation	**Approval** ○ Approved by the U.S. FDA (Omisirge; April 17, 2023).[201] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
METABOLIC DISORDERS		
Donislecel (Lantidra) CellTrans Inc.	Type 1 diabetes (juvenile diabetes)	**Approval** ○ Approved by the U.S. FDA (Lantidra; June 28, 2023).[202] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
Insulin icodec (Awiqli) Novo Nordisk AS	Type 1 diabetes (juvenile diabetes); Type 2 diabetes	**Approval** ○ Health Canada approved (Awiqli; March 12, 2024); not marketed as of June 17, 2024.[203] **Forecasted revenue** ○ Total global annual revenue forecasted to be $1 billion by 2029.*
Pegunigalsidase alfa (Elfabrio) Chiesi Farmaceutici SpA	Fabry disease (FD)	**Approval** ○ Approved by the U.S. FDA (Elfabrio; May 9, 2023).[204] ○ Approved by the EMA (Elfabrio; May 8, 2023).[205] **Forecasted revenue** ○ Forecasted annual global revenue unknown.
ONCOLOGY		
Imetelstat sodium (Rytelo) Geron Corp	Myelodysplastic syndrome; Post-essential thrombocythemia myelofibrosis (post-ET MF); Post-polycythemia vera myelofibrosis (PPV-MF)	**Approval** ○ Approved by the U.S. FDA (Rytelo; June 6, 2024).[206] **Forecasted revenue** ○ Total annual global revenue forecasted to be $1.2 billion by 2029.*

Medicine (Trade name) Company	Indication(s)	Approval status and key attributes
OPHTHALMOLOGY		
Avacincaptad pegol sodium (Izervay) Astellas Pharma Inc.	Geographic atrophy (GA)	**Approval** • Approved by the U.S. FDA (Izervay; August 4, 2023).[207] **Forecasted revenue** • Total global annual revenue forecasted to be $1.5 billion by 2029.*
WOMEN'S HEALTH		
Fezolinetant (Veozah) Astellas Pharma Inc.	Vasomotor symptoms of menopause (hot flashes)	**Approval** • Approved by the U.S. FDA (Veozah; May 12, 2023).[208] • Approved by the EMA (Veozah; December 7, 2023).[209] **Forecasted revenue** • Total global annual revenue forecasted to be $1.4 billion by 2029.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q2-2024, and are given in US dollars.

Data source: GlobalData Healthcare database.

SPOTLIGHT ON CANADA

This section includes a list of select medicines currently under review by Health Canada that may have a significant impact on future clinical practice and drug spending. Medicines included on this list may be new to Canada but have been approved in other jurisdictions.

Table 7 highlights six new medicines currently on Health Canada's Drug and Health Product SUR Lists that have a novel mechanism of action or have demonstrated improved safety and efficacy in clinical trials. Of the five medicines reported in the 2022 edition, all but one have received market authorization from Health Canada. The central nervous system drug masitinib mesylate, indicated for amyotrophic lateral sclerosis (ALS), was issued a Notice of Deficiency (2024-02), and the submission was withdrawn from Health Canada.

The SUR Lists are publicly available sources that identify pharmaceutical and biologic drug submissions with new medicinal ingredients that have been accepted for review in Canada.

TABLE 7.
Selected new medicines currently under review by Health Canada, 2023

Selection criteria

- Increased safety and efficacy
- Novel mechanism
- Gene or cell therapy

Key attributes

- Breakthrough
- Fast Track
- Priority Review
- Clinical trials in Canada
- Rare or orphan designation
- Biologic medicine
- Add-on therapy

Medicine (Trade name) Company	Anticipated indication(s)†	Description and key attributes
IMMUNOLOGICAL DISORDERS		
Leniolisib **Joenja (U.S.)** Pharming Technologies BV	Activated phosphoinositide 3-kinase delta syndrome (APDS)	○ It is a PI3K-δ selective inhibitor.[210] ○ Administered orally. ○ Approved by the U.S. FDA (Joenja tablets; March 24, 2023) for APDS.[211] **Clinical trials** ○ Based on an interim analysis of an ongoing open-label, single-arm extension study, it was well tolerated and maintained durable outcomes with up to 5 years of exposure in 37 patients with APDS.[212] ○ No other therapy for APDS was identified in Phase II development at this time.[213] **Forecasted revenue** ○ Total global annual revenue forecasted to be $260 million by 2029.*
Tapinarof **Vtama (U.S.)** Dermavant Sciences GmbH	Plaque psoriasis	○ It is a non-steroidal, topical, aryl hydrocarbon receptor (AhR) agonist.[214] ○ Administered topically once a day. ○ Approved by the U.S. FDA (Vtama; May 23, 2022) for the topical treatment of plaque psoriasis in adults.[215] **Clinical trials** ○ Clinical trials demonstrated high rates of complete skin clearance with tapinarof cream, durable effects while on treatment (a lack of tachyphylaxis for up to 52 weeks), an approximately 4-month remittive effect off therapy after achieving complete clearance and stopping treatment (i.e., duration during which psoriasis does not recur off therapy), and no rebound effects after cessation of therapy.[216] ○ There are other drugs in Phase II development (n>10), but none with the same mechanism of action as tapinarof. See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $790 million by 2029.*

Medicine (Trade name) Company	Anticipated indication(s)†	Description and key attributes
ONCOLOGY		
Avapritinib **Ayvakit (U.S.)** Blueprint Medicines Corporation	Gastrointestinal stromal tumor (GIST)	 • It is a selective tyrosine kinase inhibitor (TKI) targeting KIT D816V. • Administered orally. • Approved by the U.S. FDA (Ayvakit; tablets on June 16, 2021) for mastocytosis.[217] Approved by the EMA (Ayvakit; September 30, 2020).[218] **Clinical trials** • In a Phase II trial, it was superior to placebo in reducing uncontrolled symptoms and mast-cell burden in patients with indolent systemic mastocytosis.[219] • No other therapy for systemic mastocytosis was identified in Phase II development at this time.[220] **Forecasted revenue** • Forecasted annual global revenue $1.6 billion by 2029.*
Ivosidenib **Tibsovo (U.S.)** Servier Canada Inc.	Acute myeloid leukemia (AML)	 • It is a selective, allosteric, isocitrate dehydrogenases 1 and 2 (IDH1 and IDH2) inhibitor.[221] • Administered orally. • Approved by the U.S. FDA (Tibsovo; May 25, 2022) in combination with azacitidine (azacitidine for injection) for newly diagnosed AML with a susceptible IDH1 mutation, as detected by an FDA-approved test in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.[222] Approved by the EMA (Tibsovo; May 12, 2023).[223] **Clinical trials** • Clinical data highlighted its favourable safety profile, as a stand-alone therapy and in combination strategy. [224] • In a comparison of real-world outcomes with common first-line regimens for IDH1-mutated AML, ivosidenib plus a hypomethylating agent was associated with better outcomes than venetoclax plus a hypo-methylating agent.[225] • There are other drugs in Phase II development (n>10), but none with the same mechanism of action as ivosidenib. See Appendix A for additional information. **Forecasted revenue** • Forecasted annual global revenue $29 million by 2029.*

Medicine (Trade name) Company	Anticipated indication(s)†	Description and key attributes
Momelotinib dihydrochloride monohydrate Ojjaara (U.S.) Omjjara (EMA) GlaxoSmithKline Inc.	Myelofibrosis (MF)	○ It is an inhibitor of Janus kinase 1 (JAK1) and JAK2 and also an inhibitor of activin A receptor type 1 (ACVR1), a key regulator of iron homeostasis. ○ Administered orally, once a day. ○ Approved by the U.S. FDA (Ojjaara; September 15, 2023) for myelofibrosis patients with anemia.[226] Approved by the EMA (Omjjara; February 8, 2024).[227] **Clinical trials** ○ Clinical trials have demonstrated its efficacy in reducing spleen size, alleviating symptoms, and improving anemia, with a favourable safety profile compared to other JAK inhibitors, both in treatment-naïve and in pre-treated patients.[228, 229] ○ In anemic subgroups, momelotinib was associated with higher rates of transfusion independence and reduced/stable transfusion intensity vs. ruxolitinib.[230] ○ In addition to these benefits, it conferred notable survival outcomes in both JAK inhibitor-naïve and ruxolitinib-pretreated patients.[231] ○ There are other drugs in Phase II development (n>10), but none with the same dual mechanism of action as momelotinib. See Appendix A for additional information. **Forecasted revenue** ○ Total global annual revenue forecasted to be $939 million by 2029.*
OPHTHALMOLOGY		
Perfluorohexyl-octane Miebo (U.S.) Bausch & Lomb Inc.	Keratoconjunctivitis sicca (dry eye)	○ It is a s a semifluorinated alkane. It forms a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation. ○ Administered as topical ophthalmic drops. ○ Approved by the U.S. FDA (Miebo; May 19, 2023) for the treatment of dry eye disease.[232] **Clinical trials** ○ Compared with use of hypotonic saline solution, instillation of perfluorohexyloctane led to significant improvements in signs and symptoms in as early as 2 weeks. In a long-term, open-label safety extension study, efficacy of perfluorohexyloctane was sustained over 12 months, and the safety profile was consistent with those of previous studies. Clinical trial results indicate that treatment with perfluorohexyloctane effectively and consistently reduces the signs and symptoms of DED.[233] ○ There are other drugs in Phase II development (n>10), but none with the same mechanism of action as perfluorohexyloctane. See Appendix A for additional information. **Forecasted revenue** ○ Forecasted annual global revenue unknown.

* Consensus forecasts for global revenue data were collected from GlobalData, Q2-2024, and are given in US dollars.

† Health Canada's Drug and Health Product Submissions Under Review Lists provide the therapeutic area for the medicine under review but do not specify the indication. The indication listed in Table 7 is based on the information about the medicine in the literature and/or approvals in other jurisdictions. When there is an aligned review, in some cases the indication was confirmed by the CDA Reimbursement Review report.

Data source: GlobalData Healthcare database.

APPENDIX A

TABLE A1.
Biosimilars in Phase III or preregistration (based on data extract from 2024-04-03)

Medicine	Reference product in Canada	Other biosimilars marketed in Canada at this time (Y/N) and biosimilars under review by HC		Companies developing a biosimilar	Indication
Aflibercept	Eylea (Bayer Inc.)	N	Under HC review (as of Apr 3): • Amgen Canada Inc. • Apotex Inc. • Biosimilar Collaborations Ireland Ltd. • Celltrion HealthCare Co Ltd.	Alteogen Inc. Celltrion Inc. Formycon AG Sam Chun Dang Pharm Co Ltd.	Wet (neovascular/exudative) macular degeneration
				Amgen Inc.	Macular edema
				Celltrion Inc.	Age related macular degeneration
				Celltrion Inc.	Choroidal neovascularization
				Celltrion Inc.	Cystoid macular edema; Diabetic macular edema
Bevacizumab	Avastin (Hoffmann-La Roche Limited)	Y		Prestige BioPharma Ltd.	Non-small cell lung cancer
Denosumab	Prolia/Xgeva (Amgen Canada Inc.)	N	Under HC review (as of Apr 3): • Sandoz Canada Inc. (approved 2024-02-16 but not yet marketed)	Alvotech SA Biocon Ltd. Celltrion Inc. Eden Biologics Inc. Fresenius Kabi SwissBioSim GmbH Gedeon Richter plc I'rom Group Co Ltd. (Japan) Shanghai Henlius Biotech Inc.	Post menopausal osteoporosis
				Biocon Ltd.	Bone fracture
				Biocon Ltd.	Bone metastasis

Medicine	Reference product in Canada	Other biosimilars marketed in Canada at this time (Y/N) and biosimilars under review by HC		Companies developing a biosimilar	Indication
Eculizumab	Soliris (Alexion Pharma GmbH)	N	Under HC review (as of Apr 3): ○ Amgen Canada Inc. ○ Samsung Bioepis Co., Ltd.		Paroxysmal nocturnal hemoglobinuria
Filgrastim	Neulasta (Amgen Canada Inc.)	Y	Under HC review (as of Apr 3): ○ Curateq Biologics Private Limited		Chemotherapy induced neutropenia
Ocrelizumab	Ocrevus (Hoffmann-La Roche Limited)	N		Celltrion Inc.	Relapsing remitting multiple sclerosis (RRMS)
Omalizumab	Xolair (Novartis Pharmaceuticals Canada Inc.)	N	Under HC review (as of Apr 3): ○ Celltrion Healthcare Co Ltd.	Celltrion Inc.	Allergic asthma
				Celltrion Inc.	Chronic urticaria or hives
				Celltrion Inc.	Nasal polyps (nasal polyposis); Rhinosinusitis
				Celltrion Inc.	Food allergy
Pegfilgrastim	Neulasta (Amgen Canada Inc.)	Y	Under HC review (as of Apr 3): ○ Curateq Biologics Private Limited ○ JAMP Pharma Corporation ○ Lupin Pharma Canada Limited ○ Nora Pharma Inc.	Curateq Biologics Pvt Ltd.	Chemotherapy induced neutropenia
Pertuzumab	Perjeta (Hoffmann-La Roche Limited)	N		Shanghai Henlius Biotech Inc.	Human epidermal growth factor receptor 2 positive breast cancer (HER2+ breast cancer)
Ranibizumab	Lucentis (Novartis Pharmaceuticals Canada Inc.)	Y		Lupin Ltd.	Wet (neovascular/exudative) macular degeneration
Rituximab	Rituxan (Hoffmann-La Roche Limited)	Y	Under HC review (as of Apr 3): ○ Dr. Reddy's Laboratories SA		Non-Hodgkin's lymphoma; chronic lymphocytic leukemia; rheumatoid arthritis; granulomatosis with polyangiitis and microscopic polyangiitis

Medicine	Reference product in Canada	Other biosimilars marketed in Canada at this time (Y/N) and biosimilars under review by HC		Companies developing a biosimilar	Indication
Tocilizumab	Actemra (Hoffmann-La Roche Limited)	N	Under HC review (as of Apr 3): ○ Fresenius Kabi Canada Ltd.	Celltrion Inc. Mochida Pharmaceutical Co Ltd.	Rheumatoid arthritis
Trastuzumab	Herceptin (Hoffmann-La Roche Limited)	Y	Under HC review (as of Apr 3): ○ Accord Healthcare Inc.	Prestige BioPharma Ltd.	Human epidermal growth factor receptor 2 positive breast cancer (HER2+ breast cancer)
				Prestige BioPharma Ltd.	Adenocarcinoma of the gastroesophageal junction
				Prestige BioPharma Ltd.	Gastric cancer
Ustekinumab	Stelara (Janssen Inc.)	N	Under HC review (as of Apr 3): ○ Celltrion Healthcare Co Ltd. ○ Samsung Bioepis Co,. Ltd..	Biocon Ltd. Samsung Bioepis Co Ltd.	Psoriatic arthritis
				Biocon Ltd. Formycon AG Samsung Bioepis Co Ltd. STgen Bio Co Ltd.	Plaque psoriasis (psoriasis vulgaris)
				Biocon Ltd. Samsung Bioepis Co Ltd.	Crohn's disease (regional enteritis)
				Samsung Bioepis Co Ltd.	Ulcerative colitis

TABLE A2.
Drugs in Phase II for indications targeted by pipeline candidates, 2023

Pipeline candidate	Indication	Drugs in Phase II and mechanism of action (MoA)*
ABBVCLS-7262	Amyotrophic lateral sclerosis (ALS)	Drugs in Phase II for this indication and their MoA: • 1 phosphatidylinositol 3 phosphate 5 kinase inhibitor (apilimod); • 70 kDa ribosomal protein S6 kinase inhibitor/serine/threonine protein kinase mTOR inhibitor(monepantel); • Akt pathway activator (IPL-344, NA-704, RNS-60); • antioxidant (EH-301); • apoptosis regulator BAX Inhibitor/free radical scavenger/ insulin like growth factor I and II activator/ insulin receptor agonist/protein kinase B activator (GM-6); • arachidonate 15 lipoxygenase inhibitor (utreloxastat); • ataxin 2 inhibitor (ION-541); • boosts regulatory T-cells (COYA-101); • CD40 ligand inhibitor (tegoprubart); • cell therapy (AstroRx); • cholinergic receptor muscarinic antagonist (scopolamine); • coagulation factor V and factor VIII inhibitor (3K3A-APC); • combination (celecoxib + ciprofloxacin); • D2 and D3 dopamine receptor agonist (ropinirole); • gene therapy (Gene Therapy to Activate GDNF for Amyotrophic Lateral Sclerosis and Retinitis Pigmentosa); • glucocorticoid receptor antagonist (dazucorilant); • ikappaB kinase inhibitor / nuclear factor kappa B inhibitor (acetylcysteine zidrimer); • macrophage activator (NP-001); • macrophage colony stimulating factor 1 receptor antagonist (sotuletinib); • mitochondrial-targeted neuroprotector (MP-101); • oxidoreductase enzyme inhibitor (EPI-589); • protein phosphatase 1 regulatory subunit 15A inhibitor (icerguastat); • reverse transcriptase inhibitor (censavudine); • superoxide dismutase activator (AP-101); • others with undisclosed mechanism of action (TM-700). There are no other drugs targeting this indication with the same MoA as ABBVCLS-7262 (a eukaryotic translation initiation factor 2 subunit beta activator) in Phase II development at this time.
AD109 (atomoxetine + R-oxybutynin)	Obstructive sleep apnea (OSA)	There are no other drugs targeting this specific indication in Phase II development at this time.
Aficamten	Hypertrophic cardiomyopathy	There are no other drugs targeting this specific indication in Phase II development at this time.
Brensocatib	Bronchiectasis	Drugs in Phase II for this indication and their MoA: • mitogen activated protein kinase inhibitor (MGS-2525); • neutrophil elastase inhibitor (alvelestat); • synthetic phage (AP-PA02). There are no other drugs targeting this indication with the same MoA as brensocatib (a dipeptidyl peptidase 1 inhibitor) in Phase II development at this time.
Datopotamab deruxtecan	Breast cancer, both HR-positive/ HER2-negative and triple-negative	Drugs in Phase II for this indication and their MoA: • gene-modified cell therapy (huMNC2-CAR22, huMNC2-CAR44); • prolyl endopeptidase FAP inhibitor (AAA-614); • vaccine (nelipepimut-S). There are no other drugs for all types of breast cancer targeted by datopotamab (a TROP2-targeted antibody-drug conjugate) in Phase II development at this time.

Pipeline candidate	Indication	Drugs in Phase II and mechanism of action (MoA)*
Efruxifermin	Metabolic dysfunction-associated steatohepatitis (MASH)	Drugs in Phase II for this indication and their MoA: o 1-acylglycerol 3 phosphate o acyltransferase PNPLA3 inhibitor (AZD-2693); o 5-lipoxygenase inhibitor (epeleuton); o acetyl CoA carboxylase inhibitor; diacylglycerol O acyltransferase 2 inhibitor (combination of clesacostat tromethamine + ervogastat); o AMP activated protein kinase activator; cGMP specific 3',5' cyclic PDE inhibitor; NAD dependent protein deacetylase sirtuin 1 activator (combination of leucine + metformin hydrochloride + sildenafil citrate); o androgen receptor agonist (LPCN-1144); o arachidonate 5 inhibitor; leukotriene receptor antagonist; PDE 3, 4 inhibitor; phospholipase C inhibitor; thromboxane A2 receptor antagonist (tipelukast); o bile acid receptor agonist (CS-0159, HPG-1860, TERN-101); o cell therapy (HepaStem); o cholesterol and triglyceride synthesis dual inhibitor (gemcabene); o cytochrome P450 2E1 inhibitor; diacylglycerol O acyltransferase 1 inhibitor; hormone sensitive lipase activator (SNP-610); o focal adhesion kinase inhibitor (narmafotinib); o GLP 1 receptor agonist; glucagon receptor agonist (AZD-9550, efinopegdutide, efocipegtrutide, pemvidutide); o glucose dependent insulinotropic receptor agonist (DA-1241); o high mobility group protein B1 activator (redasemtide trifluoroacetate); o lipid modulator (berberine ursodeoxycholate); o mitochondrial pyruvate carrier inhibitor (PXL-065); o peptidyl prolyl cis trans isomerase A, B & F mitochondrial inhibitor(rencofilstat); o thyroid hormone receptor beta agonist (ALG-009, TERN-501, VK-2809). There is one other drug (NN-9499) targeting this indication with the same MoA as efruxifermin (a fibroblast growth factor receptor agonist) in Phase II development at this time.
Ensifentrine	Chronic obstructive pulmonary disease	Drugs in Phase II for this indication and their MoA: o 5-lipoxygenase inhibitor (epeleuton); o adenosine receptor A1 antagonist (PBF-680); o beta 1 and 2 adrenergic receptor antagonist (nadolol); o complement C1q subcomponent inhibitor (RLS-0071); o macrophage metalloelastase inhibitor (aderamastat); o myristoylated alanine rich C kinase substrate inhibitor (BIO-11006); o toll like receptor 2, 6, 9 agonist (PUL-042); o vaccine, inactivated (HI-1640V). There are no other drugs targeting this indication with the same MoA as ensifentrine (a PDE 3 and 4 inhibitor) in Phase II development at this time.
Fazirsiran	Alpha-1 antitrypsin deficiency (A1AD)	Drugs in Phase II for this indication and their MoA: o neutrophil elastase inhibitor (alvelestat). There are other drugs (belcesiran, INBRX-101) targeting this indication with the same MoA as fazirsiran (an alpha 1 antitrypsin Inhibitor) in Phase II development at this time.
Gemcitabine (GemRIS, TAR-200)	Non-muscle invasive bladder cancer (NMIBC) (superficial bladder cancer); Muscle invasive bladder cancer (MIBC)	Drugs in Phase II for these indications and their MoA: o vaccine (lerapolturev). There is no other drug targeting both indications with the same MoA as gemcitabine (a ribonucleoside diphosphate reductase large subunit inhibitor) in Phase II development at this time.

Pipeline candidate	Indication	Drugs in Phase II and mechanism of action (MoA)*
Iclepertin	Kidney transplant rejection	Drugs in Phase II for this indication and their MoA: • CD40 ligand inhibitor (tegoprubart[viii]); • critical regulator of the microtubule motor cytoplasmic dynein (LIS-1); • gene-modified cell therapy (TX-200); • T cell specific surface glycoprotein CD28 antagonist (FR-104); • T cell surface antigen CD2 inhibitor (siplizumab). There is no other drug targeting this indication with the same MoA as iclepertin (a sodium and chloride dependent glycine transporter 1 inhibitor) in Phase II development at this time.
Inaxaplin	Focal segmental glomerulosclerosis	Drugs in Phase II for this indication and their MoA: • B lymphocyte antigen CD19 inhibitor (VB-119); • lipid modifier (R3R01). There is no other drug targeting this indication with the same MoA as inaxaplin (an apolipoprotein L1 inhibitor) in Phase II development at this time.
Nerinetide	Acute ischemic stroke	Drugs in Phase II for this indication and their MoA: • antioxidant (LT-3001); • apoptosis regulator BAX inhibitor/ free radical scavenger/ insulin like growth factor I and II activator/ insulin receptor agonist/ protein kinase B activator (GM-6); • bifunctional epoxide hydrolase 2 inhibitor (JX-10); • cell therapy (it-hMSC, NCS-01, ReN-001); • high mobility group protein B1 activator (redasemtide); • oxygen carrier (perflenapent); • repulsive guidance molecule a inhibitor (elezanumab); • others with undisclosed mechanism of action (RNS-60). There is no other drug targeting this indication with the same MoA as nerinetide (a neuroprotective eicosapeptide) in Phase II development at this time.
Obefazimod	Ulcerative colitis	Drugs in Phase II for this indication and their MoA: • adenosine receptor A1/A3 antagonist (PBF-677); • bacteria replacement/microbiome modulator (BGP-014, VE-202A); • calcineurin inhibitor (cyclosporine CR); • cAMP specific 3',5' cyclic PDE 4B/4D inhibitor (orismilast); • E3 ubiquitin protein ligase pellino homolog 1 inhibitor (BBT-401); • integrin alpha 4/ beta 7 antagonist (MORF-057); • interleukin 1 alpha/ beta inhibitor (lutikizumab); • interleukin 2 receptor agonist (PT-101); • interleukin 7 receptor subunit alpha antagonist (lusvertikimab); • lanC like protein 2 agonist (omilancor); • melanocyte stimulating hormone receptor agonist (PL-8177); • microbial-derived immunotherapy (QBECO[ix]); • neuroimmune modulator (HM-201); • prostaglandin G/H synthase inhibitor (combination of mesalamine + hyaluronate sodium); • P selectin glycoprotein ligand 1 activator (AbGn-268); • sphingosine 1-phosphate receptor 1 agonist (amiselimod, icanbelimod); • toll like receptor 9 agonist (cobitolimod); • TNF ligand superfamily member 15 inhibitor (RG-6631); • others with undisclosed mechanism of action (KSP-0243). There is no other drug targeting this indication with the same MoA as obefazimod (a eukaryotic translation initiation factor 4E inhibitor/ interleukin 22 receptor agonist) in Phase II development at this time.

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Pipeline candidate	Indication	Drugs in Phase II and mechanism of action (MoA)*
Patidegib	Gorlin syndrome (basal cell nevus syndrome/ nevoid basal cell carcinoma syndrome)	Drugs in Phase II for this indication and their MoA: o serine/threonine protein kinase mTOR inhibitor (sirolimus). There is no other drug targeting this indication with the same MoA as patidegib (a hedgehog signaling pathway blocker) in Phase II development at this time.
Pelacarsen sodium	Cardiovascular disease; Hyperlipidemia	Drugs in Phase II for this indication and their MoA: o angiopoietin related protein 3 inhibitor (solbinsiran, zodasiran); o cholesterol and triglyceride synthesis dual inhibitor (gemcabene); o Niemann Pick C1 like protein 1 inhibitor (KT-6971); o proprotein convertase subtilisin/kexin type 9 inhibitor (AZD-0780). There is no other drug targeting the hyperlipidemia indication with the same MoA as pelacarsen (an apolipoprotein A inhibitor) in Phase II development at this time.
Prademagene zamikeracel	Epidermolysis bullosa	Drugs in Phase II for this indication and their MoA: o bacterial biofilm/growth inhibitor / intermediate filament protein modulator (Tolasure); o high mobility group protein B1 activator (redasemtide trifluoroacetate); o others with undisclosed mechanism of action (RLF-TD011). There is one drug (PTR-01) targeting this indication with the same MoA as prademagene zamikeracel (a collagen type 7 replacement) in Phase II development at this time.
Resiniferatoxin	Osteoarthritis pain	Drugs in Phase II for this indication and their MoA: o adenosine receptor A3 agonist (NTM-006); o C-C chemokine receptor type 2 antagonist (CNTX-6970); o C-C motif chemokine 17 inhibitor (GSK-3858279); o glucocorticoid receptor agonist (fluticasone); o high affinity nerve growth factor receptor inhibitor (AK-1830); o PG E2 receptor EP4 subtype antagonist (grapiprant); o PG G/H synthase 1 and 2 inhibitor (otenaproxesul); o sodium channel protein type 10 subunit alpha blocker (VX-150); o others with undisclosed mechanism of action (S-120083, TTAX-03). There is one other drug (CGS-2005) targeting this indication with the same MoA as resiniferatoxin (a transient receptor potential cation channel subfamily v member 1 activator) in Phase II development at this time.
Revumenib	Acute lymphocytic leukemia (ALL); Acute lympho-blastic leukemia; Refractory acute myeloid leukemia; Relapsed acute myeloid leukemia	Drugs in Phase II for these indications and their MoA: o anti-CD123 antibody alkylating agent (pivekimab sunirine); o butyrophilin subfamily 3 member A1 activator (ICT-01); o cell therapy (ECT-001, SMART-101); o protein kinase B inhibitor (PTX-200). There are other drugs (DS-1594b, DSP-5336, ziftomenib) targeting all indications with the same MoA as revumenib (a menin-mixed lineage leukemia inhibitor) in Phase II development at this time.

Pipeline candidate	Indication	Drugs in Phase II and mechanism of action (MoA)*
RGX-121	Mucopoly-saccharidosis II (MPS II) (Hurler syndrome)	Drugs in Phase II for this indication and their MoA: o alpha L-iduronidase replacement (AGT-181, lepunafusp alfa); o CCAAT/enhancer binding protein alpha activator (MTL-CEBPA); o chondrocyte metabolism stimulator (pentosan polysulfate sodium). There is one other drug (RGX-111) targeting this indication with the same MoA as RGX-121 (an iduronate 2 sulfatase activator) in Phase II development at this time.
Xanomeline-trospium (KarXT)	Schizophrenia; Psychosis	Drugs in Phase II for this indication and their MoA: o 5-hydroxytryptamine receptor 2A antagonist / D2 dopamine receptor antagonist (risperidone 6-12 month formulation). There are other drugs (ANAVEX-371, NBI-1117568, RL-007) targeting the schizophrenia indication with the same MoA as xanomeline-trospium (a muscarinic acetylcholine receptor agonist) in Phase II development at this time.

Abbreviations:

AMP: adenosine monophosphate; GABA: gamma-aminobutyric acid ; GLP: glucagon like peptide; GSK: glycogen synthase kinase; PDE: phosphodiesterase; PG: prostaglandin; PPAR: peroxisome proliferator activated receptor; TNF: tumour necrosis factor.

* Data source: GlobalData's Healthcare database (accessed April 2024).

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