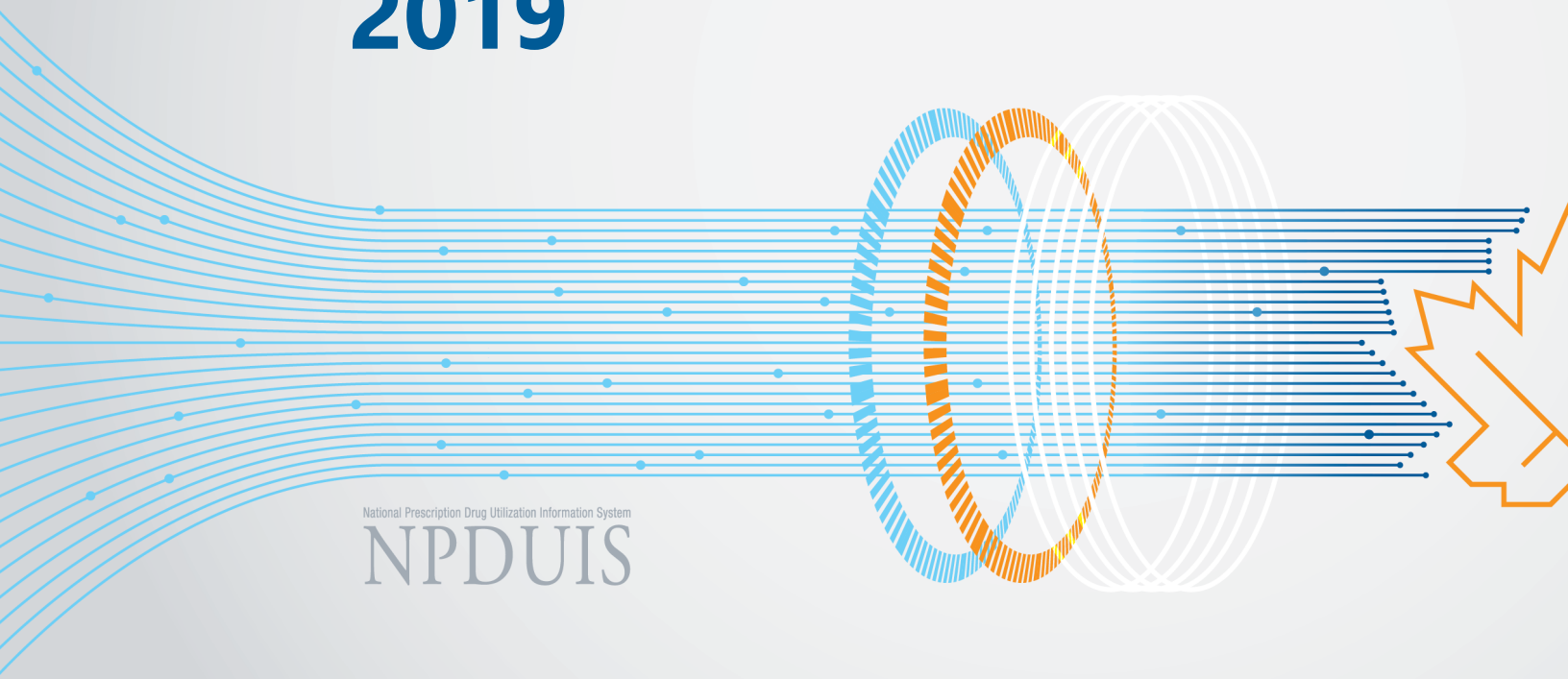
Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

MEDS

PIPELINE MONITOR 2019



National Prescription Drug Utilization Information System

NPDUIS

Canada

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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) is a research initiative 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, the Canadian Agency for Drugs and Technologies in Health (CADTH), 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

NPDUIS operates independently of the regulatory activities of the Board of the PMPRB. The research priorities, data, statements, and opinions expressed or reflected in NPDUIS reports do not represent the position of the PMPRB with respect to any regulatory matter. NPDUIS reports do not contain information that is confidential or privileged under sections 87 and 88 of the *Patent Act*, and the mention of a medicine in a NPDUIS report is not and should not be understood as an admission or denial that the medicine is subject to filings under sections 80, 81, or 82 of the *Patent Act* or that its price is or is not excessive under section 85 of the *Patent Act*.

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EXECUTIVE SUMMARY

Meds Pipeline Monitor (MPM) is a horizon scanning report that features a selection of new medicines in the late stages of clinical evaluation that may have a significant impact on future clinical practice and drug spending in Canada.

Medicines in Phase III clinical trials or in pre-registration with the US Food and Drug Administration (FDA) are considered as candidates if they have the potential to address an unmet therapeutic need, offer a novel mechanism or therapeutic benefit over existing therapies, or treat a serious condition. The final selection features medicines that treat a broad range of therapeutic areas. In addition to identifying new medicines for inclusion in the list, this edition monitors the medicines featured in the 2018 *Meds Pipeline Monitor* to report on changes to their status in the pipeline. A new section focused on Canada highlights potentially significant medicines currently under review by Health Canada.

The report collects data from two main sources: GlobalData's Healthcare database is used to identify medicines currently undergoing clinical evaluation, while Health Canada's Drug and Health Product Submissions Under Review list provides information on new medicines under assessment in Canada.

Together with its companion publication *Meds Entry Watch*, this report series monitors the continuum of new and emerging medicines in Canada and internationally, providing key information to decision makers, researchers, patients, and clinicians, among other stakeholders.

Highlights of the Meds Pipeline 2019

- In 2019, the pipeline contained 5,584 new medicines in various stages of evaluation.
- Oncology dominated the therapeutic mix, with cancer treatments representing over one third (35%) of medicines in all phases of clinical trials. Therapies for central nervous system diseases such as Alzheimer's disease and depression accounted for 14% of medicines in clinical trials.
- Nervous system treatments represented the greatest share (19%) of medicines in pre-registration with the FDA in 2019, exceeding the 15% share held by oncology.
- Of the 5,584 new medicines in the pipeline, 697 (12%) were in Phase III clinical trials and FDA pre-registration, representing a wide range of therapeutic areas. One third of these late-stage medicines had an early orphan designation approved through the FDA or EMA, which is consistent with the increasing trend in the prevalence of orphan-designated medicines entering the pharmaceutical market.
- Eight late-stage new medicines, including two gene therapies, were selected for addition to the 2019 MPM list based on their potential impact on the Canadian healthcare system. Some of these medicines may offer breakthroughs in treating previously unmet needs or may have the potential to treat large patient populations.
- Of the 30 new medicines featured in the 2018 edition of the MPM, 16 were retained on the list as they continue to satisfy the selection criteria. Five medicines, including the FDA Breakthrough-designated treatment for spinal muscular atrophy Zolgensma, had been granted market authorization by the US FDA, the EMA, and/or Health Canada as of January 2020.
- The report also highlights nine new medicines currently under review by Health Canada. Of these, more than half had forecasted global revenues nearing or exceeding $1 billion by 2025.

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LIST OF TERMS

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

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.

MEDICINE PIPELINE: A set of new medicine candidates under active research and development by biotechnology and pharmaceutical companies.

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

PHASE III CLINICAL TRIALS: Controlled or uncontrolled trials conducted after preliminary evidence suggesting efficacy of the drug has been demonstrated. These are intended to gather the additional and confirmatory information about the clinical efficacy and safety under the proposed conditions of use for the drug.[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.[v]

[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] http://www.pmprb-cepmb.gc.ca/en/npduis/view.asp?ccid=1310&lang=en

[v] http://www.appliedclinicaltrialsonline.com/are-phase-labels-still-relevant

INTRODUCTION

This ninth edition of the *Meds Pipeline Monitor* (MPM) is a continuation of the horizon scanning research formerly published under the title *New Drug Pipeline Monitor*. It features a selection of medicines in Phase III clinical trials or in pre-registration with the US Food and Drug Administration (FDA) that have the potential to significantly impact clinical practice and drug spending in Canada. This edition also includes a new Spotlight on Canada section that highlights potentially significant new drug submissions currently under review by Health Canada.

The methodology, which is detailed in the next section, uses a specific set of criteria to identify a list of pipeline candidates from the GlobalData Healthcare database, as well as a list of candidates currently under review in Canada from Health Canada's Drug and Health Product Submissions Under Review (SUR) lists. Medicines reported in the previous edition are also reviewed for this edition, including those that continue to qualify for the list of candidates as well as those that have since received market authorization. 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 entire pipeline, with an emphasis on the therapeutic breakdown of each phase of clinical evaluation. It also identifies trends observed across the pipeline in 2019.

Meds Pipeline Monitor is a companion publication to *Meds Entry Watch*, which analyzes the market dynamics 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 pipeline captures the composition of medicines in various phases of clinical evaluation at a single point in time. For the purpose of this analysis, a full list of pipeline medicines was retrieved from GlobalData's Healthcare database in September 2019.

New medicinal ingredients are identified as those with no prior approvals through the US Food and Administration (FDA), the European Medicines Agency (EMA), or Health Canada, while existing medicinal ingredients include previously approved medicines that are undergoing assessment for additional indications.

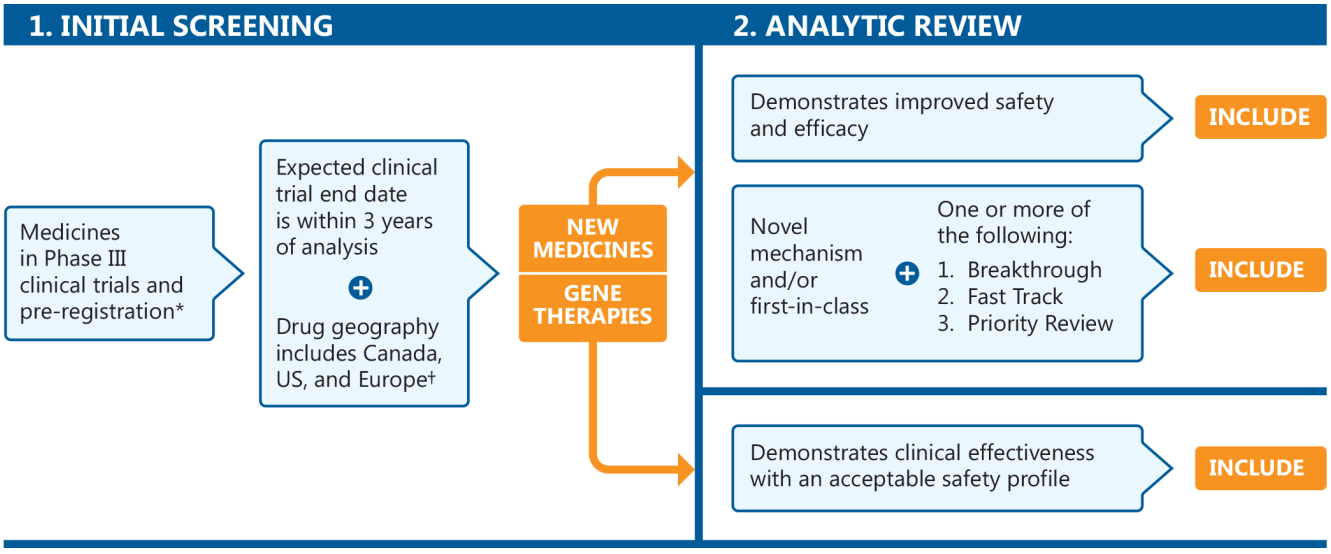
The distribution of new medicines by therapeutic area corresponds to the indication under evaluation, as reported by GlobalData. Note that a single new medicine may be undergoing multiple clinical studies for separate indications.

Meds Pipeline Monitor

The MPM focuses on new medicines in Phase III clinical trials in Canada, the United States, and Europe, or in pre-registration with the FDA. 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. The second stage considers a specific set of criteria, in addition to the results of a thorough review of clinical evidence and scientific literature.

This methodology is reviewed annually and refined as required.

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, United States, or geographic Europe (excluding Russia and Turkey).

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 with the FDA. 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 Turkey). 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.

The selection process groups pipeline candidates into two categories: (a) new medicines and (b) new gene therapies. As illustrated in Figure 1, the initial screening process for both groups is the same, but the analytic review stage is slightly different, as the available data for gene therapies is limited.

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.

Gene therapies are selected using a broader approach, as the clinical evidence available for this group is relatively limited. A gene therapy is retained on the list if the preliminary (or completed) results from Phase III trials suggest that there is evidence of clinical effectiveness with an acceptable safety profile.

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

SELECTION CRITERIA
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 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

Additional descriptive information

A profile of each successful pipeline candidate is provided, including a brief outline of 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 the 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 Institute 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	

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 have additional indications at various phases of clinical evaluation that are not mentioned in this report. The scientific description provided applies directly to the specified indication(s) for the selected medicines.

Spotlight on Canada

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

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 US FDA or the EMA.

Selection Criteria

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

Gene therapies are selected using a broader approach, based on the available clinical evidence for this group. A gene therapy is retained on the list if the preliminary (or completed) results from Phase III trials suggest that there is evidence of clinical effectiveness with an acceptable safety profile.

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 / 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 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

Additional descriptive information

As in the pipeline lists, the profile of each medicine under review includes the key attributes listed in Table 2, as well as a brief outline of 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 provided applies directly to 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, including the clinical trial end date. 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: phase of clinical development, therapeutic area, molecule type, indication, drug geography, mechanism of action, and FDA designations.

The Health Canada 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), US FDA, the EMA, and Health Canada; and information in Health Canada's ClinicalTrials 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 Turkey). 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 US 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.

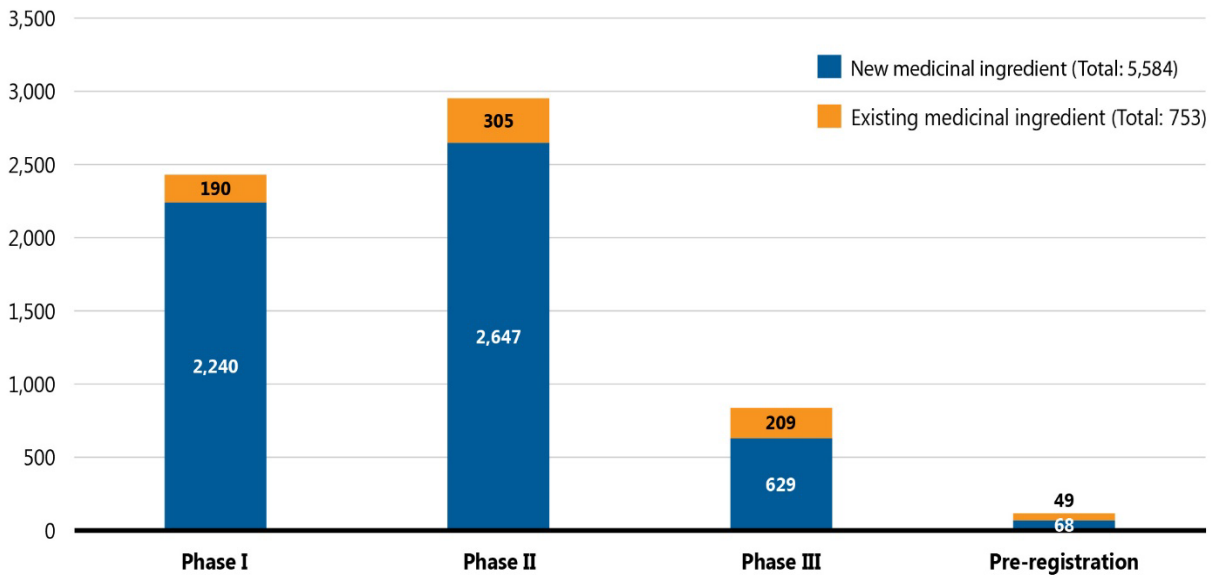
The featured lists capture the composition of the pipeline as of September 2019 and are validated as of the end of January 2020. Due to the unpredictability and fast-moving nature of pipeline medicines entering the market, some of the medicines listed in this edition may have been approved or marketed in Canada, United States, 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 and these, along with the rest of the drug pipeline will be considered for the next edition of the report.

SNAPSHOT OF THE 2019 PIPELINE

Pharmaceutical innovation is transforming the development and application of medical treatments worldwide. Over 5,500 new medicines were in clinical evaluation or in pre-registration with the FDA in 2019, representing 88% of the total pipeline.

Figure 2 provides a snapshot of the pipeline in 2019, including the number of new medicinal ingredients in each phase of clinical evaluation. Of the 5,584 new medicines, 697 (12%) were in Phase III clinical trials or in pre-registration with the FDA.

FIGURE 2. Number of pipeline medicines in each stage of clinical evaluation

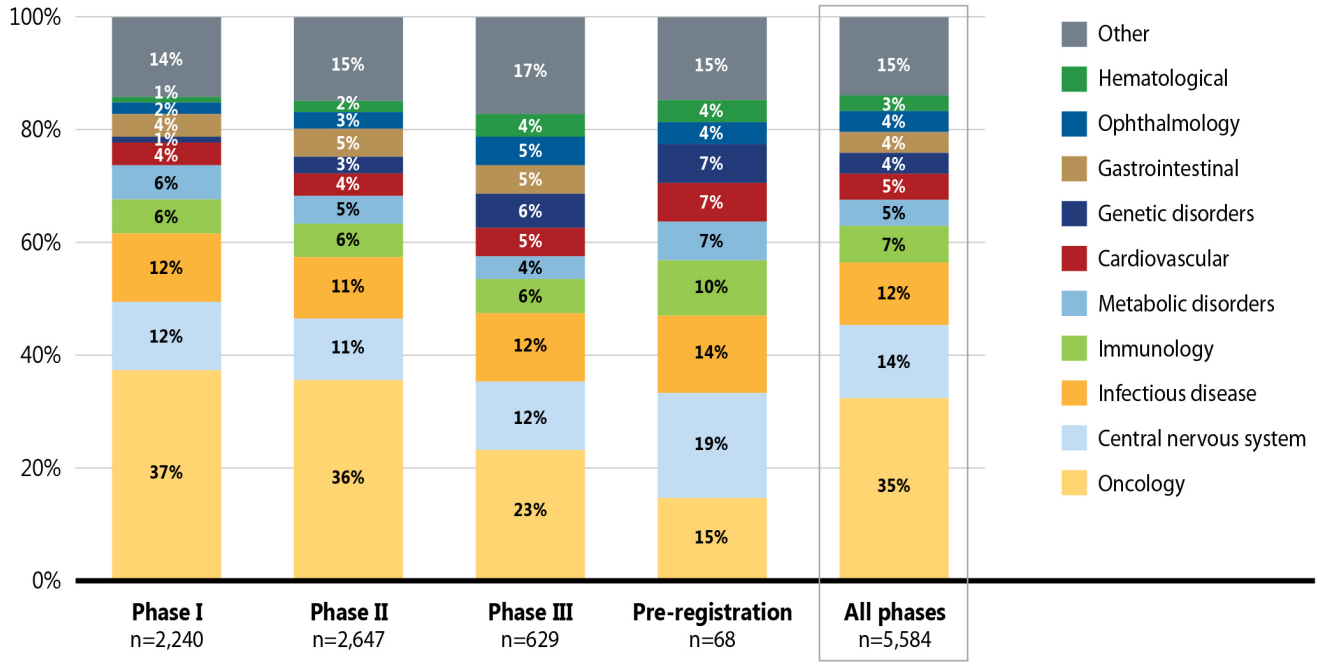


Data source: GlobalData Healthcare database (accessed September 2019).

Figure 3 illustrates the distribution of new medicines by therapeutic area from Phase I through pre-registration. Although the findings show that pipeline medicines represented a wide range of therapeutic areas in 2019, cancer treatments dominated the therapeutic mix across the pipeline, accounting for over one third (35%) of medicines in all phases of clinical evaluation. Other important pipeline therapies include those for central nervous system (CNS) diseases such as Alzheimer's disease and depression.

As a share of the medicines in pre-registration, central nervous system treatments increased to 19% in 2019, exceeding the 15% share held by oncology. This increase primarily reflects recent innovative developments in medicines for Alzheimer's disease. Novel treatments for Alzheimer's that target either amyloid protein buildup in the brain or neurotransmitter activity have an increased presence in all phases of the pipeline, in response to growing unmet needs and despite setbacks from previously unsuccessful clinical trials. There were 128 medicines for the treatment of Alzheimer's disease in the pipeline in 2019, 16% of which were in Phase III and pre-registration.

FIGURE 3. Therapeutic class distribution of pipeline medicines by phase of clinical evaluation, 2019



Data source: GlobalData Healthcare database (accessed September 2019).

MEDS PIPELINE MONITOR 2019

The following tables list the selection of new pipeline medicines in 2019 and those retained from the 2018 edition of the *Meds Pipeline Monitor*, as well as medicines featured in the previous edition of the report that have since gained market authorization. These medicines will be monitored in future editions of this report.

Applying the screening criteria described in the Methodology section, 8 of the 697 pipeline medicines in late stages of clinical evaluation, including 2 gene therapies, were selected for inclusion in the 2019 new medicines list (Table 4). Likewise, 16 late-stage medicines were retained from the 2018 list as they continued to satisfy the same criteria (Table 5).

Five medicines that were featured in the 2018 edition of the MPM, including two from the list of gene therapies, had gained market authorization in the US, Europe, or Canada as of January 2020. These medicines are listed in Table 6.

TABLE 4. Selected new medicines for 2019

SELECTION CRITERIA						KEY ATTRIBUTES			
Increased safety and efficacy	Novel mechanism	Gene therapy	Breakthrough	Fast Track	Priority Review	Clinical trials in Canada	Rare or orphan designation	Biologic medicine	Add-on therapy

MEDICINE (TRADE NAME) COMPANY	INDICATION(S)*	DESCRIPTION AND KEY ATTRIBUTES
CARDIOVASCULAR		
Bempedoic acid Esperion Therapeutics Inc.	Hyperlipidemia atherosclerosis	• Oral, first-in-class, lipid-lowering therapy. • Unique mechanism of action: adenosine triphosphate-citrate lyase inhibition (ACL), an enzyme involved in fatty acid and cholesterol synthesis.[1] • Reduced low-density lipoprotein cholesterol (LDL-C) as monotherapy, combined with ezetimibe, and added to statin therapy, with LDL-C lowering most pronounced when it was combined with ezetimibe in patients who cannot tolerate statins.[1,2,3] • Has been shown to be safe in combination with statins as well as ezetimibe, appears to effectively lower LDL-C, and has the potential to reduce the risk of muscle-related adverse events, which can limit the utilization and effectiveness of statin therapy.[4,5] • Total global revenue forecasted to be $521 million by 2025.*
CENTRAL NERVOUS SYSTEM		

Gantenerumab Hoffmann-La Roche Ltd	Alzheimer's disease	• A fully human monoclonal antibody that binds aggregated amyloid-β (Aβ) and removes Aβ plaques by Fc receptor-mediated phagocytosis. • Several Phase III studies of its effect on cognition and functioning in participants with prodromal Alzheimer's disease are ongoing. [6,7,8,9] • Being tested in the dominantly inherited Alzheimer's network trials unit (DIAN-TU).[10] • There are several ongoing Phase III trials in Canada.[11,12,13] • Total global revenue forecasted to be $55 million by 2025.*
Gepirone hydrochloride ER (Travivo [US]) Fabre-Kramer Pharmaceuticals, Inc.	Major depressive disorder (MDD)	• A 5-HT1A receptor agonist belonging to the buspirone family. • Differs from the SSRIs in only affecting the 5-HT (1A) receptor.[14] • Has been shown to be more effective than selective serotonin reuptake inhibitors (SSRIs), as it treats the psychiatric disorders without causing sexual dysfunction.[15] • Possesses greater selectivity for the 5-HT1A receptor than SSRIs.[15] • "Could be a breakthrough therapeutic agent in the treatment of anxiety and MDD."[15]
ENDOCRINOLOGY		
Donaperminogene seltoplasmid (VM202) Helixmith Co., Ltd	Diabetic neuropathic pain	• First-in-class non-viral plasmid DNA gene therapy that contains the instructions to produce more of a protein called hepatocyte growth factor (HGF). HGF has multiple roles in the body: it is involved in angiogenesis (the formation of new blood vessels) and is a neurotrophic factor or a chemical that improves the survival and growth of neurons (nerve cells).[16] • The results from previous studies suggest that it provides the same magnitude of pain relief as reported with pregabalin or gabapentin.[17] • In study NCT02427464, intramuscular injections were administered.[18] In a double-blind, placebo-controlled study, it was shown to have no significant adverse events and demonstrate a significant reduction at 3 months in the mean pain score and continued reductions in pain at 6 and 9 months: 48.4% of patients experienced a ≥50% reduction in pain compared to 17.6% of placebo patients.[19] • A Phase III trial in the treatment of diabetic foot ulcers is ongoing.[20] • Total global revenue forecasted to be $783 million by 2025.*
IMMUNOLOGY		
Imlifidase (Idefirix [EU]) Hansa Biopharma AB	Kidney transplant rejection	• An endopeptidase derived from Streptococcus pyogenes which has specificity for human IgG, and when infused intravenously results in rapid cleavage of IgG.[21]

		• May represent "a ground breaking new method of desensitization for patients who otherwise might have no hope for receiving a lifesaving transplant." [21]
ONCOLOGY		
Nadofaragene firadenovec (Instiladrin [US]) FKD Therapies Oy	Non-muscle-invasive bladder cancer (NMIBC)	• A gene therapy consisting of an adenovirus containing the gene interferon (IFN)-alpha2b. • Administered by catheter directly into the bladder where the virus introduces the active gene into cells of the bladder lining to do its work.[22] • Being developed particularly for NMIBC that is not responsive to bacillus Calmette-Guérin (BCG) therapy, the current main treatment option for early bladder cancer. • In Phase III trials.[23]
Plitidepsin (Aplidin) PharmaMar, S.A.	Relapsed or refractory multiple myeloma (MM)	• A cyclic depsipeptide that potently inhibits MM cell growth and induces apoptosis.[24,25] • Exerts pleiotropic effects on cancer cells, most likely by binding to the eukaryotic translation eEF1A2. This ultimately leads to cell-cycle arrest, growth inhibition and induction of apoptosis via multiple pathway alterations.[26] • In patients with relapsed or refractory MM, its activity seems to be enhanced after addition of dexamethasone while remaining well tolerated.[24] • In a Phase III trial, efficacy data, the reassuring safety profile, and its novel mechanism of action suggest that, in combination with dexamethasone, it can be an alternative option in patients with relapsed/refractory MM after at least three prior therapy lines.[27]
OPHTHALMOLOGY		
Abicipar pegol Allergan PLC	Wet (neovascular/ exudative) macular degeneration	• A long-acting anti-vascular endothelial growth factor (VEGF) administered by intravitreal injection given every 3 months (compared to monthly with existing agents); reduces treatment burden.[28,29] • A designed ankyrin repeat protein (DARPin)[30] targeting vascular endothelial growth factor-A (VEGF-A).[31] • Total global revenue forecasted to be $456 million by 2025.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2019, and are given in US dollars.
Data source: GlobalData Healthcare database. The database search for new medicines added to the MPM was performed in September 2019.

TABLE 5. Pipeline medicines retained from the 2018 *Meds Pipeline Monitor*

SELECTION CRITERIA						KEY ATTRIBUTES			
Increased safety and efficacy	Novel mechanism	Gene therapy	Breakthrough	Fast track designation	Priority Review	Clinical trials in Canada	Orphan designation	Biologic	Add-on therapy

MEDICINE (TRADE NAME) COMPANY	INDICATION(S)*	DESCRIPTION AND KEY ATTRIBUTES
GASTROINTESTINAL AND METABOLIC DISORDERS		
Cenicriviroc Allergan PLC	Liver fibrosis; Non-alcoholic steatohepatitis (NASH)	• A dual chemokine receptor type 2 (CCR2) and type 5 (CCR5) antagonist, in treatment-experienced, HIV-infected individuals.[32] • For oral treatment of non-alcoholic steatohepatitis (NASH) with liver fibrosis.[33] After one year of treatment, twice as many patients achieved improvement in fibrosis and no worsening of NASH compared with placebo.[33] • Non-alcoholic fatty liver disease (NAFLD) has an increasing prevalence worldwide. At present, no specific pharmacotherapy is approved for NAFLD.[34] • In studies to date, safety and tolerability were comparable to placebo.[33] • Phase III study is ongoing.[35] • Total global revenue forecasted to be $27 million by 2025.*
Setmelanotide Rhythm Pharmaceuticals, Inc.	Genetic disorders; Obesity	• First-in-class melanocortin-4 receptor (MC4R) agonist to treat rare genetic disorders of obesity. • Leads to weight loss in in obese individuals with complete pro-opiomelanocortin (POMC) deficiency. While POMC deficiency is very rare, 1%-5% of severely obese individuals harbour heterozygous mutations in MC4R.[36] • Phase III studies are ongoing.[37,38] • Total global revenue forecasted to be $682 million by 2025.*
GENETIC DISORDERS		
Elivaldogene tavalentivec (Lenti-D) bluebird bio, Inc.	Adrenoleuko-dystrophy (ADL)	• A Lenti-D gene therapy for X chromosome-linked ADL, a devastating neurologic disorder with an estimated birth incidence of 1 in 17,000 newborns. ADL is a metabolic disorder that impairs peroxisomal beta-oxidation of very-long-chain fatty acids. • CD34+ cells are obtained from the patient by means of apheresis and transduced with the Lenti-D lentiviral vector. The patient receives

		conditioning with busulfan and cyclophosphamide, after which the Lenti-D gene product, which is made up of the transduced CD34+ cells, is infused. • Early results of the STARBEAM study (ALD-102; Phase II/III) suggest that Lenti-D gene therapy may be a safe and effective alternative to allogeneic stem-cell transplantation in boys with early-stage cerebral ADL.[39] • Total global revenue forecasted to be $202 million by 2025.*
HEMATOLOGICAL		
Fitusiran Alnylam Pharmaceuticals Inc.; Genzyme, a Sanofi Co.	Hemophilia A; Hemophilia B	• A small interfering RNA (siRNA) developed to suppress the hepatic synthesis of antithrombin. • Current hemophilia treatment involves frequent intravenous infusions of clotting factors, which is associated with variable hemostatic protection, a high treatment burden, and a risk of the development of inhibitory alloantibodies. • Once-monthly subcutaneous administration of fitusiran resulted in dose-dependent lowering of the antithrombin level and increased thrombin generation in participants with hemophilia A or B who did not have inhibitory alloantibodies.[40] • Phase III trials are ongoing.[41,42,43,44] • Total global revenue forecasted to be $1.2 billion by 2025.*
Vadadustat Otsuka Holdings Co., Ltd; Akebia Therapeutics, Inc.	Anemia in chronic kidney disease (CKD; renal anemia)	• A titratable prolyl hydroxylase domain (PHD) enzyme inhibitor that represents a novel pharmacological treatment of anemia. • Has been shown to increase hemoglobin (Hb) levels[45] and to maintain mean Hb concentrations in patients on hemodialysis previously receiving epoetin.[46] • Phase III trials are ongoing.[47] • Total global revenue forecasted to be $845 million by 2025.*
INFECTIOUS DISEASE		
Cabotegravir ViiV Healthcare UK Ltd	HIV infections (AIDS)	• A potent integrase strand transfer inhibitor; formulated as an oral tablet for daily administration and as a long-acting injectable nanosuspension. • Has a long half-life and can be formulated into a long-acting nanosuspension for parenteral administration (intramuscular at 4 weekly and 8 weekly intervals).[48] • Few interactions with commonly used concomitant medications.[48] • May provide an alternative therapeutic option for both the treatment and prevention of HIV-1 infection that does not necessitate adherence to a daily regimen.[49]

		• In combination with dual nucleoside reverse transcriptase inhibitor (NRTI) therapy had potent antiviral activity during the induction phase; as a two-drug maintenance therapy, cabotegravir plus rilpivirine provided antiviral activity similar to efavirenz plus dual NRTIs until the end of week 96.[50] • Offers an alternative to daily regimens and may improve preexposure prophylaxis (PrEP) adherence.[51] • Currently under review by Health Canada. • Total global revenue forecasted to be $876 million by 2025.*
Fostemsavir tromethamine ViiV Healthcare UK Ltd; Bristol-Myers Squibb Co.; GlaxoSmithKline PLC	HIV infections (AIDS)	• A next generation CD4 attachment inhibitor that is active regardless of viral tropism, without cross-resistance to any of the existing antiretroviral compounds.[52] • In one study, 82% of patients treated with fostemsavir and an optimized background ARV regimen achieved virological suppression below 50 copies/mL in HIV-infected treatment-experienced individuals.[52] • Total global revenue forecasted to be $329 million by 2025.*
MUSCULOSKELETAL SYSTEM		
Palovarotene Ipsen S.A.	Myositis ossificans progressive; Fibrodysplasia ossificans progressiva (FOP)	• A novel highly selective retinoic acid receptor gamma agonist. • Claimed to reverse the structural, functional, and inflammatory features of cigarette smoke-induced emphysema.[53] • Phase III trials for treatment of FOP are ongoing.[54] • Total global revenue forecasted to be $1.2 billion by 2025.*
ONCOLOGY		
Ipatasertib Genentech, Inc.	Metastatic hormone refractory (castration-resistant, androgen-independent) prostate cancer	• An oral, v-Akt murine thymoma viral oncogene homolog (Akt) inhibitor. • In metastatic castration-resistant prostate cancer (mCRPC), combined blockade with abiraterone and ipatasertib showed superior antitumour activity to abiraterone alone, especially in patients with phosphatase and tensin homolog (PTEN)-loss tumours.[55] • Improved outcomes in a subset of patients with metastatic triple-negative breast cancer (TNBC) when combined with paclitaxel in the first-line setting.[56,57] Targeted therapies for TNBC—which accounts for around 20% of breast cancers—remain unavailable. • Phase III trials in breast cancer[58,59] and prostate cancer[60] are ongoing. • Total global revenue forecasted to be $586 million by 2025.*

Melphalan flufenamide hydrochloride (Melflufen, Ygalo) Oncopeptides AB	Refractory multiple myeloma; Relapsed multiple myeloma (MM)	• Peptide-based alkylating agent; a novel dipeptide prodrug of Melphalan. • Overcomes drug-resistance and improves multiple myeloma patient outcomes.[61] • Phase III trials are ongoing.[62] • Total global revenue forecasted to be $468 million by 2025.*
Quizartinib dihydrochloride (Vanflyta) Daiichi Sankyo Co., Ltd	Refractory acute myeloid leukemia (AML); Relapsed acute myeloid leukemia (AML)	• A small molecule receptor tyrosine kinase inhibitor targeting FLT3 that is administered orally once daily. FLT3 is a receptor tyrosine kinase that is commonly expressed in AML and is mutated in approximately 25% of AML patients. • Data from the QuANTUM-R study (NCT02039726) confirmed the efficacy and safety of quizartinib that was observed in previous trials and showed the value of therapy targeting FLT3-ITD. It is the first trial to demonstrate improved overall survival for FLT3-ITD–associated AML patients who are treatment resistant or who relapsed after prior therapy. • Preliminary data from the QuANTUM-R study shows improved overall survival for FLT3-ITD–associated AML patients who are treatment resistant or who relapsed after prior therapy. • Phase III trials are ongoing.[63] • Total global revenue forecasted to be $162 million by 2025.*
Tavokinogene telseplasmid (ImmunoPulse, Tavo) OncoSec Medical Inc.	Metastatic melanoma	• An immunomodulatory cytokine that delivers the immune-stimulating protein interleukin-12 (IL-12) into the tumour microenvironment. • Administered using ImmunoPulse, a device that electroporates into the tumour. • A combination of tavokinogene telseplasmid and pembrolizumab was effective at reducing tumours in advanced melanoma patients who had failed prior anti-programmed cell death protein (PD-1) therapies, according to early results of a Phase IIb trial (includes a Canadian site).[64, 65]
Ublituximab (Utuxin) TG Therapeutics, Inc.; LFB S.A.	Refractory chronic lymphocytic leukemia (CLL); Relapsed chronic lymphocytic leukemia (CLL); Relapsing multiple sclerosis (RMS)	• A next generation glycoengineered anti-CD20 monoclonal antibody. • Next-generation with higher complement-dependent cytotoxicity and antibody-dependent cellular cytotoxicity against malignant B-cells.[66] • Demonstrated efficacy in patients with high-risk CLL and B-non-Hodgkin lymphoma in both first line, subsequent lines, and in rituximab refractory patients.[66] • In combination with ibrutinib, resulted in rapid and high response rates.[67] • Phase III in RMS are ongoing.[68] • Total global revenue forecasted to be $619 million by 2025.*

OPTHALMOLOGY		
Lenadogene nolparvovec (Lumevoq [EU]) GenSight Biologics S.A.	Leber's hereditary optic neuropathy (LHON)	• A recombinant adeno-associated viral vector serotype 2 (rAAV2/2) containing the wild-type ND4 gene (rAAV2/2-ND4). • It is administered through intravitreal injection containing 9E10 viral genomes in 90uL balanced salt solution (BSS) plus 0.001% Pluronic F68®. • In Phase III trials for the treatment of optic atrophy or hereditary Leber[69,70] due to the mutation of the G11778A ND4 gene.
Timrepigene emparvovec [AAV2-REP1, NSR-REP-1] Biogen Inc.	Choroideremia	• An adeno-associated viral vector (AAV2) encoding rab escort protein 1. • Administered as a sub-retinal injection after vitrectomy. • Choroideremia is an X-linked inherited chorioretinal dystrophy leading to blindness by late adulthood. It is estimated that the prevalence of CHM is between 1 in 50,000–100,000 people. Currently there is no effective treatment.[71] • Phase I and II studies with NSR-REP1 in patients with choroideremia have produced encouraging results, suggesting that it is possible not only to slow or stop the decline in vision, but also to improve visual acuity in some patients.[72] • In a small number of patients, it was associated with maintenance or improvement of visual acuity, although no significant difference was found from control eyes. All safety issues were associated with the surgical procedure and none were judged severe.[73] • Phase III registrational trial (STAR) in patients with choroideremia has been initiated in many countries, including Canada.[74,75] • Total global revenue forecasted to be $159 million by 2025.*
Zuretinol acetate Retinagenix LLC	Leber congenital amaurosis (LCA); Retinitis	• Oral retinoid; it is a synthetic retinoid replacement for 11-cis-retinal. • Could "achieve significant improvement in visual function and acuity as an alternative to gene therapy in inherited retinal diseases. Its oral dosing would, if approved, differentiate it as a potential therapy, particularly for patients who may not be amenable to more invasive options, such as younger children, due to intraocular surgical difficulties in underdeveloped eyes."[76] • Total global revenue forecasted to be $105 million by 2025.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2019, and are given in US dollars.
Data source: GlobalData Healthcare database.

TABLE 6. Pipeline medicines from the 2018 *Meds Pipeline Monitor* that have gained market authorization

SELECTION CRITERIA						KEY ATTRIBUTES			
Increased safety and efficacy	Novel mechanism	Gene therapy	Breakthrough	Fast track designation	Priority Review	Clinical trials in Canada	Orphan designation	Biologic	Add-on therapy

MEDICINE (TRADE NAME) COMPANY	INDICATION(S)*	DESCRIPTION AND KEY ATTRIBUTES
CENTRAL NERVOUS SYSTEM		
Onasemnogene abeparvovec (Zolgensma) AveXis, Inc.	Spinal muscular atrophy (SMA)	• A non-replicating recombinant AAV9 virus vector-based gene therapy containing the complimentary deoxyribonucleic acid (cDNA) of the human survival motor neuron (SMN) gene under the control of the cytomegalovirus (CMV) enhancer/chicken-β-actin-hybrid promoter (CB). • Administered as a one-time infusion. • The START trial (Phase I) demonstrated a dramatic increase in survival and transformative improvement in achievement of developmental milestones compared to the natural history of SMA Type 1.[77] Phase III trials in infants diagnosed with SMA are ongoing.[78, 79, 80] • A long-term study has been initiated for continuous safety monitoring for up to 15 years (estimated completion date: 2033).[81] • Marketed in the US in May 2019 for the treatment of pediatric patients aged less than 2 years with SMA and bi-allelic mutations in SMN1. • Total global revenue forecasted to be $2.46 billion by 2025.*
Ubrogepant (Ubrelvy [US]) Allergan PLC	Migraine	• A next generation oral calcitonin gene-related peptide receptor antagonist. • Safe and effective in the acute treatment of migraine in a wide range of patients, including those who had an insufficient response to a triptan or those in whom triptans were contraindicated, as well as in patients who had moderate to severe cardiovascular risk. • In Phase III trials (ACHIEVE II), in adults with migraine, acute treatment with ubrogepant compared with placebo led to significantly greater rates of pain freedom at 2 hours.[82] • Total global revenue forecasted to be $486 million by 2025.*
INFECTIOUS DISEASE		
Lefamulin (Xenleta) Nabriva Therapeutics PLC	Community-acquired bacterial pneumonia (CABP)	• Novel pleuromutilin antibiotic; exhibits a unique mechanism of action through inhibition of protein synthesis by binding to the peptidyl transferase center of the 50S bacterial ribosome, thus preventing the binding of transfer RNA for peptide transfer.[83]

		• Has demonstrated efficacy against the most common bacteria responsible for CABP, including strains exhibiting resistance to macrolides, fluoroquinolones, tetracyclines, vancomycin, and beta-lactams.[84] • In Phase III trials for community-acquired bacterial pneumonia.[85] • Approved by the FDA in August 2019. • Total global revenue forecasted to be $253 million by 2025.*
ONCOLOGY		
Selinexor (Xpovio) Karyopharm Therapeutics Inc.	Relapsed or refractory multiple myeloma	• First-in-class, oral selective inhibitor of nuclear export (SINE). It links to and inhibits XPO1 (CRM1), a nuclear export protein. • In a Phase II trial (STORM), it was given in combination with low-dose dexamethasone and shrank tumours in 25.4% of these patients, including two patients whose tumours were completely gone. Responses lasted a median of 4.4 months. • In combination with dexamethasone, it resulted in objective treatment responses in patients with myeloma refractory to currently available therapies.[86] • Approved by FDA in July 2019. • Total global revenue forecasted to be $548 million by 2025.*
HEMATOLOGICAL		
LentiGlobin BB305 (Zynteglo) bluebird bio, Inc.	Beta-thalassaemia major	• A gene therapy (autologous CD34+ cells encoding βA-T87Q-globin gene) for the treatment of beta-thalassemia major, a rare and potentially debilitating blood disorder. • Administered as a single dose straight into the blood (intravenous infusion) following a course of busulfan chemotherapy.[87] • May improve survival and quality of life by reducing or eliminating the need for blood transfusions and iron-chelation therapy. • In Phase III trials.[88, 89] • Approved in the EU in June 2019. • Total global revenue forecasted to be $1.08 billion by 2025.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2019, and are given in US dollars.
Data source: GlobalData Healthcare database.

SPOTLIGHT ON CANADA

This new 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 are new to Canada, but may have been approved in other jurisdictions.

Table 7 highlights nine new medicines currently on Health Canada's Drug and Health Product Submissions Under Review (SUR) list that have a novel mechanism of action or demonstrated improved safety and efficacy in clinical trials. The SUR is a publicly available source that identifies 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

SELECTION CRITERIA			KEY ATTRIBUTES						
Increased safety and efficacy	Novel mechanism	Gene therapy	Breakthrough	Fast Track	Priority Review	Clinical trials in Canada	Rare or orphan designation	Biologic	Add-on therapy

MEDICINE (TRADE NAME) COMPANY	INDICATION(S)*	DESCRIPTION AND KEY ATTRIBUTES
CENTRAL NERVOUS SYSTEM		
Fremanezumab (Ajovy) Teva Canada Ltd	Migraine prevention	• A humanized monoclonal antibody targeting calcitonin gene-related peptide (CGRP). • Represents a new approach to migraine therapy. This is the first identification of an anti-migraine drug that appears to be selective for Aδ-fibers (peripherally) and HT neurons (centrally).[90] • In a Phase III trial, it was shown to be effective and well tolerated in patients with difficult-to-treat migraine who had previously not responded to up to four classes of migraine preventive medications.[91] • As a monoclonal antibody, it was not associated to liver toxicity and is not expected to interact with other drugs.[92] • Total global revenue forecasted to be $843 million by 2025.*
DERMATOLOGY		
Tildrakizumab (Ilumetri) Sun Pharma Global FZE	Plaque psoriasis	• A high-affinity, humanized monoclonal antibody selectively targeting the p19 subunit of IL-23, a key cytokine for Th17 cells.[93,94] • Among the first drugs with specific action against IL-23 to be approved by the FDA and the EMA.[95]

		• Represents an evolving treatment strategy in chronic plaque psoriasis.[93] • Demonstrated significant clinical improvement and a favourable safety profile. In Phase III trials, it demonstrated superior efficacy vs. etanercept treatment.[94] • Its simple dosing, prolonged duration of action, and mild adverse event profile make it a practical option for patients.[94] • Total global revenue forecasted to be $253 million by 2025.*
GASTROINTESTINAL		
Tenapanor (Ibsrela) Knight Therapeutics Inc.	Irritable bowel syndrome (IBS)	• A first-in-class, small-molecule inhibitor of the gastrointestinal sodium/hydrogen exchanger 3 (NHE3).[96] • Has been shown to significantly increase stool frequency and reduce abdominal symptoms in patients with IBS-C.[96] • In Phase III trials, it significantly reduced elevated serum phosphate in patients with hyperphosphatemia receiving maintenance hemodialysis.[97] • Approved by FDA in September 2019. • Total global revenue forecasted to be $490 million by 2025.*
GENITOURINARY AND SEX HORMONES		
Ospemifene (Osphena, Senshio) Duchesnay Inc.	Menopause	• An oral, third-generation selective estrogen receptor modulator, used to treat moderate-to-severe dyspareunia due to postmenopausal vulvovaginal atrophy (VVA).[98,99] • Significantly improves the structure and pH levels of the vagina, reducing dyspareunia.[99] • An indirect comparison suggests that it has an efficacy, safety, and tolerability profile comparable to or better than local vaginal estrogens in the treatment of VVA.[100] • Patients had significantly greater adherence and persistence vs. local estrogen therapies. It had the lowest mean outpatient costs vs. local estrogen therapies. Total all-cause healthcare costs were also significantly less vs. local estrogen therapies.[101] • Total global revenue forecasted to be $61 million by 2025.*
INFECTIOUS DISEASE		
Baloxavir marboxil (Xofluza) Hoffmann-La Roche Ltd	For influenza A or B virus infections	• An oral, selective cap-dependent endonuclease inhibitor; new mechanism of action.[102] • The time to alleviation of symptoms was similar with that of oseltamivir. It was associated with greater reductions in viral load one day after initiation of the regimen vs. placebo or oseltamivir.[103]

		• Due to the possibility of viral mutations and resistance, it is important to have antivirals with different mechanisms available, especially in the case of a new pandemic strain.[102] • Total global revenue forecasted $965 million by 2025.*
Cabotegravir ViiV Healthcare UK Ltd	HIV infections (AIDS)	• A potent integrase strand transfer inhibitor; formulated as an oral tablet for daily administration and as a long-acting injectable nanosuspension. • Has a long half-life and can be formulated into a long-acting nanosuspension for parenteral administration (intramuscular at 4 weekly and 8 weekly intervals).[48] • Few interactions with commonly used concomitant medications.[48] • May provide an alternative therapeutic option for both the treatment and prevention of HIV-1 infection that does not necessitate adherence to a daily regimen.[49] • In combination with dual nucleoside reverse transcriptase inhibitor (NRTI) therapy had potent antiviral activity during the induction phase; as a two-drug maintenance therapy, cabotegravir plus rilpivirine provided antiviral activity similar to efavirenz plus dual NRTIs until the end of week 96.[50] • Offers an alternative to daily regimens and may improve preexposure prophylaxis (PrEP) adherence.[51] • Total global revenue forecasted to be $876 million by 2025.
NEUROLOGY		
Siponimod fumarate (Mayzent) Novartis Pharmaceuticals Canada Inc.	Multiple sclerosis (MS)	• An oral selective sphingosine 1-phosphate receptor subtypes 1 and 5 (S1PR1,5) modulator.[104] • A synthetic molecule belonging to the sphingosine-1-phosphate (S1P) modulator family, which has putative neuroprotective properties and well-characterized immunomodulating effects mediated by sequestration of B and T cells in secondary lymphoid organs.[105] • Exhibits selective affinity for types 1 and 5 S1P receptor, leading to a lower risk of adverse events that are mainly induced by S1P3 receptor activation, such as bradycardia and vasoconstriction.[105] • In Phase II trials, it was associated with a significant reduction in disability progression in secondary progressive (SP) MS patients vs. placebo.[105] • Total global revenue forecasted to be $1.4 billion by 2025.*
ONCOLOGY		
Darolutamide (Nubeqa) Bayer Inc.	Prostate cancer	• An oral, high-affinity androgen receptor (AR) antagonist, with a distinct chemical structure compared to other AR antagonists, which has activity

		against known AR mutants that confer resistance to other second-generation anti-androgens.[106,107] • The Phase III ARAMIS study shows that it delays metastasis in men with castration-resistant prostate cancer by a median of 22 months vs. placebo.[108,109] • Approved by FDA in 2019. • Total global revenue forecasted to be $995 million by 2025.*
Entrectinib (Rozlytrek) Hoffmann-La Roche Ltd	Non-small cell lung cancer (NSCLC); Leukemia	• An orally available, CNS-active, highly potent, and selective kinase inhibitor against TRKA/B/C, ROS1, and ALK kinase activities.[110] • Has shown potent anti-neoplastic activity and tolerability in various neoplastic conditions, particularly NSCLC.[111] • Approved by FDA in 2019. • Total global revenue forecasted to $421 million by 2025.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2019, and are given in US dollars.
Data source: GlobalData Healthcare database.

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