2018 Drugs to Watch

2018 Drugs to Watch
The Year of the Blockbuster
What is the Drugs to Watch report?

- A yearly publication by Clarivate Analytics where we look at the future of drugs that will be approved over the coming year.

- Each of the drugs featured in the report is anticipated to be launched in 2018 with expected annual revenue within five years in excess of $1 billion.

- In 2018 there are 12 drugs that made the list with a total anticipated revenue of $22.6B in 2022.
2018: The year of the blockbuster

- A blockbuster drug is a therapy that enters the market and reaches more than $1B in yearly sales in a certain timeframe.
- These drugs are able to achieve blockbuster sales because many have the potential to
- become the new standard of care or represent a new treatment option.

2018 is “The Year of the Blockbuster”

- 12 new drugs entering the market in 2018 are anticipated to achieve blockbuster sales within 5 years.
- 2018 is a year with more potential blockbuster drug launches since the debut of the Drugs to Watch series in 2013.
- Despite political and regulatory uncertainties in the US and EU markets, the pace of pharmaceutical innovation continues to accelerate.
# The 2018 Drugs to Watch

<table>
<thead>
<tr>
<th>RANK</th>
<th>DRUG</th>
<th>DISEASE</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
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<td>Hemophilia A with factor VIII inhibitors</td>
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<td>2,583</td>
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<td>Non-metastatic CRPC</td>
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<td>1,368</td>
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<td>Epidiolex (plant-derived cannabidiol)†,§,**</td>
<td>Dravet syndrome and Lennox-Gastaut syndrome</td>
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<td>11</td>
<td>Steglatro (ertugliflozin)**</td>
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<td>308</td>
<td>439</td>
<td>634</td>
<td>1,072</td>
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</table>

Data were obtained from the Cortellis Competitive Intelligence database, accessed March 05, 2018 [Source: Thomson Reuters I/R/E/S]. Forecasts are in U.S.$ million. CRPC=cadaveric-resistant prostate cancer. TTR=transthyretin. *=biological drug, †=Breakthrough Therapy designation. ‡=Fast Track designation. §=RNA Interference. ¶=Orphan Drug designation. ‖=Priority Review. **=small molecule. ††=novel integrase inhibitor. † †=first-in-class. ¶¶=vaccine.
How was the list chosen?

- Data for this report was compiled from the Cortellis database, from Clarivate Analytics
  
  - Using the advanced search functions, drugs in phase 2 or phase 3 trials, at the pre-registration or registration stage, or already launched early in 2018 were selected
  
  - The dataset was then filtered for drugs that had total forecast sales of $1 billion or more in 2022
  
  - This filtering process produced a list of 28 drugs, which were then manually reviewed to determine whether these products were likely to go to market in 2018, based on factors such as the company’s expected approval or launch date
  
  - Following this manual review, 12 “Drugs to Watch” for 2018 were selected
  
  - Each drug was subsequently studied and evaluated in its individual market context for the report
Why is the list important?

• Many of the drugs identified as potential blockbusters could become the new standard-of care for a variety of diseases. Some are first time cures for rare orphan diseases for which there is a high unmet need or are first-in-class drugs. They both represent and support a continued push by the biopharma industry to pioneer real innovations.

Highlights in the class include:

• Five drugs on the list are first-in-class and four are for orphan diseases
• Two are drugs for diabetes and are projected to garner significant sales in a crowded market due to superior efficacy and safety
• The first ever approved RNA interference therapeutic; it is a potential treatment for a rare, inherited, progressively debilitating and often fatal disease called transthyretin (TTR)-mediated amyloidosis
• More than half of these drugs have been granted Priority Review, Breakthrough Therapy or Fast Track designations. In contrast to 2017, where more than half of the drugs on our blockbuster list were cancer treatments, only one blockbuster expected to launch in 2018 is for cancer
How credible is the list?

- In March 2017, Clarivate Analytics named eight drugs entering the market to achieve blockbuster status by 2021. Seven of the eight drugs named entered the market as predicted and there was one exception.

- All are still anticipated to be future blockbusters.

- Novo Nordisk’s Ozempic was also listed in our 2017 report, but following approval in late 2017 was launched in early 2018.

- Two drugs on the 2017 list (Eli Lilly’s Olumiant and Merck Serono/Pfizer’s Bavencio) have reduced sales forecasts, but are still predicted to exceed $1B in sales in 2022.
Behind the Blockbusters: our next webinar in the series

Rare disease research trends:

- **Date**: June 12, 2018
- **Time**: 9:00 am EDT, 2:00 pm BST, 3:00 pm CEST

This talk will focus on:

- the history of rare and orphan disease research
- the recent approvals
- where the field is headed
The 2018 List in Greater Detail

• The 2018 Drugs to Watch Forecast contains a number of market disruptors that have the potential to be truly transformative for patients
  • Two of the drugs on the list were for diabetes
  • The first-ever approved drug that is based on Micro RNA technology
  • Five of the drugs are for rare diseases
  • There were first-in-class molecules

• Drugs on this list are valuable additions to existing treatments as well as disruptions to certain markets and first-in-class treatment options for some indications

• More than half of these drugs had been granted some sort of accelerated regulatory designation
Diabetes background

• Diabetes is a group of metabolic diseases classified by chronic hyperglycemia resulting from defects in insulin secretion, insulin action or both. \(^1\)

• The chronic hyperglycemia of diabetes is associated with serious long-term complications including and macrovascular disease \(^2\)

• Diabetes patients require continuous medical care incorporating multifactorial risk-reduction strategies in addition to glycemic control \(^3\)

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\(^1\) Forbes, J.M. and Cooper, M.E., 2013; Morsink, L.M. et al., 2013
\(^2\) Matheus, A.S. et al., 2013; Kong, A.P. and Chan, J.C., 2015
\(^3\) 2018 (American Diabetes Association, January 2018)).
Causes of Diabetes

- The risk factors for type 2 diabetes are well established and include the following:
  - Family history
  - Prothrombotic factors
  - Age
  - Obesity/adiposity
  - Racial/ethnic group
  - Hypertension
  - Physical inactivity
  - History of gestational diabetes
  - Dyslipidemia
  - Polycystic ovary syndrome (PCOS)
  - Inflammation
  - Cigarette smoking

- Evidence is accumulating to support the roles of several other suggested risk factors, including several classes of therapeutic drugs (Fathallah, N. et al., 2015) and toxic agents (Huang, C.Y. et al., 2015), solid organ transplantation and associated immunosuppressive drug therapy (Porrini, E.L. et al., 2016), prolonged exposure to fine particulate matter (air pollution) (Weinmayr, G. et al., 2015), severe and prolonged stress/low stress resilience (Crump, C. et al., 2016), male gender (Gregg, E.W. et al., 2014), low birth weight and fetal undernutrition (Chen, L. et al., 2011)
Diabetes incidence and prevalence

- Diabetes is a global epidemic of diabetes, with 8%-9% (387 million) of the world’s population living with diabetes in 2014

- There are numerous chronic complications and comorbidities associated with diabetes and poor glycemic control

<table>
<thead>
<tr>
<th>Region/Country</th>
<th>Age group (years)</th>
<th>Incidence rate (%)</th>
<th>Incidence number</th>
<th>Population*</th>
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<thead>
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<th>Prevalence rate (%)</th>
<th>Prevalence number</th>
<th>Population*</th>
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<td><strong>LATIN AMERICA</strong></td>
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<td>7.1</td>
<td>5,712,499</td>
<td>80,457,737</td>
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</tbody>
</table>
Economic burden of Diabetes

- Diabetes is a chronic disease, and the severity of its complications and the means required to control them, the cost of diabetes is disproportionately high.

- According to the World Economic Forum, people with diabetes in low- and middle-income countries lose 8% of potential work time due to their disease, and those in high-income countries lose 2% of potential work time.

- According to one analysis the economic burden of diabetes in the period 2011-2030 will be USD 1.7 trillion.

- The global absolute cost of diabetes in 2015 was USD 1.31 trillion, equivalent to 1.8% of the global gross domestic product (GDP).
  - Indirect costs (lost productivity due to increased morbidity and mortality) accounted for approximately 35% of the total burden.
Current treatment options

• The objective of diabetes therapy is to achieve the best possible glycemic control while avoiding hypoglycemia.

• Current treatment guidelines emphasize three major components of treatment of the patient with type 2 diabetes:
  • lifestyle modification (including diet and exercise),
  • normalization of blood glucose levels,
  • and aggressive management of cardiovascular risk factors to prevent micro- and macrovascular complications.\(^1\)

• Few antidiabetic drugs have been approved for use in children and adolescents, with the result that these patients have limited options.\(^2\)

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\(^1\) American Diabetes Association, January 2018
\(^2\) Tamborlane, W.V. and Klingensmith, G., 2013
Glucose and insulin signaling

- Most of the food we eat is turned into glucose, a form of sugar that is used by the body for energy.
- Beta cells in the pancreas produce insulin, a hormone that enables muscles and other tissues to absorb glucose from the blood.
- The maintenance of whole-body glucose homeostasis is dependent upon a normal insulin secretory response by the pancreatic beta cells and a normal tissue sensitivity to the independent effects of hyperinsulinemia and hyperglycemia to augment glucose uptake.
Glucose and insulin signaling

- The combined effects of insulin and hyperglycemia to promote glucose disposal are dependent on three mechanisms:
  - Stimulation of glucose uptake by the splanchnic tissues
  - Suppression of endogenous (primarily hepatic) glucose production
  - Stimulation of glucose uptake by peripheral tissues, primarily muscle; muscle glucose uptake is regulated by flux through two major metabolic pathways: glycolysis (of which approximately 90% represents glucose oxidation) and glycogen synthesis.
- Type 2 diabetes arises when the body is unable to use the insulin it produces in an effective manner (insulin resistance or type 2 diabetes).
Targets for the intervention of Diabetes
Insulin secretagogues

- Insulin secretagogues are a widely used class of oral antidiabetic agents that induce hypoglycemic effects via the stimulation of insulin release.

- The major incretin hormones are glucose-dependent insulinotropic polypeptide (GIP) and the truncated form of glucagon-like peptide-1 (GLP-1).

- When blood glucose levels are elevated, incretins act on the pancreas to potentiate both early- and late-stage insulin secretion. They also decrease glucagon secretion and the rate of gastric emptying.
GLP-1 Pipeline

- In 2005, exenatide (Byetta) became the first molecule in this novel class of antidiabetic drugs to obtain regulatory approval.
- A systematic review concluded that GLP-1 drugs are moderately effective in lowering HbA1c compared to placebo, but that they were more effective in improving postprandial glycemia as compared to older antidiabetic drugs.
- The American Diabetes Association has concluded that available evidence supports the use of incretin-based therapies in the treatment of diabetes patients who require effective glycemia control as well as control of body weight;
Ozempic for type 2 diabetes

The hormone insulin, which is produced by the pancreas, is responsible for controlling the amount of glucose in the blood. Diabetes is a chronic disease that occurs either when the pancreas does not produce insulin (type 1) or when the pancreas does not produce enough insulin or the body’s cells do not react to insulin (type 2). Approximately 90% of patients with diabetes are living with type 2 diabetes.\(^\text{15}\)

More than 425 million adults are living with diabetes globally. By 2045, this number is projected to rise to 629 million. In 2017, diabetes caused at least $727 billion in health expenditure.\(^\text{16}\)

Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.\(^\text{15}\) But the risk factors related to these complications can be reduced through effective control of blood sugar levels.
Ozempic

One class of medication that is used to treat type 2 diabetes is known as glucagon-like peptide-1 (GLP-1). GLP-1 treatments help stimulate the body’s own insulin release, limit how much sugar gets into the blood from the liver and slow down how quickly food leaves the stomach.  

As predicted in the Drugs to Watch 2017 report, Novo Nordisk’s weekly GLP-1 analog Ozempic (semaglutide) was approved for treatment of type 2 diabetes that year based on positive data from the SUSTAIN program. However, the late approval in December 2017 delayed the expected year-end launch to February 2018.  

In the SUSTAIN trial, Ozempic demonstrated superiority in blood glucose and weight control over existing options, including Januvia (sitagliptin), Bydureon (controlled-release exenatide) and Lantus (insulin glargine). Like Novo Nordisk’s market-leading GLP-1 analog Victoza (liraglutide), Ozempic has demonstrated a positive cardiovascular effect, reducing stroke risk by 39% and myocardial infarction risk by 26%.  

STROKE RISK
REDUCED BY 39%

MYOCARDIAL INFARCTION
RISK REDUCED BY 26%
The GLP-1 market

Once-daily Victoza has lost market share to longer acting, weekly GLP-1 analogs, particularly Eli Lilly’s Trulicity (dulaglutide), but data released in 2017 from SUSTAIN 7 showed that Ozempic achieved greater HbA1c reductions (i.e., a measure of average blood sugar levels over weeks/months) compared with Trulicity (1.5 versus 1.1 percentage points at the lowest doses tested). Data from the SUSTAIN 7 study also showed that patients treated with Ozempic had doubled the weight loss versus patients treated with Trulicity (4.6 kg versus 2.3 kg).

Cardiovascular outcomes for Trulicity are being assessed in the REWIND study, and data are expected from 2018 onwards. With a positive cardiovascular effect already demonstrated for Ozempic, it will put pressure on Trulicity and help Novo Nordisk regain market share, although Trulicity is anticipated to lead the GLP-1 market by 2022, with forecasts of $4.090 billion for Trulicity, $3.912 billion for Victoza and $3.469 billion for Ozempic.

Injectable GLP-1 analogs are commonly used after therapy with oral drugs has failed. However, Novo Nordisk’s once-daily oral formulation of semaglutide (assessed in the PIONEER program) could be a game-changing development for the treatment of type 2 diabetes. Availability of an oral GLP-1 formulation could result in earlier switching from small-molecule oral antidiabetic medications to GLP-1 analogs, which are viewed as more efficacious and have a proven cardiovascular benefit. Semaglutide is also being assessed for treatment of obesity (in view of its weight loss effects) and non-alcoholic steatohepatitis (i.e., fatty liver disease) and thus presents a competitive threat to a range of drugs on the market.

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<th>TRULICITY</th>
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<td>HbA1c reductions, percentage points at the lowest doses tested</td>
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<td>1.1</td>
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<td>weight loss kg, SUSTAIN 7</td>
<td>4.6</td>
<td>2.3</td>
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<table>
<thead>
<tr>
<th></th>
<th>TRULICITY</th>
<th>VICTOZA</th>
<th>OZEMPIC</th>
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<tr>
<td>2022 Expected sales</td>
<td>$4.090B</td>
<td>$3.912B</td>
<td>$3.469B</td>
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Targets for the intervention of Diabetes
Modulators of glucose uptake

• The sodium-glucose cotransporter (SGLT), actively transports glucose by coupling with Na+.
  • The inhibition of renal SGLTs leads to suppression of tubular glucose reabsorption and the excretion of excess plasma glucose into urine

• SGLT-1 is involved in glucose transport in the small intestine, while both SGLT-2 and SGLT-1 receptors on early and late proximal tubules, respectively, are involved in the kidney

• Dapagliflozin, the first selective SGLT-2 inhibitor, was approved and launched in 2012 for the treatment of type 2 diabetes
SGLT2 inhibitors

• There has been some debate regarding the relative merits of selective SGLT-2 versus dual SGLT-1/2 inhibitors

• The potential cardiovascular effects of SGLT-2 inhibitors continue to be evaluated

• In late 2016, the U.S. FDA approved empagliflozin for the reduction of risk of cardiovascular death in adult patients with T2D and cardiovascular disease

<table>
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<th>Drug Name</th>
<th>Organization</th>
<th>Mechanism of Action</th>
<th>Status</th>
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<td>SGLT-2 Inhibitors/ Expression Inhibitors</td>
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<td>Boehringer Ingelheim/ Lilly</td>
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<td>SBM-TFC-039</td>
<td>Wanbang Biopharma</td>
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<td>Sichuan Haisco Pharmaceutical</td>
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<td>JRP-493</td>
<td>Prous Institute for Biomedical Research</td>
<td>SGLT-2 Inhibitors</td>
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11. Steglatro for type 2 diabetes

In view of the growing burden of type 2 diabetes, the race is on to develop new and efficacious treatments to help clinicians and their patients manage blood sugar levels. In addition to insulins and GLP-1 therapies, several other classes of drugs are available for the treatment of type 2 diabetes, including sodium glucose co-transporter-2 (SGLT-2) inhibitors.

SGLT-2’s reduce the amount of glucose being absorbed in the kidneys so that it is passed out in the urine and reduce the amount of glucose in the blood.88

In addition to the 2018 market entry of the potential GLP-1 analog blockbuster, Ozempic, a new SGLT-2 inhibitor, Steglatro (ertugliflozin), is also expected to launch in early 2018 for type 2 diabetes.
Steglatro and the type 2 diabetes market

Although SGLT-2 inhibitors are the newest oral treatment options for diabetes, Steglatro will be a late entrant to an increasingly crowded market and will compete with first-to-market Invokana (canagliflozin; Johnson & Johnson; launched in 2013), Farxiga (dapagliflozin; AstraZeneca; launched in early 2014) and Jardiance (empagliflozin; Boehringer Ingelheim; launched in late 2014). Steglatro does, however, have specific strengths that will help it gain market share, including significant HbA1C reductions in combination with Merck’s DPP-4 market leader Januvia (sitagliptin) in the first-line setting as shown in the VERTIS SITA trial (HbA1C reductions of up to 1.7 versus 0.4 percentage points for the combination and placebo, respectively).

Steglatro is also efficacious as a monotherapy (see VERTIS Mono), in combination with metformin (see VERTIS MET trial), and combined with Januvia versus Januvia alone (see VERTIS Factorial trial). All of these studies showed significant weight loss and blood-pressure-lowering effects, which led to FDA approval of Steglatro as a monotherapy and in fixed-dose combinations with Januvia (as Steglujan) and metformin (as Segluromet) in December 2017.

A cardiovascular outcomes study (VERTIS CV) for Steglatro is ongoing. Results of this study are expected in 2019.

Positive cardiovascular data are key to helping Steglatro consolidate a place among the other SGLT-2 inhibitors.

Cardiovascular benefits from Jardiance’s paradigm-shifting EMPA-REG OUTCOME trial were included in the label for Januvia in December 2016. CANVAS data for Invokana were filed in October 2017 and outcomes data from the DECLARE study of Farxiga are also expected in 2019.

In 2016, Invokana was the market-leading SGLT-2 inhibitor and the only one with blockbuster sales ($1.407 billion). However, cardiovascular benefits, among other strengths, are predicted to result in a rapid rise in sales of this drug class and Steglatro is expected to be a significant contributor. By 2022, Farxiga is forecast to lead the market ($2.025 billion), followed by Jardiance ($1.713 billion), and another novel class member sotagliflozin (a dual SGLT-1 and SGLT-2 inhibitor from Lexicon/Sanoﬁ). Sotagliflozin is likely to be filed for approval in the first half of 2018 and could enter the market in 2019 and is forecast to generate 2022 sales of $1.193 billion, followed by $1.087 billion for Steglatro and $652 million for Invokana. A decline in sales for Invokana could be a result of the amputations observed in the CANVAS trial, which led to a black box warning for this medicine.
06. Patisiran for hereditary transthyretin-mediated amyloidosis

Transthyretin amyloidosis is a slowly progressive condition characterized by the buildup of abnormal deposits of a protein called amyloid (amyloidosis) in the body’s organs and tissues. In most cases, the condition is inherited. The exact prevalence of the disease is unknown, but it is less common among Americans of European descent, where it affects about one in 100,000 people. The cardiac form of transthyretin amyloidosis is more common among people with African ancestry, affecting between 3% and 3.9% of African Americans and approximately 5% of people in some areas of West Africa.
Patisiran is the first FDA approved RNA interference drug

- Small interfering RNA (siRNA) is a class of short double-stranded RNA molecules (21- to 25-nucleotides in length), which can mobilize the RNA interference (RNAi) pathway
- Synthetic siRNAs are produced and transfected into the cell either by polymer based transfection reagents, by cationic lipid or by electroporation
RNA interference offer key advantages as potential therapeutic approaches for a broad range of indications

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Details</th>
</tr>
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<tbody>
<tr>
<td>Unrestricted choice of targets and specificity</td>
<td>Small molecule drugs or antibody-based drugs have a limited range of protein targets. siRNA may be used to interfere with the expression of nearly any gene transcript in a specific manner.</td>
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<tr>
<td>High degree of safety</td>
<td>siRNA acts on the post-translational stage of gene expression, so it does not interact with DNA and thereby avoids the mutation and teratogenicity risks of gene therapy.</td>
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<tr>
<td>High efficacy</td>
<td>Only a few molecules of siRNA per cell are required to produce effective gene silencing.</td>
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<tr>
<td>Increasing molecular and genetic evidences</td>
<td>Comprehensive nucleotide sequence databases have been established, including human genomic databases, cDNA databases and disease gene databases, which have laid a solid foundation for siRNA drug development.</td>
</tr>
<tr>
<td>Pharmaceutical attractiveness</td>
<td>siRNA is suitable for drug use because it does not require genome integration and can be easily synthesized.</td>
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</table>

- It has been reported that synthetic siRNA is able to knock down targets in various diseases in vivo, including hepatitis B, human papilloma virus, ovarian cancer, bone cancer, hypercholesterolemia, and liver cirrhosis

**siRNA Therapeutic products are being tested in 5 phase 3 clinical programs**

Number of clinical studies by phase and RNA type (2011-2017)

<table>
<thead>
<tr>
<th>Phase</th>
<th>siRNA</th>
<th>Other RNA Technologies</th>
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<tr>
<td>Phase 1</td>
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<tr>
<td>Phase 3</td>
<td>9</td>
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</table>

- Five phase 3 clinical trials have already been conducted testing siRNA candidates
- The vast majority of clinical trials conducted for siRNA technologies has been in phase 1 and 2. For these stages, siRNA account for half of the total of clinical trials involving RNA technologies

* Other RNA technologies include microRNA, RNAs vaccines, RNAi, RNA modulators and shRNAs

Reference: Clarivate Analytics Cortellis
Patisiran for hereditary transthyretin-mediated amyloidosis

Transthyretin amyloidosis is a slowly progressive condition characterized by the buildup of abnormal deposits of a protein called amyloid (amyloidosis) in the body’s organs and tissues. In most cases, the condition is inherited. The exact prevalence of the disease is unknown, but it is less common among Americans of European descent, where it affects about one in 100,000 people. The cardiac form of transthyretin amyloidosis is more common among people with African ancestry, affecting between 3% and 3.9% of African Americans and approximately 5% of people in some areas of West Africa.
Patisiran and the market for transthyretin amyloidosis treatments

In December 2017, shortly after reporting top-line data, Alnylam completed its NDA submission for patisiran, an intravenously administered RNA interference (RNAi) therapeutic targeting the transthyretin gene. Together with Sanofi, Alnylam filed for EU approval that same month.

Patisiran was filed for treatment of patients with debilitating hereditary transthyretin-mediated amyloidosis. If successful, patisiran will be the first FDA-approved RNAi therapeutic. The FDA granted patisiran Priority Review with a PDUFA date in August 2018, and Fast Track and Breakthrough Therapy designations. The FDA also expanded patisiran’s Orphan Drug designation from transthyretin familial amyloid polyneuropathy to the broader indication of hereditary transthyretin-mediated amyloidosis.

In the EU, the EMA granted accelerated assessment. Launch of this treatment in both the U.S. and the EU is expected later in 2018, putting patisiran on track to become the standard of care for hereditary transthyretin-mediated amyloidosis.

The current standard of care for this disease is liver transplantation but the risks of surgery, acute liver rejection and increased risk of infection make it an option only in patients in good clinical condition who can tolerate the intervention.

Vyndaqel (tafamidis, Pfizer), a first-in-class anti-amyloid therapy, is currently the only approved anti-amyloid treatment for transthyretin familial amyloid polyneuropathy. However, this therapy is limited to treatment for early-stage disease, and is not yet approved in the U.S.
Patisiran

Competitor drugs, expected sales in 2022

INOTERSEN
$533M in 2022

VYNDAQEL
$170M in 2022

Patisiran has potential to be a best-in-class treatment. In the APOLLO phase 3 trial in patients with transthyretin familial amyloid polyneuropathy (including those with cardiac symptoms), patisiran showed significant improvement of neurological impairment (with a 34-point difference in the mNIS+7 scale [a composite measure of neurological impairment] at 18 months), improved quality of life and reduced disease symptoms and disability with an encouraging safety profile.45

Treatment benefit was better than with Ionis’ potential competitor inotersen, an antisense drug that inhibits transthyretin. In the phase 3 NEURO-TTR study, inotersen showed a 19.7-point treatment benefit compared with placebo at month 15.46 Additionally, inotersen was associated with safety signals, including cases of severe thrombocytopenia.

Inotersen was filed for approval ahead of patisiran in November 2017, in both the U.S. and EU.47,48 While it is likely to be the first of the two to be approved (PDUFA date is in July 2018), patisiran is set to reap the greatest revenue due to its superior efficacy and safety. In 2019, the first full year following launch, patisiran sales of $373 million are forecast, rising to $1.212 billion in 2022. Inotersen sales are forecast at $106 million in 2019 and $533 million in 2022. Vyndaqel sales of $170 million are forecast for 2022.
Behind the Blockbusters: our next webinar in the series

Rare disease research trends:

• **Date:** June 12, 2018
• **Time:** 9:00 am EDT, 2:00 pm BST, 3:00 pm CEST
• **Register:** [bit.ly/2GqfI0I](bit.ly/2GqfI0I)

This talk will focus on:

• the history of rare and orphan disease research
• the recent approvals
• where the field is headed
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