

JUST THE FACTS

30.3 MILLION

AMERICANS HAVE DIABETES.¹

7.2 MILLION

AMERICANS ARE UNDIAGNOSED¹

DIABETES IS THE

7TH LEADING

CAUSE OF DEATH IN
THE UNITED STATES²

\$327 BILLION,

COST OF DIAGNOSED DIABETES IN
THE UNITED STATES¹

MEDICINES IN DEVELOPMENT | 2019 REPORT

DIABETES



A Note from PhRMA President
and CEO **Stephen J. Ubl**

We are in a new era of medicine, one where innovative treatments for chronic conditions like diabetes are transforming and improving the lives of patients.

Biopharmaceutical companies are developing more than 160 new treatments for diabetes, including some that would offer an oral medicine option for Type 1 diabetes patients who currently administer insulin daily.

While diabetes patients need help managing their blood glucose levels, the reality is that many also need help affording the insulin and other medicines that keep them healthy. Patients' out-of-pocket costs continue to increase even though insurers receive significant discounts and rebates on insulin. That's because they often don't share those savings with patients. For example, patients with high-deductible plans sometimes have to pay the full list price for their insulin. Other plans require high copays or co-insurance at the pharmacy counter.

The status quo must change. America's biopharmaceutical companies are committed to addressing patient affordability challenges and to changing the incentives in the supply chain so that more of the \$166 billion in rebates and discounts given to middlemen help lower patients' costs at the pharmacy counter. Through this and other market-based solutions like delinking supply chain payments from the list price of a medicine and providing first dollar coverage of insulin in high deductible health plans, we can reduce out-of-pocket costs so patients don't bear a bigger financial burden than their insurance companies.

Researchers and scientists are working on cutting-edge treatments that will make managing diabetes easier, and we are fighting for ways to make these innovations more affordable for patients.



More Than **160** Medicines in Development for Diabetes and Related Conditions

Diabetes is a major public health issue in the United States, and projections suggest the number of those impacted by the disease will continue to grow. According to the Centers for Disease Control and Prevention (CDC), the number of Americans with diabetes is projected to double or even triple by 2050. The incidence of diabetes is also increasing for those under the age of 20. From 2002 to 2012, the incidence of type 1 diabetes increased 1.8 percent every year and type 2 diabetes increased 4.8 percent every year.³

Today, the facts are alarming. Diabetes affects more than 30 million Americans, a figure that includes seven million who are undiagnosed.¹ There are 1.5 million new cases diagnosed each year.¹ Despite advances in treatment, diabetes still remains the 7th leading cause of death in the United States, with more than 80,000 deaths attributed to diabetes in 2016.²

Diabetes treatment has improved tremendously over the years. Today, a range of insulin therapies and various other antidiabetic medicines help patients manage their condition. Even with these advances, diabetes remains a complex disease to treat. It often requires diligent management and frequent testing in addition to monitoring and coordinating on diet and exercise. Often, this must be done along with a range of treatments to maintain healthy and stable blood glucose (sugar) levels. As a result of these challenges, significant unmet need remains for patients struggling to adhere to available treatment regimens and for those who are unable to achieve adequate glycemic control with these options. These difficulties may be driven either by the unique characteristics of their disease, other co-morbid conditions or simply the inherent challenges of everyday diabetes management.

For example, medicines being taken for other conditions can exacerbate diabetes complications such as excessive weight, kidney problems or heart disease. In particular, some blood pressure medicines—such as thiazide diuretics—can cause blood sugar elevation, and others can alter lipid levels, as patients often respond differently to various insulins in terms of absorption and how long the insulin remains active in the body.

A patient's diet and exercise habits and daily schedules may further dictate which types of insulin are more appropriate and likely to support successful disease management. Likewise, some patients may be particularly averse to needles, and others—particularly older patients—may face challenges with vision, dexterity or forgetfulness. The reality is there is no one-size-fits all approach to diabetes management as the disease itself varies from patient to patient, and there is a range of patient needs.

Uncontrolled diabetes with persistent high blood sugars can lead to serious and costly health complications, such as heart disease, painful neuropathy, blindness, kidney disease/failure and lower-extremity amputations. All of these issues underscore the need for a wide variety of treatment options that meet the diverse needs of the millions of Americans struggling to manage the disease.

What is Diabetes?

Diabetes is a chronic condition where there is too much glucose in the blood. Normally, the pancreas makes insulin to help glucose enter the body's cells where it is used for energy. In patients with diabetes, the body does not make enough insulin, makes none at all, or does not use it properly, leading to high blood glucose levels. There are two main types of diabetes:

Type 1 diabetes: A condition in which the body is unable to produce insulin. This tends to develop in childhood and is generally treated with either daily insulin (human insulin or insulin analogs) injections or continuous subcutaneous insulin infusion via an insulin pump. Daily insulin therapy generally falls into two main categories: basal and bolus. Basal, or background, insulins are long-acting and intended to provide a consistent base level of insulin in the body throughout the day. Bolus insulins are rapid-acting and designed to modulate glucose spikes occurring after meals or other instances where blood glucose may be high. Patients generally inject basal insulins once a day, supplementing with bolus insulin injections at meal times. Alternatively, those wearing an insulin pump directly administer consistent levels of rapid-acting insulin to provide a base level throughout the day while also enabling additional bolus delivery to modulate spikes.

Type 2 diabetes: A condition in which the body does not produce enough insulin or becomes unable to use insulin properly. This often requires patients to manage high glucose levels with meal planning, weight loss and exercise. When these measures are not enough, patients may initiate treatment with antidiabetic medicines to help achieve better glycemic control. The majority of type 2 antidiabetic medicines are oral medicines.^{6,7} The use of multiple antidiabetic medicines is also common among type 2 diabetes patients, particularly over time. If these treatments are insufficient and/or insulin dependence builds over time, some patients may add insulin to their management protocol—often for example, beginning with basal insulin and subsequently adding bolus insulin. The range of insulin dependence varies considerably for type 2 patients depending on individual need.⁸

To help meet the unmet needs of diabetes patients, biopharmaceutical research companies continue to research and develop innovative treatment options for patients. Today, there are 167 medicines in development for type 1 and type 2 diabetes and diabetes-related conditions.⁴ All of the medicines are in clinical trials or awaiting review and approval by the U.S. Food and Drug Administration (FDA). The 167 medicines include:

- **77 medicines for type 2 diabetes:** In type 2 diabetes, which comprises up to 95 percent of diagnosed diabetes cases, the body is resistant to the action of insulin.⁵ To combat this resistance, the pancreas makes even more insulin until it fails to produce enough insulin to overcome the resistance, causing blood glucose levels to be higher than normal.
- **32 medicines for type 1 diabetes:** Type 1 diabetes, which comprises about five percent of diagnosed diabetes cases, is an autoimmune disease where the body does not produce insulin as a result of the immune system attacking the insulin-producing cells of the pancreas.⁵ Type 1 diabetes, which is usually diagnosed in children and young adults, requires lifelong insulin treatment for survival.
- **68 medicines for diabetes-related conditions:** These include chronic kidney disease due to diabetes (diabetic nephropathy), painful diabetic neuropathy, diabetic macular edema and diabetic gastroparesis.

Diabetes Medicines in the Pipeline

Biopharmaceutical research companies continue to explore new and varied approaches to fight diabetes and diabetes-related conditions. Among the 167 medicines in the development pipeline today, some potential innovations include:

Type 1 and Type 2 Diabetes

A potential first-in-class oral medicine in development provides a new way to address type 1 and type 2 diabetes by acting on two different targets in the body. It is a dual inhibitor of both sodium-glucose co-transporter types 1 and 2 (SGLT1 and SGLT2), which are molecules that also help move glucose in and out of the body's cells independent of insulin. This movement is important for the absorption of glucose in the body both by the intestine (glucose absorption from food) and by the kidney (which determines how much glucose leaves the body via urine).

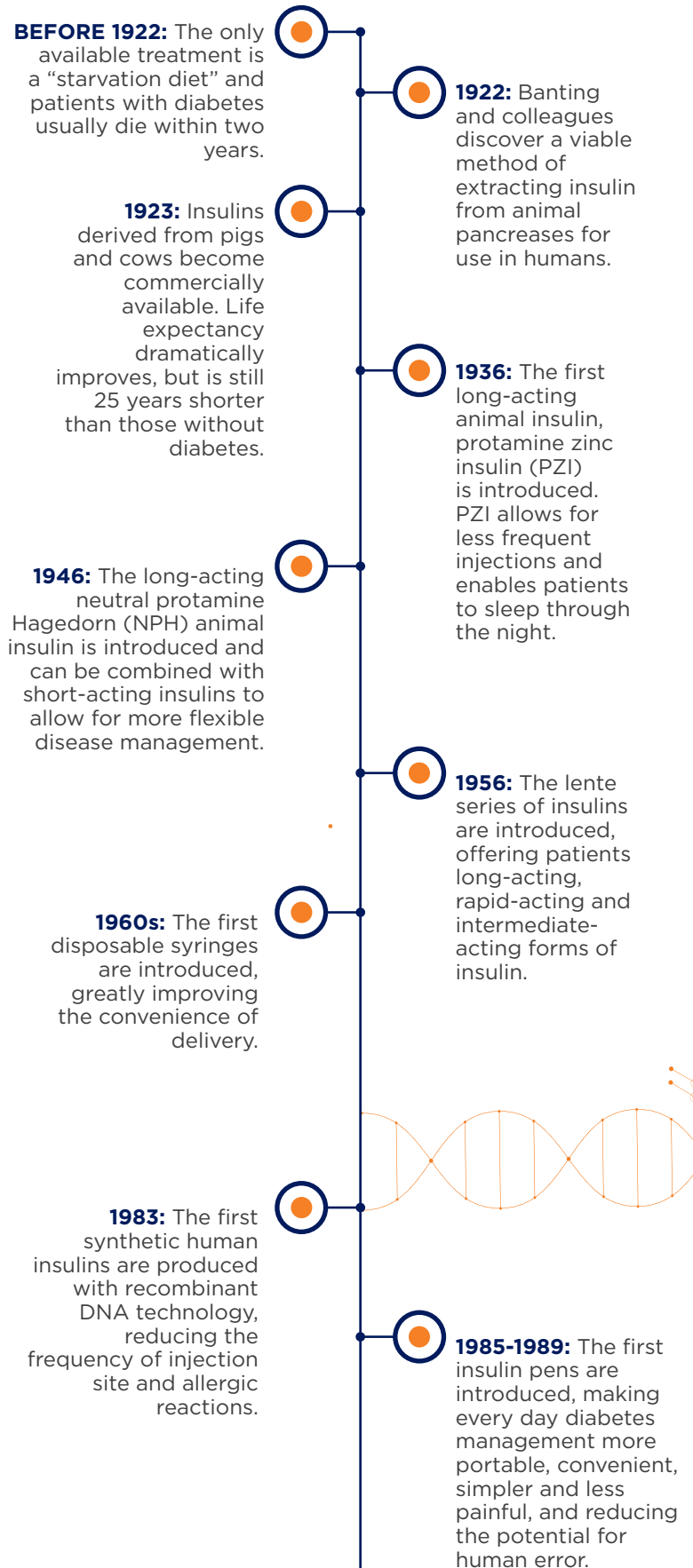
Type 1 Diabetes

A fully recombinant monoclonal antibody is in development for treating patients with newly-diagnosed type 1 diabetes. It is combined with an approved subcutaneous GLP-1 agonist, liraglutide, which is indicated as an adjunct to diet and exercise to improve glycemic control and to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes. The antibody targets the protein interleukin-21 (IL-21), which is involved in communication between cells and plays a role in regulating the immune system. In type 1 diabetes, the immune system mistakenly attacks beta cells in the pancreas. These cells normally produce insulin. Targeting IL-21 provides a mechanism to modify the immune system, which may help mitigate the attack on the pancreas and preserve beta cells.

Type 2 Diabetes

An oral version of an already approved glucagon-like peptide (GLP-1) receptor agonist is in development for type 2 diabetes. The approved subcutaneous medicine is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. It lowers blood glucose levels and reduces body weight. The oral version is being developed as a once-daily treatment, giving patients an injection-free option to manage their diabetes.

ADVANCEMENTS OF INSULIN TREATMENTS OVER TIME



Diabetic Gastroparesis

Both type 1 and type 2 diabetes can affect nerves throughout the body, including the vagus nerve, which controls how quickly the stomach empties after eating or drinking. When this nerve is damaged, digestion slows down and food stays in the body longer than it should, causing diabetic gastroparesis. A medicine in development for diabetic gastroparesis, and derived from natural ghrelin, has been enhanced to stimulate gastrointestinal motility with greater potency and enhanced stability and pharmacokinetics (absorption, distribution, metabolism and excretion).

Other cutting-edge treatments in development for diabetes include an artificial pancreas that is a closed-loop drug-device system that monitors blood glucose levels automatically and provides insulin or a combination of insulin and a second hormone to patients with type 1 diabetes; and drug-device combination products can deliver continuous and consistent drug therapy for long periods of time while minimizing peak drug level related side effects in type 2 diabetes.



1996: The first rapid-acting insulin analog, insulin lispro, more closely resembles the natural physiological release of insulin and provides greater flexibility by allowing for closer administration to meals.

2000-2005: Rapid-acting insulin aspart and insulin glulisine and long-acting insulin levemir expand the insulin analog choices available to patients.

2014: A more portable inhaled rapid-acting insulin allows for greater flexibility of mealtime administration.

2015-2018: More concentrated high dose options of various insulin analogs enable fewer injections for some patients.

2018: An improved formulation of insulin aspart provides quicker onset, allowing for greater patient flexibility to administer insulin before, during, or even after meals.

2000: The first long-acting insulin analog, insulin glargine, mimics the characteristics of healthy pancreas release, allowing for a more stable effect and less frequent, once-a-day dosing.

2015: Two ultra-long-acting insulin analogs offer patients 24-hour (or sometimes even longer) coverage and greater flexibility in dosing for patients with shifting schedules.

2017: A pre-filled “junior” pen for children offers more precise dosing adjustments due to low-insulin requirements, greater accuracy, reduced injection force and torque and a memory function for prior dosing.

Type 2 Diabetes: Prevention and Early Detection

Unlike type 1 diabetes, type 2 diabetes can be prevented or delayed. Early detection and effective treatment play a key role in keeping people with diabetes healthy. Early detection can help to reduce the risk of serious complications such as premature heart disease, stroke, blindness, limb amputations and kidney failure. Key strategies for preventing the disease or successfully managing the disease include staying at a healthy weight, being physically active, managing blood glucose levels, treating high blood pressure, lowering unhealthy levels of cholesterol and not smoking.

While prediabetes puts people at a higher risk for developing type 2 diabetes, they will not automatically develop this disease. For some people with prediabetes, early treatment can actually return blood glucose levels to the normal range. Research shows that people can lower their risk for type 2 diabetes by 58 percent by losing 5 to 7 percent of their body weight (10 to 14 pounds for patients that weigh 200 pounds) and exercising moderately (e.g. brisk walking) 30 minutes a day, five days a week.⁹

Improving Adherence for Better Outcomes and Cost Savings

While maintaining a healthy weight and exercise can help prevent and manage type 2 diabetes, medicines play a key role in helping to manage a patient's disease, maintain healthy glucose levels and prevent serious disease complications. But of the 30 million Americans with diabetes, only 19 million receive treatment and just 8 million receive treatment that allows them to reach their treatment goals – leaving more than half of those treated for diabetes with uncontrolled disease.¹⁰

Continuous advances in the treatment of diabetes over the past decade alone have dramatically simplified treatment regimens and improved patient adherence and quality of life. More than 20 additional medicines have become available to meet the diverse needs of both type 1 and type 2 diabetes patients. More than 10 oral combination medicines have been approved, each combining more than one class of diabetes medicines, reducing pill burden for patients and barriers to treatment compliance. Diabetes patients on combination medicines are more likely to be adherent to treatment regimens, use fewer health care resources and have an increased life expectancy compared to those on multiple single dose therapies. Three medicines stemming from two classes of medicines known as SGLT2 inhibitors and GLP1 agonist receptors have been shown to reduce risk of major adverse cardiac events, such as cardiac stroke or death.^{11,12} Additionally, recent advances in insulin therapy and products that combine insulin into innovative delivery devices have also continued to meet the diverse needs of patients.

While patient adherence to diabetes medicines can lead to better health outcomes, it also leads to reduced health care costs. One study estimates that improved adherence among patients with diabetes could result in over 1 million avoided emergency departments visits and hospitalizations, for potential saving of \$8.3 billion each year.¹³ A study of Medicare patients with diabetes showed proper adherence to diabetes medicines was associated with \$4,000 in reduced total Medicare (including medicine) spending over two years.¹⁴ While patients with higher adherence levels also incur higher pharmacy costs, they are associated with about 10 percent lower annual health care expenditures compared to those who are less adherent.¹⁵ Interruptions in insulin therapy can increase medical costs by nearly 30 percent, underscoring the importance of addressing persistence to therapy.¹⁶

Looking ahead, companies continue to strive to fulfill the unmet needs of diabetes patients. For example, insulin manufacturers have announced plans alongside digital health platform manufacturers to develop products which connect dosing data from insulin pen devices with diabetes management solutions, such as data from continuous glucose monitoring systems and blood glucose meters. Innovations such as these allow for connection of real-time monitoring and precise dosing information. This reduces monitoring burden on patients and allows for more precise and effective delivery of insulin—a significant paradigm shift in treatment.

A Researchers Profile Advancing Diabetes Innovation



Laura Michael

Senior Director, Outcomes and Translation, Diabetes and Complications Therapeutic Area, Eli Lilly and Company

Daily Discoveries

Dr. Laura Michael started her career at Eli Lilly and Company (Lilly) researching cardiovascular disease and the complications that frequently arise from it. Working in this field, she grew increasingly interested in the connections between heart health and type 2 diabetes, especially because so many diabetes patients suffer from serious cardiovascular complications. Today, she leads a team of researchers who are working to develop new medicines to help manage and prevent complications from type 2 diabetes, such as heart and kidney failure.

The Driving Force

Addressing the unmet needs of patients is by far the most important driver of her work, but Laura notes that there's something more that energizes her on a daily basis. "I think if you asked 10 scientists, nine of them will probably say that there is a family history that led them to their interest in science and to a specific field of medicine," says Laura. "My mother's side of the family suffered from heart problems, like heart attack and stroke, and my dad's side suffered from diabetes."

Challenges, Chance and Looking Forward

"You've probably noticed a lot of talk about precision or personalized medicine—diabetes is a classic example. People think diabetes is the same disease for everyone, but that's not the way it works," says Laura. "One of the biggest challenges we face is the fact that the disease is so different for each individual patient. For example, a type 2 diagnosis could be the result of genetics or it could be something environmental. And if it's the latter, there are so many different environmental factors that could contribute to diabetes. Then once you get past the diagnosis, you have to look at the way the disease presents itself in different patients, which can vary widely as well."

For patients, though, Laura says that connected care is the most exciting thing on the horizon. "We're seeing more and more devices that self-regulate medication, such as insulin, so that patients can go about their day without worrying so much about it," says Laura. "It's truly remarkable, and something scientists could barely dream up just a few decades ago. It's just another example of how far we've come, but it's also important to remember that there's so much more we can do. I'm just excited to be on the frontlines in shaping that future."

"Pharmaceuticals have the effect of improving or maintaining an individual's health . . . adhering to a drug regimen for a chronic condition such as diabetes or high blood pressure may prevent complications . . . taking the medication may also avert hospital admissions and thus reduce the use of medical services."

— Congressional Budget Office¹⁷

Diabetes and Minorities in the United States

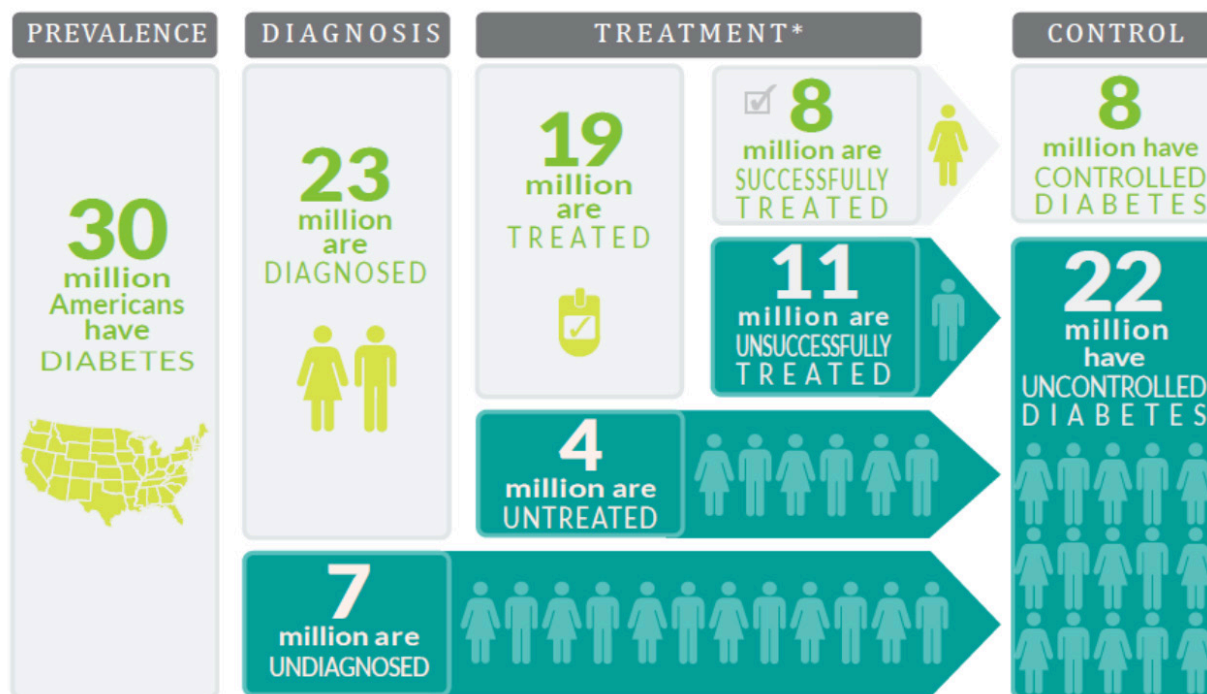
Racial and ethnic minorities in the United States—many of whom are born with a predisposition to diabetes—are disproportionately affected by the disease. According to the Office of Minority Health (OMH) at the FDA, racial and ethnic minorities have a higher burden of diabetes and worse diabetes control as well as being more likely to experience complications. For example, the death rate from diabetes among Hispanics is 50 percent higher than for non-Hispanic whites.

OHM cites a combination of risk factors for the disparities, including poverty, lack of access to health care and cultural attitudes and behaviors. These risk factors can be barriers to preventing diabetes and effectively managing the disease once diagnosed. Additionally, diabetes can progress faster in minorities due to poor diet, obesity, lack of physical exercise and lack of access to consistent health care services.

According to the American Diabetes Association, African Americans, Mexican Americans, American Indians, Native Hawaiians, Pacific Islanders and Asian Americans are all at a greater risk of developing type 2 diabetes. Of all adults diagnosed with diabetes, 7.4 percent are non-Hispanic white, while eight percent are Asian American, 12.1 percent are Hispanic, 12.7 percent are non-Hispanic black and 15.1 percent are American Indian/Alaska Native.

Diabetes: An Example of Underdiagnosis and Undertreatment

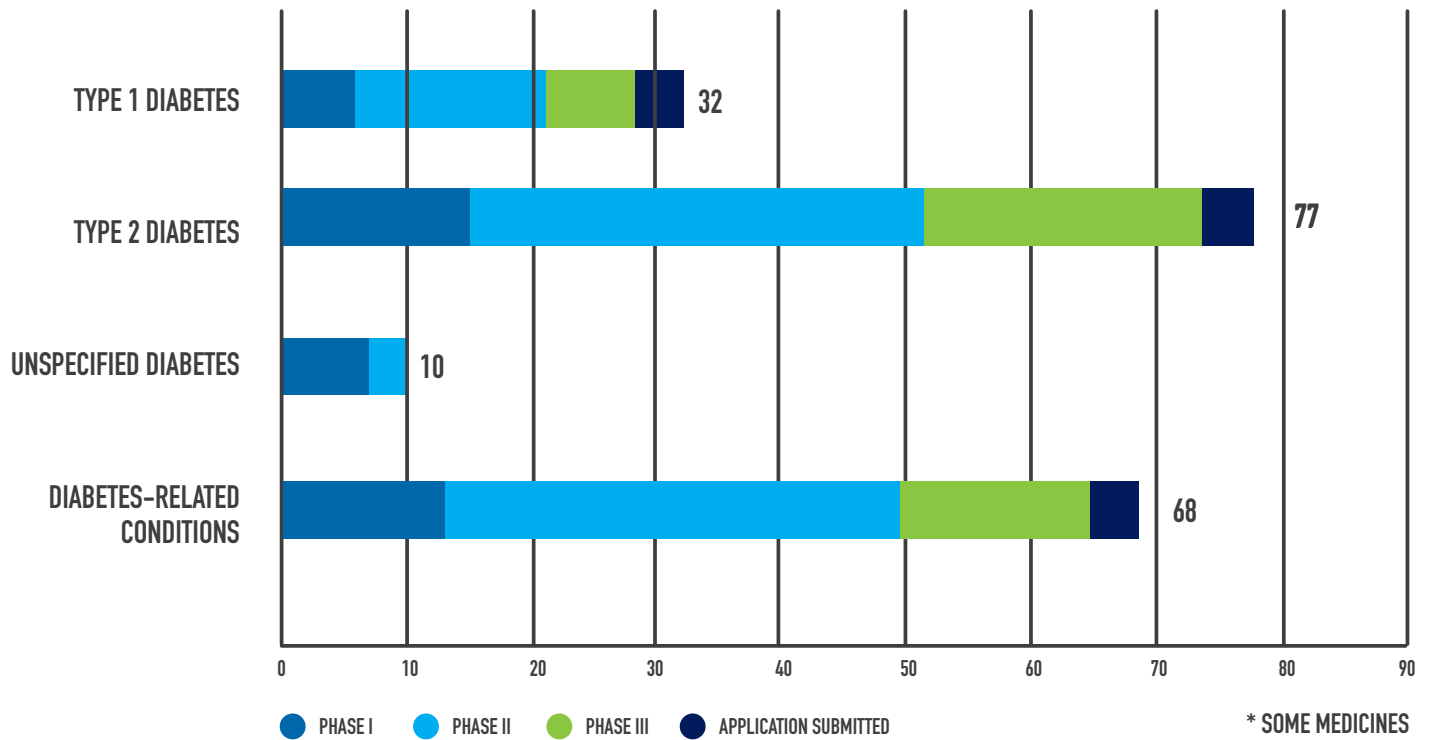
Uncontrolled diabetes can lead to kidney failure, amputation, blindness and stroke. Care for people with diagnosed diabetes accounts for 1 in 4 health dollars in the US.³



Treatment includes blood sugar control (medicines, diet and exercise) and testing to prevent complications. Data rounded to whole numbers.

Sources: American Diabetes Association³; IHS Life Sciences analysis of CDC data⁴

Medicines in Development for Diabetes and Related Conditions*



* SOME MEDICINES ARE IN MORE THAN ONE CATEGORY.

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