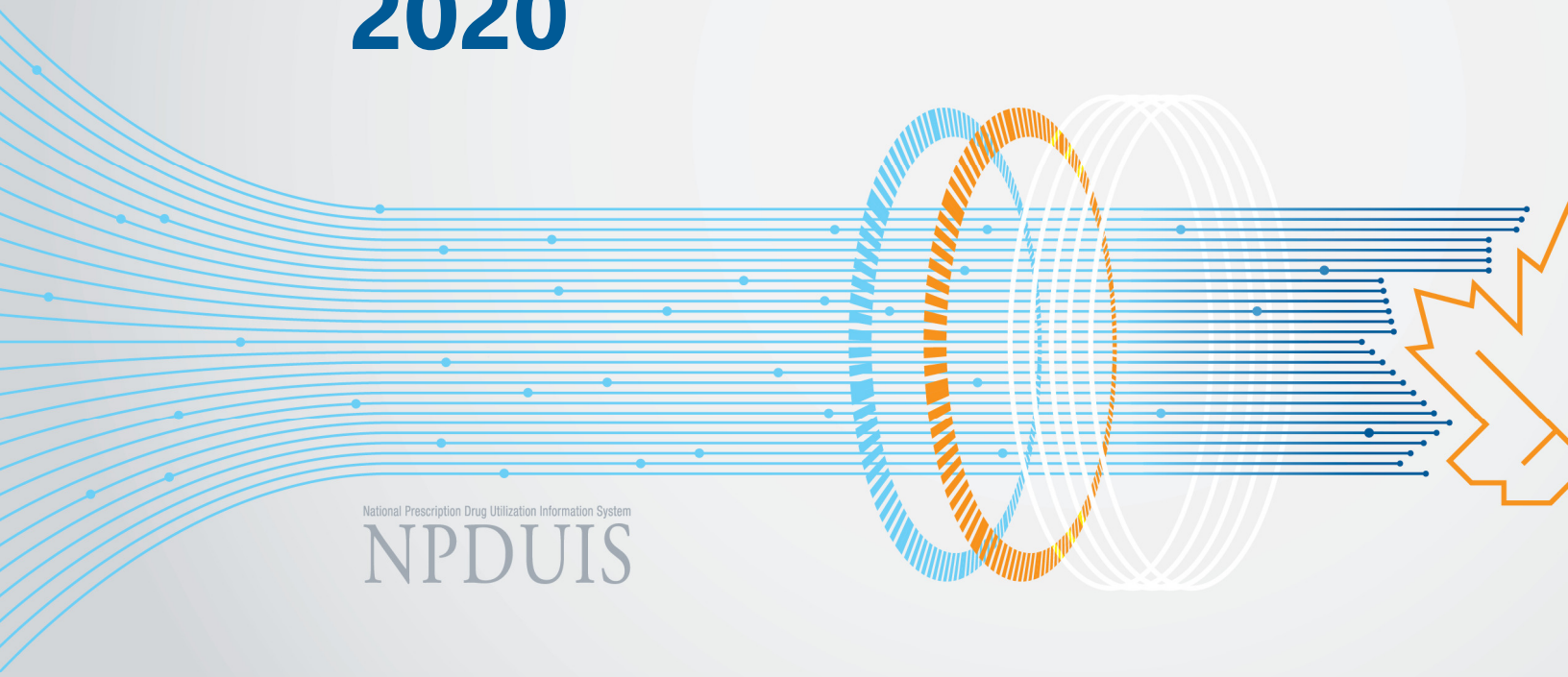
Patented Medicine Prices Review Board
Conseil d'examen du prix des médicaments brevetés

MEDS

PIPELINE MONITOR 2020



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 pre-registration are considered as candidates 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 final selection features medicines that treat a broad range of therapeutic areas. In addition to identifying new medicines for inclusion in the list, medicines featured in the 2019 *Meds Pipeline Monitor* are also reviewed to report on changes to their status in the pipeline. A section focused on Canada highlights potentially significant medicines currently under review by Health Canada.

This edition of the report includes a new section on COVID-19, which provides an overview of medicines undergoing Phase I, II, and III clinical trials or in pre-registration for the treatment and prevention of the novel coronavirus disease.

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 review 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 2020

- In 2020, the pipeline contained 6,946 new medicines in various stages of evaluation, of which 13% were in Phase III clinical trials and pre-registration, representing a wide range of therapeutic areas.
- Oncology continued to dominate the therapeutic mix in 2020, with cancer treatments representing one third (35%) of medicines in all phases of clinical trials. Treatments for infectious diseases held the second largest share of the pipeline, at 13%, and are expected to grow in importance in response to the COVID-19 pandemic.
- Over one third of medicines in Phase III clinical trials or pre-registration 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.
- Sixteen late-stage new medicines, including five gene therapies, were selected for addition to the 2020 MPM 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 24 new medicines featured in the 2019 edition of the MPM, 11 were retained on the list as they continued to satisfy the selection criteria.

- The report also highlights six of the new medicines currently under review by Health Canada. Four of these medicines have forecasted global revenues of over US $1 billion annually by 2026.
- As of November 2020, 427 vaccines and therapies were undergoing evaluation for the prevention and treatment of COVID-19.

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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]

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.

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.[v]

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.[vi]

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

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

INTRODUCTION

This tenth edition of the *Meds Pipeline Monitor* (MPM) features a selection of medicines in Phase III clinical trials or pre-registration in 2020 that have the potential to significantly 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 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. This edition of the report also highlights select vaccines and other medicines undergoing evaluation for the treatment and prevention of COVID-19, in global markets as well as in Canada. The medicines assessed for this portion of the analysis include new therapies as well as previously marketed treatments that have been repurposed.

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 July 2020.

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. 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.

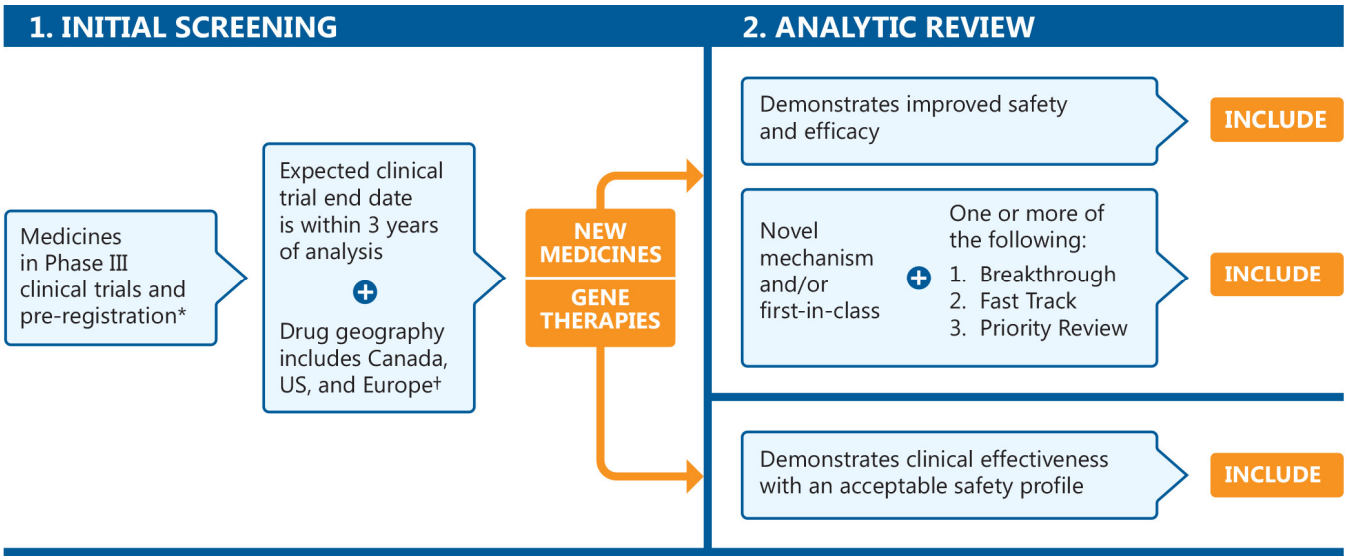
The list of medicines used for the analysis of orphan medicines in the pipeline was retrieved in November 2020. For the purposes of this analysis, orphan medicines were defined as new medicines that had been granted an orphan designation by the US FDA or the EMA.

Meds Pipeline Monitor

The MPM focuses on new medicines in Phase III clinical trials or pre-registration in Canada, the United States, and Europe. 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, the 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. 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

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 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	

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.

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 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 / 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

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 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.

Emerging COVID-19 Therapies

Vaccines and medicines under development worldwide with an indication for COVID-19 were extracted for this section of the report, based on a development stage of Phase I, II, and III clinical trials or pre-registration. All such medicines were assessed for this analysis, both new and existing. New medicines were identified as those that have not yet been marketed for any indication, while existing medicines include previously marketed therapies undergoing evaluation for new indications related to the treatment of COVID-19.

In light of the rapid development of the medicines in this category of the pipeline, the data for this analysis was extracted in November 2020.

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 the following: phase of clinical development, therapeutic area, molecule type, indication, drug geography, mechanism of action, and regulatory 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 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 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.

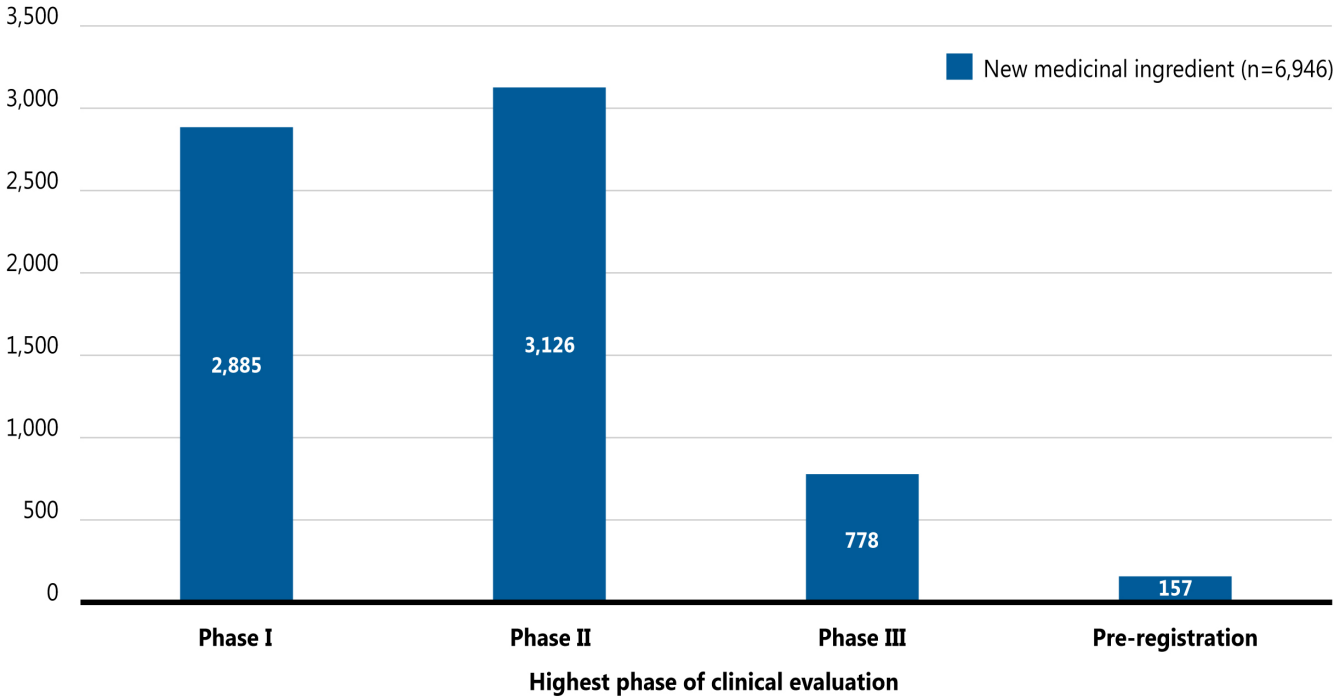
Unless otherwise specified, the featured lists capture the composition of the pipeline as of July 2020 and are validated as of the end of November 2020. Due to the unpredictability and fast-moving nature of pipeline medicines entering the market, some of the medicines listed in this edition may have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

SNAPSHOT OF THE 2020 PIPELINE

Pharmaceutical innovation is transforming the development and application of medical treatments worldwide. Nearly 7,000 new medicines were in clinical evaluation or in pre-registration in 2020.

Figure 2 provides a snapshot of the pipeline in 2020, including the number of new medicinal ingredients in each phase of clinical evaluation. Of the 6,946 new medicines, 935 (13%) were in Phase III clinical trials or in pre-registration.

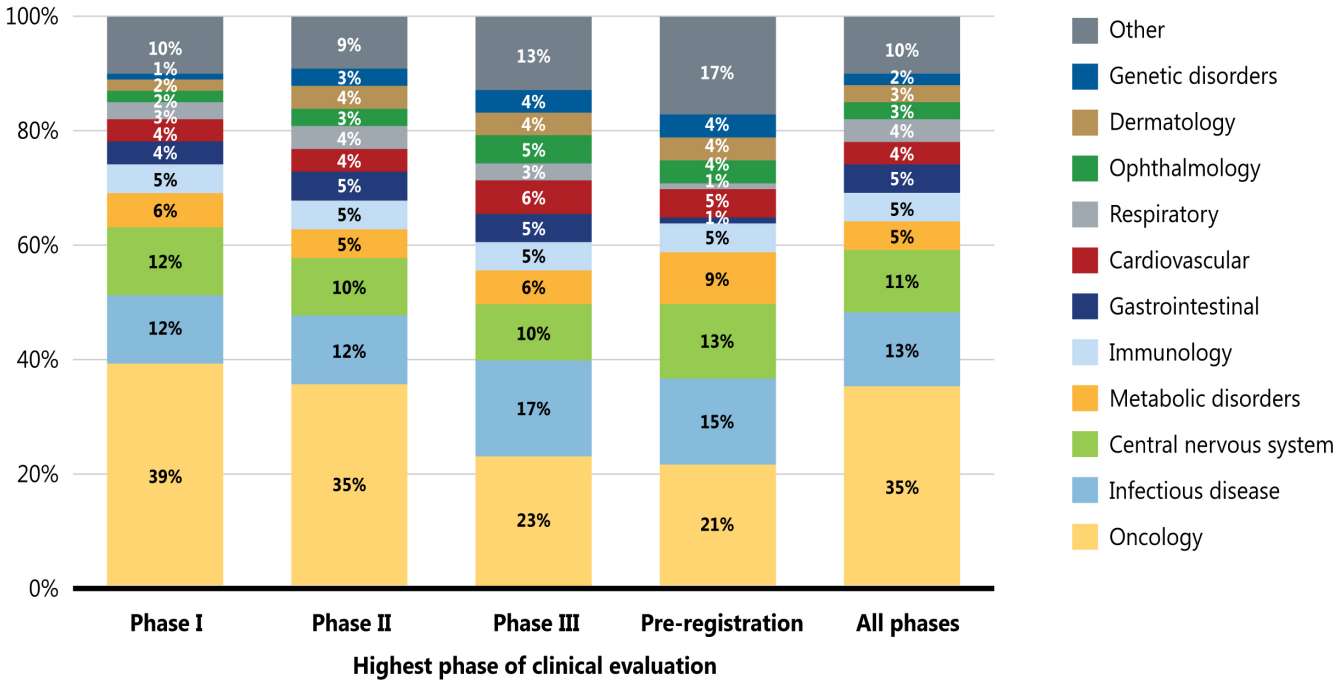
FIGURE 2. Number of new medicines in each phase of clinical evaluation, 2020



Data source: GlobalData Healthcare database (accessed July 2020); IQVIA MIDAS.

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 2020, 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 infectious diseases (such as COVID-19) and central nervous system therapies.

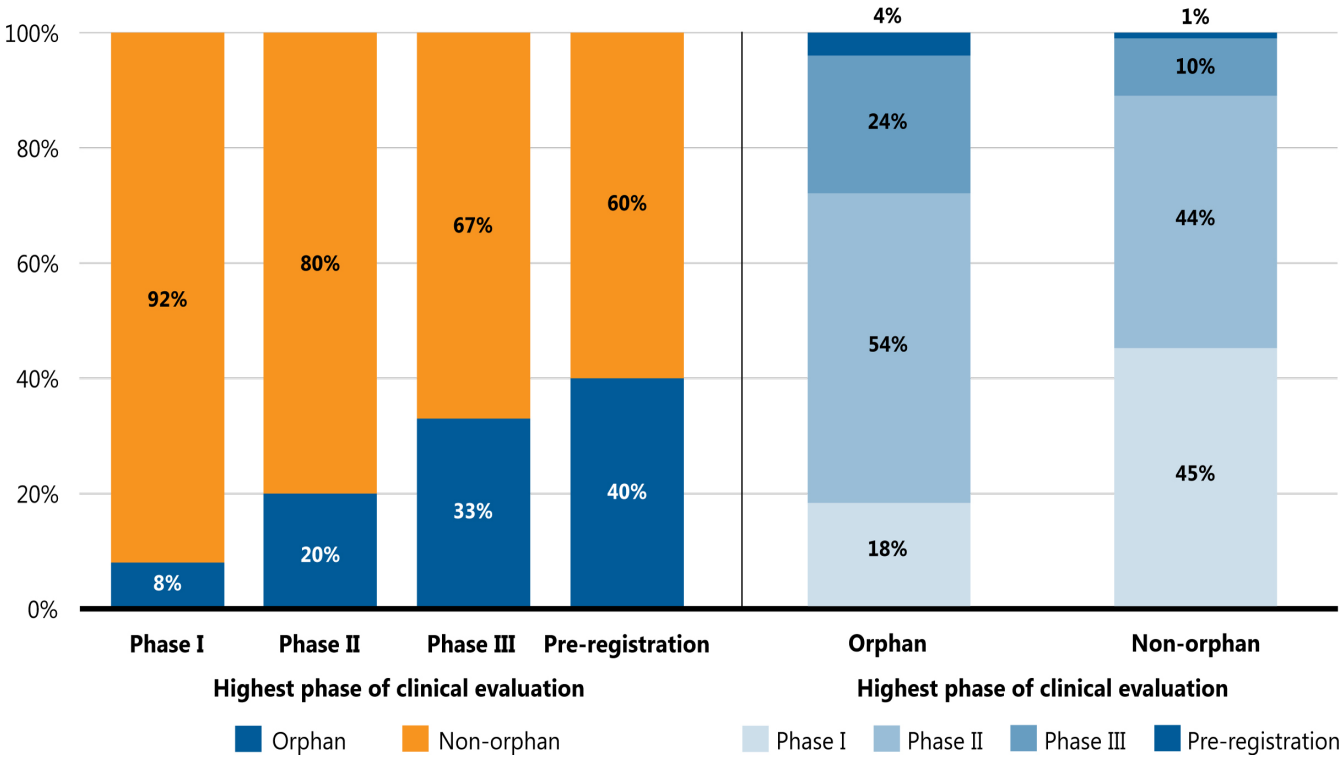
FIGURE 3. Therapeutic class distribution of pipeline medicines by phase of clinical evaluation, 2020



Data source: GlobalData Healthcare database (accessed July 2020).

Orphan medicines, as designated by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA), accounted for a notable proportion of the total medicine pipeline in 2020. Figure 4 provides the shares of orphan and other medicines in the pipeline from Phase I to pre-registration. Orphan medicines made up a greater share of medicines in the latter stages of clinical evaluation, accounting for 8% of pipeline medicines in Phase I clinical trials and 40% of those in pre-registration. A distribution of orphan medicines by highest phase of clinical evaluation indicates that, compared to non-orphan medicines, rare disease treatments are more highly concentrated in the advanced phases of evaluation.

FIGURE 4. Share of orphan medicines in the pipeline by highest phase of clinical evaluation, 2020



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 Turkey). 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 November 2020).

MEDS PIPELINE MONITOR 2020

The following tables list the selection of new pipeline medicines in 2020, those retained from earlier editions of the *Meds Pipeline Monitor*, as well as medicines featured in previous editions that have since gained market authorization. These pipeline medicines will continue to be monitored in future editions of this report.

Applying the screening criteria described in the Methodology section, 16 of the 935 pipeline medicines in late stages of clinical evaluation, including 5 gene therapies, were selected for inclusion in the 2020 new medicines list (Table 4). Likewise, 12 late-stage medicines were retained from the 2019 list as they continued to satisfy the same criteria (Table 5).

Three new medicines featured in the 2019 edition of the MPM had received market authorization in the US, Europe, or Canada as of November 2020. These medicines are listed in Table 6.

TABLE 4. Selected new medicines for 2020

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		
Inclisiran Novartis AG	Atherosclerosis	• Inclisiran is a small interfering ribonucleic acid (siRNA) molecule monoclonal antibody being investigated for the treatment of hypercholesterolemia.[1] • Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition is a new strategy to reduce LDL cholesterol (LDL-C), that is currently pursued by monoclonal antibodies. A promising novel approach to target PCSK9 is using small interfering RNAs to inhibit hepatic PCSK9 synthesis.[2] • In the ORION-11 phase III, it achieved sustained, additional 50% LDL-C reduction in patients receiving background statin therapy.[3,4] • It may be an option as a cholesterol-lowering medication, where it would likely be used in high risk patients or in patients who are unable to achieve their LDL-C targets despite maximally tolerated statin therapy or who are intolerant to statin therapy.[5] • Total global revenue forecast $2.1 billion by 2026.*

CENTRAL NERVOUS SYSTEM		
Aducanumab Biogen Inc.	Alzheimer's disease	• A recombinant human monoclonal antibody that binds primarily to aggregated forms of Aβ, including soluble oligomers and insoluble fibrils, but reportedly does not bind Aβ monomers.[6] • Given once a month by infusion in Phase III trials. • Met its primary goal in Phase III EMERGE trial, with patients receiving the highest dose of aducanumab experiencing a significant reduction in the progression of cognitive and functional impairments.[7] • Currently under review by the FDA. • Total global revenue forecasted to be $11.0 billion by 2026.*
GENETIC DISORDERS		
Pegunigalsidase alfa Chiesi Farmaceutici SpA	Fabry disease (FD)	• A novel PEGylated, covalently cross-linked form of α-galactosidase A enzyme replacement therapy (ERT).[8] • In the 12-month on-treatment Phase III BRIDGE study, interim data analysis indicates significant improvement in kidney function in patients switched from agalsidase alfa (Replagal) to pegunigalsidase alfa.[9] • May represent an advance in ERT for FD, based on its unique pharmacokinetics and apparent low immunogenicity.[10] • Currently under review by the FDA. • Total global revenue forecasted to be $39 million by 2026.*
HEMATOLOGICAL DISORDERS		
Etranacogene dezaparvovec UniQure NV	Hemophilia B (factor IX deficiency)	• A recombinant AAV5 vector that includes a gene cassette containing the factor IX (FIX) Padua variant under the control of a liver-specific promoter.[11] • In clinical studies, it resulted in clinically relevant increases in factor IX (FIX) activity, cessation of bleeds, and abrogation of the need for FIX replacement.[12] • A one-time dose offers the potential to shift the disease to a milder phenotype and reduce or abrogate the bleed risk and FIX concentrate consumption.[13] • Total global revenue forecasted to be $695 million by 2026.*

Fidanacogene elaparvovec (previously SPK-9001) Pfizer Inc	Hemophilia B (factor IX deficiency)	• A hepatotropic bioengineered adeno-associated virus (AAV) based vector that delivers a high activity factor IX (FIX) transgene driven by a liver-specific promoter.[14] • Study data for 15 patients receiving one infusion demonstrated a marked reduction in bleeding frequency and exogenous FIX use at 52 weeks post-infusion.[15] • It is hoped that, once treated, patients will be able to produce factor IX themselves, rather than having to regularly inject factor IX.[16] • Total global revenue forecasted to be $252 million by 2026.*
IMMUNOLOGY		
Anifrolumab AstraZeneca Plc	Systemic lupus erythematosus	• Binds to the type I interferon receptor, blocking the activity of type I interferons such as interferon-α and interferon-β.[17] • Very promising agent for cutaneous lupus erythematosus (CLE), for which no specific approved therapies are available and resistance to conventional treatments is common.[18,19] • Positive results from the Phase III TULIP-2 study: patients who received anifrolumab were more likely to have reductions in the glucocorticoid dose and in the severity of skin disease than were patients who received placebo.[20] • Monthly intravenous administration resulted in a higher percentage of patients with a response (as defined by a composite endpoint) at week 52 than did placebo.[21] • Total global revenue forecasted to be $419 million by 2026.*
Mirikizumab Eli Lilly and Co.	Plaque psoriasis (psoriasis vulgaris)	• A first-in-class, monoclonal antibody that binds to the p19-subunit of IL-23 (IL-23p19 inhibitor).[22] • In the OASIS-2 study, where it was compared to Cosentyx (secukinumab), it demonstrated superiority at week 52 in terms of the proportion of patients with a static Physician's Global Assessment (sPGA) of (0,1) with at least a 2-point improvement and the proportion of patients with at least a 90% and 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI 90/PASI 100).[23] • Total global revenue forecasted to be $994 million by 2026.*

INFECTIOUS DISEASE		
Ibrexafungerp Scynexis Inc.	Aspergillosis; Blastomycosis; Candidiasis; Coccidioido-mycosis; Histoplasmosis; Systemic candidiasis; Vulvovaginal candidiasis	• A first-in-class, orally administered glucan synthase inhibitor that interferes with the synthesis of the fungal cell wall polymer β-(1,3)-d-glucan.[24] • A Phase III trial showed that oral ibrexafungerp may be an effective treatment for invasive candidiasis infections that could help patients avoid the need for long-term IV treatment and hospital stays, especially for those intolerant or refractory to standard antifungal treatment or in whom long term IV treatment is not feasible.[25,26] • Total global revenue forecasted to be $419 million by 2026.*
METABOLIC DISORDERS		
Dasiglucagon Zealand Pharma AS	Hypoglycemia	• A human glucagon analog that also consists of 29 amino acids, 7 of which have been substituted when compared with native glucagon. This results in an improved stability and reduced the tendency to form fibrils when dissolved in aqueous solution.[27] • It is being developed to offer a stable ready-to-use pen rescue treatment for severe hypoglycemia. • The pivotal Phase III trial, in which it was compared to a placebo and injectable glucagon, demonstrated that a single dose of dasiglucagon rapidly increases blood glucose levels in patients with type 1 diabetes following insulin-induced hypoglycemia.[28] • Currently under review by the FDA. • Total global revenue forecasted to be $311 million by 2026.*
Teplizumab Provention Bio Inc.	Type 1 diabetes (juvenile diabetes)	• An Fc receptor-nonbinding anti-CD3 monoclonal antibody.[29] • Multiple studies involving patients with type 1 diabetes have shown that it reduces the loss of beta-cell function, even as long as seven years after diagnosis.[30] • The first disease-modifying drug with data showing a long-term delay to insulin dependence.[31] • Currently under review by the FDA. • Total global revenue forecasted to be $743 million by 2026.*

ONCOLOGY		
Idecabtagene vicleucel (bb2121) Bristol-Myers Squibb Co.	Refractory multiple myeloma; Relapsed multiple myeloma	• A B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell immunotherapy.[32,33] • Targets BCMA, which is found almost exclusively on the surfaces of malignant plasma cells to the exclusion of other cell types.[34] • The Phase III KarMMa trial is evaluating it in patients with relapsed and refractory multiple myeloma.[35] • Granted accelerated assessment status by the EMA in March 2020.[36] • Total global revenue is forecasted to be $1.7 billion by 2026.*
Lisocabtagene maraleucel Juno Therapeutics Inc.	Diffuse large B-cell lymphoma; Follicular lymphoma; Non-Hodgkin lymphoma; Primary CNS lymphoma; Primary mediastinal B-cell lymphoma	• A CD19-directed chimeric antigen receptor (CAR) T-cell therapy that provides a valuable new treatment option for patients with relapsed/refractory (R/R) B-cell non-Hodgkin lymphoma.[37] • However, considerable toxicity, mainly cytokine release syndrome and neurotoxicity, limits general applicability of these CD19-directed CAR T-cell therapies.[38] • For individuals with refractory disease and those who relapse after conventional therapies, CAR T-cells are an important treatment option and have led to remissions in otherwise refractory patients.[39] • In Phase I trials, it resulted in a high rate of rapid and durable complete responses in patients with aggressive relapsed or refractory large B-cell lymphoma.[40] • Total global revenue forecasted to be $1.1 billion by 2026.*
Ofranergene obadenovec Vascular Biogenics Ltd	Epithelial ovarian cancer	• A first-in-class, targeted anti-cancer gene therapy with a dual mechanism: anti angiogenic/vascular disruption and induction of an anti-tumour directed immune response; used in combination with paclitaxel for patients with platinum-resistant ovarian cancer.[41] • Favourable tumour responses and overall survival outcomes were associated with induction of an immunotherapeutic effect. [42] • Total global revenue forecasted to be $84 million by 2026.*
Pevonedistat Millennium Pharmaceuticals Inc.; Takeda	Myelodysplastic syndromes (MDS)	• A potent, selective, first-in-class NEDD8-activating enzyme (NAE) inhibitor.[43] • NAE has been identified as a tractable target in chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma.[44] • In a Phase III trial, pevonedistat plus azacitidine increased overall survival, event-free survival, and response rates compared with azacytidine alone

		in higher-risk myelodysplastic syndromes and low-blast acute myelocytic leukemia (AML).[45] • Had a comparable safety profile to azacitidine alone in patients with higher-risk MDS / chronic myelomonocytic leukemia (CMML).[46] • Total global revenue forecasted to be $498 million by 2026.*
Umbralisib tosylate TG Therapeutics Inc	Extranodal marginal zone B-cell lymphoma (mucosa-associated lymphoid tissue or MALT-lymphoma); Follicular lymphoma (FL); Nodal marginal zone B-cell lymphoma; Splenic marginal zone B-cell lymphoma	• An oral, once-daily treatment that works by inhibiting the proteins PI3K-delta and CK1-epsilon, referred to as a dual phosphoinositide-3-kinase-δ (PI3K-δi) inhibitor. PI3K-delta is an enzyme important for many cell activities.[47,48] • In the UNITY-NHL trial, patients who had received at least two prior lines of therapy achieved an overall response rate (ORR) greater than 40%, which was the primary endpoint.[49] • Shows high rates of response in clinical trials and an improved safety profile with fewer severe adverse events.[50] • Currently under review by the FDA. • Total global revenue forecasted to be $486 million by 2026.*
RESPIRATORY		
Tezepelumab Amgen Inc.	Asthma	• A first-in-class, fully human IgG2λ monoclonal antibody that binds human thymic stromal lymphoprotein (TSLP), prevents interaction with its receptor, and consequently, inhibits multiple downstream inflammatory pathways.[51] • Has shown safety, tolerability, and efficacy as an add-on therapy for patients with severe uncontrolled asthma.[52] • In Phase II trials, patients who received add-on tezepelumab had lower rates of clinically significant asthma exacerbations than those who received placebo.[53] • Total global revenue forecasted to be $1.5 billion by 2026.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2020, and are given in US dollars.

Data source: GlobalData Healthcare database.

TABLE 5. Pipeline medicines retained from the 2019 *Meds Pipeline Monitor*

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
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.[54,55,56,57] • Being tested in the dominantly inherited Alzheimer's network trials unit (DIAN-TU).[58] • There are several ongoing Phase III trials in Canada.[59,60,61] • Total global revenue forecasted to be $108 million by 2026.*
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.[62] • For oral treatment of non-alcoholic steatohepatitis (NASH) with liver fibrosis.[63] After one year of treatment, twice as many patients achieved improvement in fibrosis and no worsening of NASH compared with placebo.[64] • Non-alcoholic fatty liver disease (NAFLD) has an increasing prevalence worldwide. At present, no specific pharmacotherapy is approved for NAFLD.[65] • In studies to date, safety and tolerability were comparable to placebo.[66] • It may ameliorate the detrimental fibrotic events that persist in treated HIV.[67] • Phase III study is ongoing.[68] • Total global revenue forecasted to be $85 million by 2026.*

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.[69] • Phase III study is ongoing.[70] • Total global revenue forecasted to be $119 million by 2026.*
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.[71] • Phase III trials are ongoing.[72,73,74,75] • Total global revenue forecasted to be $521 million by 2026.*
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[76] and to maintain mean Hb concentrations in patients on hemodialysis previously receiving epoetin alfa.[77] • Phase III trials are ongoing.[78] • Total global revenue forecasted to be $1.1 billion by 2026.*

ONCOLOGY		
Ipatasertib Genentech, Inc.	Metastatic hormone refractory (castration-resistant, androgen-independent) prostate cancer	• A first-in-class, 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.[79] • Improved outcomes in a subset of patients with metastatic triple-negative breast cancer (TNBC) when combined with paclitaxel in the first-line setting.[80,81] Targeted therapies for TNBC—which accounts for around 20% of breast cancers—remain unavailable. • Phase III trials in breast cancer[82,83] and prostate cancer[84] are ongoing. • Early promising results in prostate cancer.[85] • Total global revenue forecasted to be $1.3 billion by 2026.*
Melphalan flufenamide hydrochloride (Melflufen, Ygalo) Oncopeptides AB	Refractory multiple myeloma; Relapsed multiple myeloma (MM)	• Peptide-based alkylating agent; a novel dipeptide prodrug of melphalan plus flufenamide that rapidly delivers a cytotoxic payload into tumour cells.[86] • Overcomes drug-resistance and improves multiple myeloma patient outcomes.[87] • Phase III trials are ongoing.[88] • Total global revenue forecasted to be $547 million by 2026.*
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).[89,90]
Ublituximab (Utuxin) TG Therapeutics, Inc.; LFB S.A.	Refractory chronic lymphocytic leukemia (CLL); Relapsed chronic lymphocytic leukemia (CLL); Relapsing	• A next generation glycoengineered anti-CD20 monoclonal antibody. • Next-generation with higher complement-dependent cytotoxicity and antibody-dependent cellular cytotoxicity against malignant B-cells.[91]

	multiple sclerosis (RMS)	• Demonstrated efficacy in patients with high-risk CLL and B-non-Hodgkin lymphoma in both first line, subsequent lines, and in rituximab refractory patients.[92] • In combination with ibrutinib, resulted in rapid and high response rates in CLL.[93] • Phase III in RMS are ongoing.[94] • Total global revenue forecasted to be $497 million by 2026.*
OPHTHALMOLOGY		
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.[95] • 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.[96] • 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.[97] • Phase III registrational trial (STAR) in patients with choroideremia has been initiated in many countries, including Canada.[98,99] • Total global revenue forecasted to be $242 million by 2026.*
Zuretinol acetate Retinagenix LLC 	Leber congenital amaurosis (LCA); Retinitis	 • Oral retinoid; it is a synthetic retinoid replacement for 11-cis-retinal. • The drug candidate facilitates the recovery or restoration of visual function by acting as a replacement for missing 11-cis-retinal and restoring a key biochemical component of the visual (retinoid) cycle.

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2020, and are given in US dollars.
Data source: GlobalData Healthcare database. The database search for new medicines added to the MPM was performed in July 2020.

TABLE 6. Pipeline medicines from the 2019 *Meds Pipeline Monitor* that have gained market authorization

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 (Nexletol) 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.[100] • 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.[101,102,103] • 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.[104,105] • Approved by the FDA on February 21, 2020. • Total global revenue forecasted to be $784 million by 2026.*
GASTROINTESTINAL AND METABOLIC DISORDERS		
Setmelanotide (Imcifree) 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.[106] • Phase III studies are ongoing.[107,108] • Approved by the FDA on November 27, 2020. • Total global revenue forecasted to be $845 million by 2026.*

IMMUNOLOGY		
Imlifidase (Idefirix) 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.[109] • May represent "a groundbreaking new method of desensitization for patients who otherwise might have no hope for receiving a lifesaving transplant." [110] • Approved by the EU on August 25, 2020. • Total global revenue forecasted to be $144 million by 2026.
INFECTIOUS DISEASE		
Cabotegravir (Cabenuva, Vocabria) 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).[111] • Few interactions with commonly used concomitant medications.[112] • 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.[113] • 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.[114] • Offers an alternative to daily regimens and may improve preexposure prophylaxis (PrEP) adherence.[115] • Approved by Health Canada on March 18, 2020. • Total global revenue forecasted to be $1.3 billion by 2026.*
Fostemsavir tromethamine (Rukobia) 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.[116] • 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.[117] • Results from a Phase III trial showed that patients with multidrug-resistant HIV-1 infection with limited therapy options receiving the drug had a significantly greater decrease in the HIV-1 RNA level than

		those who received placebo during the first eight days. Efficacy was sustained through 48 weeks.[118] • Approved by the FDA on July 2, 2020. • Total global revenue forecasted to be $429 million by 2026.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2020, 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 are new to Canada but may have been approved in other jurisdictions.

Table 7 highlights six 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. Of the nine medicines reported in the 2019 edition, seven have since received market authorization from Health Canada while two were retained for the current list.

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, 2020

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
CARDIOVASCULAR		
Inclisiran Novartis AG	Atherosclerosis	• Inclisiran is a small interfering ribonucleic acid (siRNA) molecule monoclonal antibody being investigated for the treatment of hypercholesterolemia.[119] • Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition is a new strategy to reduce LDL cholesterol (LDL-C), that is currently pursued by monoclonal antibodies. A promising novel approach to target PCSK9 is using small interfering RNAs to inhibit hepatic PCSK9 synthesis.[120] • In the ORION-11 phase III, it achieved sustained, additional 50% LDL-C reduction in patients receiving background statin therapy.[121,122] • It may be an option as a cholesterol-lowering medication, where it would likely be used in high risk patients or in patients who are unable to achieve their LDL-C targets despite maximally tolerated statin therapy or who are intolerant to statin therapy.[123] • Total global revenue forecast $2.1 billion by 2026.*

HEMATOLOGICAL		
Roxadustat (Ai Ruizhuo) AstraZeneca Canada Inc.	Anemia in chronic kidney disease (CKD)	• A first-in-class oral hypoxia-inducible factor prolyl hydroxylase inhibitor.[124] • Corrects anemia through multiple pathways by mimicking a response to reduced oxygen levels.[125] • Clinical trials have shown that it can significantly reduce hepcidin, causing iron insufficiency, which causes erythrocytes to fail to mature normally, and can potentially be used for the treatment of inflammation-induced anemia in CKD.[126,127] • Total global revenue forecasted to be $1.5 billion by 2026.*
IMMUNOLOGY		
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.[128,129] • Among the first drugs with specific action against IL-23 to be approved by the FDA and the EMA.[130] • Represents an evolving treatment strategy in chronic plaque psoriasis.[131] • Demonstrated significant clinical improvement and a favourable safety profile. In Phase III trials, it demonstrated superior efficacy vs. etanercept treatment.[132] • The 12-week dosing regimen for maintenance has one advantage: as patients experience subcutaneous injections as burdensome, it may help achieving higher patient adherence and compliance.[133] • Approved by the FDA (Ilumya; 2018-03-20). • Total global revenue forecasted to be $245 million by 2026.*
ONCOLOGY		
Binimetinib (Mektovi)**; Encorafenib** (Braftovi) Pfizer Canada ULC	For unresectable or metastatic melanoma	• Binimetinib is a reversible inhibitor of the selective mitogen-activated protein kinase (MEK1/2)[134]; encorafenib is a kinase inhibitor. Both medicines are used together in the treatment of metastatic melanoma. • The favorable survival results and the attractive toxicity profile suggest that the combination of binimetinib with encorafenib is an intriguing standard option when targeted therapies are considered as first line treatment in BRAF mutated melanoma patients.[135] • Approved by the FDA (Mektovi; Braftovi; 2018-06-27). • Total global revenue forecasted to be $1.2 billion by 2026.*

Idecabtagene vicleucel (bb2121) Bristol-Myers Squibb Co.	Refractory multiple myeloma; Relapsed multiple myeloma	• A B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell immunotherapy.[136,137] • Targets BCMA, which is found almost exclusively on the surfaces of malignant plasma cells to the exclusion of other cell types.[138] • The Phase III KarMMa trial is evaluating it in patients with relapsed and refractory multiple myeloma.[139] • Granted accelerated assessment status by the EMA in March 2020.[140] • Total global revenue is forecasted to be $1.7 billion by 2026.*
GENITOURINARY AND SEX HORMONES		
Ospemifene (Osphena, Senshio) Duchesnay Inc.	Dyspareunia	• An oral, third-generation selective estrogen receptor modulator, used to treat moderate-to-severe dyspareunia due to postmenopausal vulvovaginal atrophy (VVA).[141,142] • Significantly improves the structure and pH levels of the vagina, reducing dyspareunia.[143] • 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.[144] • Compared to local estrogen therapies, showed significantly greater patient adherence and persistence, lowest mean outpatient costs, and significantly lower total all-cause healthcare costs.[145] • Approved by FDA (Osphena; 2013-02-26). • Total global revenue forecasted to be $30 million by 2026.*

* Consensus forecasts for global revenue data were collected from GlobalData, Q4-2020, and are given in US dollars.

Data source: GlobalData Healthcare database.

EMERGING COVID-19 THERAPIES

This new section of the *Meds Pipeline Monitor* includes an overview of new and existing pipeline medicines that are under evaluation for indications related to the prevention and treatment of COVID-19. An analysis of global markets provides information on COVID-19 medicines in all phases of clinical trials and pre-registration. In addition, a review of processes for the expedited development of medicines for COVID-19 in Canada demonstrates the potential impact of this fast-moving pipeline on the Canadian market.

Global markets

There is significant uncertainty in the COVID-19 drug pipeline worldwide. Published information to confirm safety and efficacy of the various treatments for COVID-19 is limited, and the available information is continuously evolving.[146]

In addition to the wide variety of vaccines under development, many novel and repurposed medicines are currently being evaluated in clinical trials for their potential benefits in the treatment of COVID-19. These include antivirals, interferons, antimalarials, antiparasitics, biologics (monoclonal antibodies and interleukin receptor antagonists), cellular therapies (mesenchymal stem cells and natural killer cells), convalescent plasma, and cytokine adsorbers.[147]

A breakdown of COVID-19 pipeline vaccines and treatments by phase of clinical evaluation is given in Figure 5. For this snapshot, data was extracted for medicines indicated for the treatment of COVID-19 with a development stage of Phase I, II, III, or pre-registration. These medicines are presented in three categories: vaccines, which are used to prevent infection of the novel coronavirus; COVID-19 treatments (new), which are new medicines used for the prevention or reduction of some of the complications associated with COVID-19 (e.g., pneumonia or respiratory complications, cytokine storm, and hyperinflammation); and COVID-19 treatments (existing), which are previously marketed medicines that have been repurposed to treat COVID-19 or its symptoms.

Figure 6 breaks down the COVID-19 candidate vaccines by category and highest development

Brief Insights

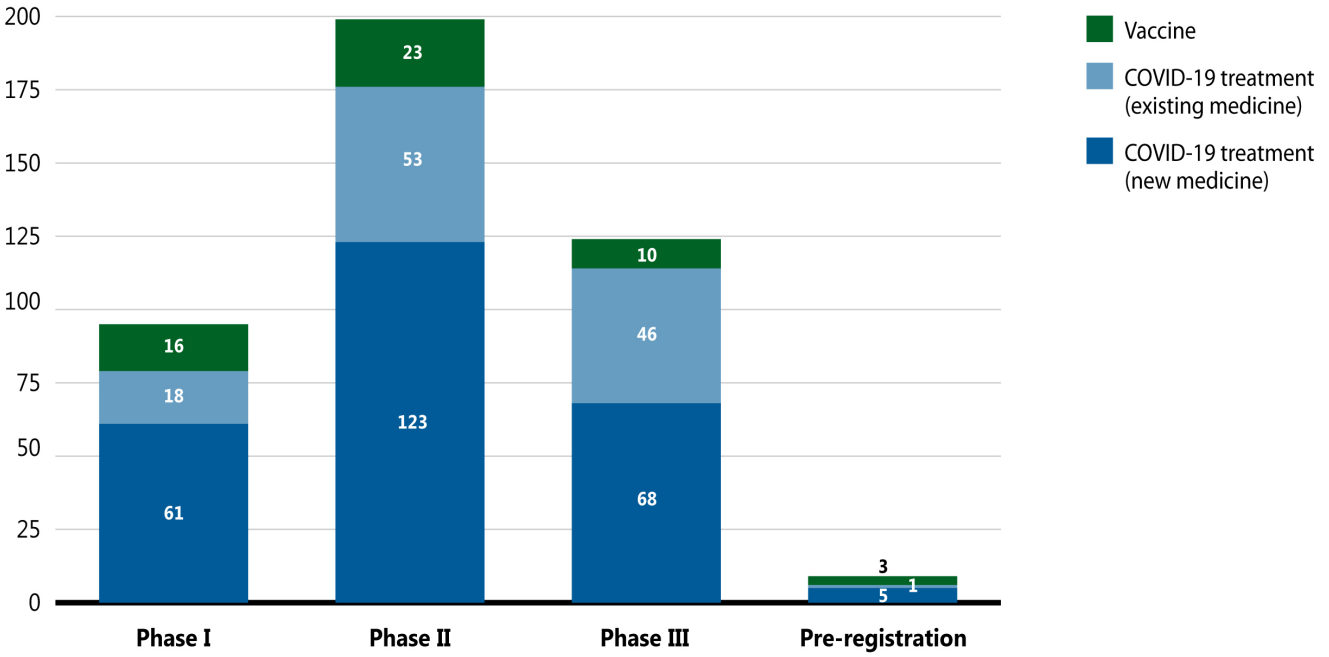
The pipeline for COVID-19 medicines is growing rapidly, with clinical investigations of novel and existing drugs:

- Gilead's remdesivir received FDA approval in October 2020, and is now approved in the EU, Japan, India, Singapore, Australia, and South Korea for treatment of hospitalized patients.
- The corticosteroid dexamethasone has been approved in the UK, Japan, and Taiwan.
- The FDA granted an emergency use authorization (EUA) for convalescent plasma to treat hospitalized COVID-19 patients.
- The FDA granted an EUA for Eli Lilly's monoclonal antibody bamlanivimab (LY-CoV555) to treat mild to moderate COVID-19. Health Canada has also granted authorization (with conditions).
- The FDA issued an EUA for Eli Lilly's Olumiant (baricitinib) in combination with remdesivir for the treatment of hospitalized COVID-19 patients requiring supplemental oxygen.
- The FDA also granted an EUA for Regeneron's REGN-COV2 antibody for treatment of mild to moderate COVID-19 for patients with positive SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Source: Pharma COVID-19 Bulletin, GlobalData (November 30, 2020); Health Canada (November 2020).

phase.[vii] Vaccines fall into various categories based on their mechanism of action; for example, while live attenuated vaccines target the whole virus, subunit and recombinant vaccines target one specific part of the virus.

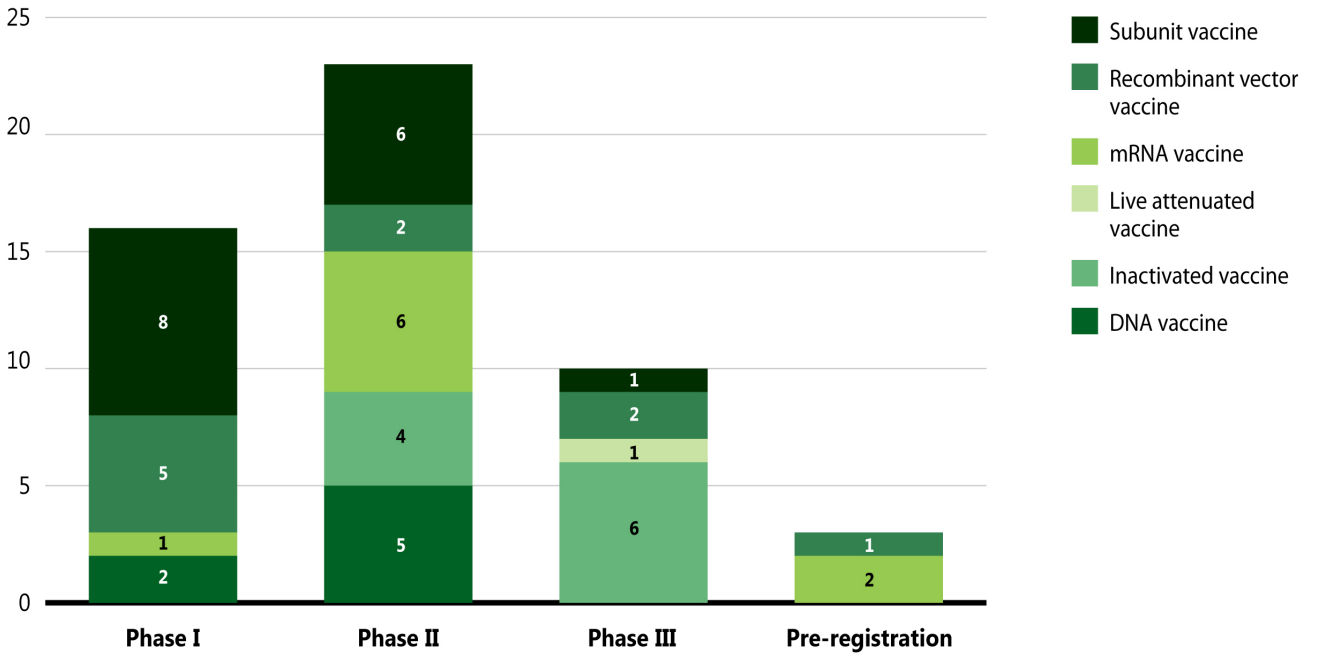
FIGURE 5. Number of COVID-19 vaccines and treatments in the pipeline, by phase of clinical evaluation, 2020



Data source: GlobalData (accessed November 2020).

[vii] Candidate vaccines in both clinical and preclinical evaluation are also reported by the World Health Organization. For a current list, visit their website: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

FIGURE 6. Distribution of COVID-19 vaccines by category and phase of clinical evaluation, 2020



Data source: GlobalData (accessed November 2020).

Canada

Canada has issued specific processes and guidance to expedite access to medicines during the COVID-19 pandemic. On August 25, 2020, the Public Health Agency of Canada released the federal/provincial/territorial public health response plan for ongoing management of COVID-19 to help guide decision-making in order to respond to future waves of the pandemic.[148]As of November 2020, five interim orders have been issued by the Minister of Health in response to COVID-19.[149,150,151,152,153] For example, the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19*,[154] signed by the Minister of Health on September 16, 2020, allows for the issuance of an expedited authorization for the importation, sale, and advertising of drugs used in relation to COVID-19, and the *Interim Order Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19*, approved on May 23, 2020, introduced an alternate pathway to facilitate clinical trials for potential COVID-19 drugs and medical devices, while upholding strong patient safety requirements and validity of trial data.[155]

As of November 2020, Health Canada had received five applications for drug and vaccine authorizations under the interim order (Table 8). Two of the five medicines—remdesivir and bamlanivimab (LY-CoV555)—had received conditional authorizations, while the remaining three applications were pending. In addition, 71 clinical trials for COVID-19 medicines and vaccines had been authorized by Health Canada at the time of the analysis,[156] with GlobalData reporting more than 90 planned and ongoing clinical trials in Canada.

Canada has joined the COVAX facility, a global initiative organized by the WHO, Gavi, the Vaccine Alliance, and the Coalition for Epidemic Preparedness Innovations (CEPI), formed to accelerate the development and manufacture of COVID-19 vaccines, as well as diagnostics and treatments, and to guarantee rapid, fair, and equitable access for people in all countries.[157]

TABLE 8. COVID-19 treatment and vaccine applications received by Health Canada, 2020

APPLICANT	MEDICINAL INGREDIENT(S)	THERAPEUTIC AREA	DATE APPLICATION WAS RECEIVED	OUTCOME OF APPLICATION	DATE OF DECISION/OUTCOME
Eli Lilly Canada, Inc.	Bamlanivimab (LY-CoV555)	Immune sera and immunoglobulins, for human use	2020-10-12	Authorized (with terms and conditions)	2020-11-20
Moderna Therapeutics, Inc.	mRNA-1273 vaccine	Vaccines, for human use	2020-10-12	Pending	N/A
Pfizer Canada ULC/BioNTech SE	mRNA vaccine BNT162b2	Vaccines, for human use	2020-10-09	Pending	N/A
AstraZeneca Canada, Inc.	Adenovirus vaccine vector (ChAdOx1)	Vaccines, for human use	2020-10-01	Pending	N/A
Gilead Sciences Canada, Inc.	Remdesivir	Antivirals for systemic use, for human use	2020-06-19	Authorized (with conditions)	2020-07-27

Data source: Heath Canada, Drug and vaccine authorizations for COVID-19: List of applications received (accessed November 2020): https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/applications.html

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