2018 Drugs to Watch

The Year of the Blockbuster

June 2018
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 five 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 U.S. 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>
<th>COMPANY (HQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemlibra (emicizumab)*,†,¶,††</td>
<td>Hemophilia A with factor VIII inhibitors</td>
<td>496</td>
<td>1,457</td>
<td>2,356</td>
<td>3,362</td>
<td>4,002</td>
<td>Roche (Switzerland)/Chugai (Japan)</td>
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<tr>
<td>2</td>
<td>Biktarvy (tenofovir alafenamide + emtricitabine + bictegravir)**,§,††</td>
<td>HIV infection</td>
<td>896</td>
<td>2,282</td>
<td>3,387</td>
<td>4,296</td>
<td>3,716</td>
<td>Gilead (U.S.)</td>
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<tr>
<td>3</td>
<td>Ozempic (semaglutide)*</td>
<td>Type 2 diabetes</td>
<td>260</td>
<td>862</td>
<td>1,576</td>
<td>2,583</td>
<td>3,469</td>
<td>Novo Nordisk (Denmark)</td>
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<tr>
<td>4</td>
<td>Erleada (apalutamide)¶,**</td>
<td>Non-metastatic CRPC</td>
<td>25</td>
<td>500</td>
<td>1,200</td>
<td>1,600</td>
<td>2,000</td>
<td>Johnson &amp; Johnson (U.S.)</td>
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<tr>
<td>5</td>
<td>Shingrix (Zoster vaccine recombinant, adjuvanted)§§</td>
<td>Shingles</td>
<td>242</td>
<td>537</td>
<td>879</td>
<td>1,202</td>
<td>1,368</td>
<td>GlaxoSmithKline (UK)</td>
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<tr>
<td>6</td>
<td>Patisiran§,¶,††</td>
<td>Hereditary TTR amyloidosis</td>
<td>83</td>
<td>373</td>
<td>726</td>
<td>1,104</td>
<td>1,212</td>
<td>Alnylam (U.S.)/Genzyme (U.S.)</td>
</tr>
<tr>
<td>7</td>
<td>Epidiolex (plant-derived cannabidiol)†,¶,‡‡</td>
<td>Dravet syndrome and Lennox-Gastaut syndrome</td>
<td>19</td>
<td>266</td>
<td>645</td>
<td>936</td>
<td>1,191</td>
<td>GW Pharmaceuticals (UK)</td>
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<tr>
<td>8</td>
<td>Aimovig (erenumab)*,††</td>
<td>Migraine</td>
<td>115</td>
<td>361</td>
<td>685</td>
<td>941</td>
<td>1,170</td>
<td>Amgen (U.S.)/Novartis (Switzerland)</td>
</tr>
<tr>
<td>9</td>
<td>Lanadelumab*†,¶,††</td>
<td>Hereditary angioedema</td>
<td>74</td>
<td>350</td>
<td>629</td>
<td>902</td>
<td>1,153</td>
<td>Shire (Ireland)</td>
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<tr>
<td>10</td>
<td>Elagolix §,**,††</td>
<td>Endometriosis</td>
<td>57</td>
<td>268</td>
<td>549</td>
<td>896</td>
<td>1,152</td>
<td>AbbVie (U.S.)</td>
</tr>
<tr>
<td>11</td>
<td>Steglatro (ertugliflozin)**</td>
<td>Type 2 diabetes</td>
<td>220</td>
<td>482</td>
<td>769</td>
<td>1,024</td>
<td>1,087</td>
<td>Pfizer (U.S.)/Merck (U.S.)</td>
</tr>
<tr>
<td>12</td>
<td>Sublocade (once-monthly buprenorphine)†,¶,**</td>
<td>Opioid dependence</td>
<td>121</td>
<td>308</td>
<td>439</td>
<td>634</td>
<td>1,072</td>
<td>Indivior (UK)</td>
</tr>
</tbody>
</table>

Data were obtained from the Cortellis Competitive Intelligence database, accessed March 05, 2018 [Source: Thomson Reuters I/B/E/S]. Forecasts are in U.S.$ million. CRPC=cancer-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 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. Four are for rare diseases
• Two are drugs for diabetes and are projected to garner significant sales in a crowded market due to superior efficacy and safety
• An 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 – two webinars in the series

New standards of care on the horizon for Type II Diabetes while the first RNAi therapy hits the market:
  • the current treatment options for Type II diabetes
  • a look into the future of diabetes treatments
  • the history and science of RNAi therapy
  • recent approvals and what’s on the horizon for gene therapies


Rare disease research trends:
  • the history of rare and orphan disease research
  • the recent approvals
  • where the field is headed
Behind the Blockbusters – in-depth blog series on all 12 drugs

Drugs to Watch profiled so far on Life Sciences Connect

- Pfizer and Merck’s Steglatro for Type II Diabetes
- Amgen and Novartis’s Aimovig for migraine
- Novo Nordisk’s Ozempic for Type II Diabetes
- GlaxoSmithKline’s Shingrix for shingles

https://clarivate.com/blog/category/life-sciences-connect/
The 2018 list in greater detail

- The 2018 Drugs to Watch forecast contains a number of therapies that have the potential to be truly transformative for patients
  - Multiple first-in-class molecules
  - Four that target rare diseases, including one harnessing RNA interference technology
  - Two of the drugs on the list were for diabetes
  - Range of therapeutic areas from HIV to opioid addiction

- 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 accelerated regulatory designation
What is a rare or orphan disease?

- A disease or disorder is defined as rare in Europe when it affects fewer than 1 in 2000.

- A disease or disorder is defined as rare in the USA when it affects fewer than 200,000 Americans at any given time. This definition was created by Congress in the Orphan Drug Act of 1983.

- One rare disease may affect only a handful of patients in the EU (European Union), and another may touch as many as 245,000. In the EU, as many as 30 million people may be affected by one of over 6000 existing rare diseases.

- 80% of rare diseases have identified genetic origins whilst others are the result of infections (bacterial or viral), allergies and environmental causes, or are degenerative and proliferative.

- 50% of rare diseases affect children.

https://www.rarediseaseday.org/article/what-is-a-rare-disease
Rare disease vs orphan disease

• **Rare Disease:** A disease or disorder is defined as rare in the USA when it affects fewer than 200,000 Americans at any given time.

• **Orphan disease:** A disease that has not been adopted by the pharmaceutical industry because it provides little financial incentive for the private sector to make and market new medications to treat or prevent it.

• There are also lists of diseases, mostly genetic disorders, that are regarded as being rare. As a group they have nothing in common apart from their rarity, but the lists vary strikingly in length; for example, that published by the US National Organization for Rare Disorders contains about 1200 items, while NIH's Office of Rare Diseases publishes a list of over 6000,
How many rare and orphan diseases are there?

- There may be as many as 7,000 rare diseases.

- The total number of Americans living with a rare disease is estimated at between 25-30 million.

- In the United States, only a few types of rare diseases are tracked when a person is diagnosed.

- These include certain infectious diseases, birth defects, and cancers. It also includes the diseases on state newborn screening tests.

### Rare Diseases by the Numbers

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cases</th>
</tr>
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<tbody>
<tr>
<td>Brugada syndrome</td>
<td>50</td>
</tr>
<tr>
<td>Protoporphyria, erythropoietic</td>
<td>50</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>475</td>
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<tr>
<td>Melanoma, familial</td>
<td>46.8</td>
</tr>
<tr>
<td>Autism, genetic types</td>
<td>45</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>45</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>42</td>
</tr>
<tr>
<td>Great vessels transposition</td>
<td>32.5</td>
</tr>
<tr>
<td>Focal dystonia</td>
<td>30</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>30</td>
</tr>
<tr>
<td>Non-Hodgkin malignant lymphoma</td>
<td>30</td>
</tr>
<tr>
<td>Retinitis pigmentosa</td>
<td>27.5</td>
</tr>
<tr>
<td>Gelineau disease</td>
<td>26</td>
</tr>
</tbody>
</table>
What causes rare diseases?

• There are many different causes of rare diseases. The majority are thought to be genetic, directly caused by changes in genes or chromosomes. In some cases, genetic changes that cause disease are passed from one generation to the next. In other cases, they occur randomly in a person who is the first in a family to be diagnosed.

• Many rare diseases, including infections, some rare cancers, and some autoimmune diseases, are not inherited. While researchers are learning more each year, the exact cause of many rare diseases is still unknown.
Why study rare diseases?
2018 Drugs to Watch for rare and orphan diseases

01. Hemlibra for hemophilia A with factor VIII inhibitors

06. Patisiran for hereditary transthyretin-mediated amyloidosis

07. Epidiolex for Dravet syndrome and Lennox-Gastaut syndrome

09. Lanadelumab for hereditary angioedema
01. **Hemlibra** for hemophilia A with factor VIII inhibitors

Hemophilia A is one of the most common congenital severe bleeding disorders, which globally affects around 350,000 people. The disorder is the result of a deficiency in the clotting protein factor VIII and therapy to prevent or treat bleeding is via recombinant factor VIII replacement. However, as a consequence of treatment, up to 30% of patients with severe hemophilia A can develop antibodies (i.e., inhibitors) to factor VIII, which bind to factor VIII and impair its clotting action. Factor VIII inhibitors are the most serious and challenging complication of hemophilia treatment, increasing morbidity and mortality since bleeds no longer respond to standard factor replacement therapy.
What is hemophilia?

- Hemophilia is a rare bleeding disorder caused by the partial reduction or total absence of clotting factors.

- The two main types of hereditary hemophilia are hemophilia A, which is caused by insufficiency or lack of the coagulation protein factor VIII, and hemophilia B (sometimes called Christmas disease), caused by insufficiency or lack of clotting factor IX.

- Acquired hemophilia is an autoimmune disorder that develops when a patient with a negative family history of hemophilia forms autoantibodies to clotting factors in the bloodstream (inhibitors), leading to factor VIII depletion (Baudo, F. and de Cataldo, F., 2015; Mingot-Castellano, M.E. et al., 2017).

- Approximately nine out of ten hemophiliacs have type A.

Source: Clarivate Integrity Disease Briefings
Incidence, Prevalence and cost of hemophilia

- The global incidence of acquired hemophilia has been estimated at 1.6 per 1,000,000 annually. ¹

- The prevalence of hemophilia B varies considerably by country, ranging from 2.69 +/- 1.61 per 100,000 males in high-income countries to 1.20 +/- 1.33 per 100,000 males in the rest of the world. The highest rate is reported in Ireland, which has a prevalence of 8.07 per 100,000 males.

- Average Medicaid expenditures for a patient with hemophilia in the U.S. in 2008 were nearly USD 143,000.

- Coagulation factor concentrates accounted for 70-82% of total costs.

¹Baudo, F. et al., 2010
²Viiala, N.O. et al., 2009
³Stonebraker, J.S. et al., 2010

Source: Clarivate Integrity Disease Briefings

From Clarivate IPD
01. Hemlibra for hemophilia A with factor VIII inhibitors

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Hemlibra

- A novel approach to treating hemophilia A, Roche/Chugai’s once-weekly Hemlibra (emicizumab) is a bispecific antibody that simultaneously binds to both factor IXa and factor X, bringing them into spatially appropriate position to mimic the function of factor VIII.

- The FDA approved Hemlibra in November 2017, which led to a product launch in late December 2017.

- Launches in both Europe and Japan are expected in 2018. Sales of $496 million have been forecast for 2018, reaching blockbuster status in 2019 with $1.457 billion and increasing steeply to $4.002 billion in 2022.

- Hemlibra the first agent to be approved in close to 20 years in this disease setting,
**Hemlibra**

- From 2018, market leading Feiba and NovoSeven are expected to see significant sales losses due to competition from Hemlibra.

- HAVEN 3 data released in November 2017 shows superiority of Hemlibra in hemophilia without inhibitios versus standard factor VIII prophylaxis.

- Bioverativ’s first long-acting recombinant factor VIII replacement therapy Eloctate has taken significant market share from Shire’s long-term market-leading recombinant factor VIII replacement therapy Advate.

- Hemlibra will challenge standard-of-care factor VIII replacement therapy with its novel action, impressive efficacy and potential monthly dosing.
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>
</thead>
<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>
</tr>
<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>
</tr>
<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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</tbody>
</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

Patisiran for hereditary transthyretin-mediated amyloidosis

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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 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.\(^\text{45}\)

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.\(^\text{46}\) 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.\(^\text{47,48}\) 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.
Epidiolex for Dravet syndrome and Lennox-Gastaut syndrome

Epilepsy is a chronic disorder of the brain that affects people of all ages. About 50 million people worldwide have epilepsy, making it one of the most common neurological diseases globally. However, two rare forms of epilepsy exist, Dravet syndrome and Lennox-Gastaut syndrome, which affect people during childhood.

Lennox-Gastaut syndrome is a form of severe epilepsy and is characterized by multiple types of seizures and intellectual disability. People with Lennox-Gastaut syndrome begin having frequent seizures in early childhood, usually between the ages of 3 and 5 years. More than three-quarters of affected individuals have tonic seizures, which cause the muscles to stiffen (contract) uncontrollably.

Dravet syndrome is another severe form of epilepsy. It appears during the first year of life with frequent febrile seizures (fever-related seizures).
Epilepsy

• Epilepsy is a chronic neurological condition that confers susceptibility to recurrent, unprovoked seizures caused by abnormal neuronal firing in the brain.

• Epilepsy is one of the most common neurological disorders, affecting approximately 50 million people worldwide.

• According to the Centers for Disease Control and Prevention, the total direct and indirect cost of epilepsy in the United States is estimated to be USD 15.5 billion per year.

Source: Clarivate Integrity Disease Briefings
Epidiolex for Dravet syndrome and Lennox-Gastaut syndrome

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Dravet syndrome is another severe form of epilepsy. It appears during the first year of life with frequent febrile seizures (fever-related seizures).
Epidiolex

- Epidiolex (plant-derived cannabidiol) has the potential to become the first cannabinoid-based anti-epileptic medication

- Efficacy data have been compelling in both disease settings, supporting the possibility of approval in patients with Dravet syndrome

- Epidiolex treatment led to a 39% decrease in the frequency of seizures at 14 weeks versus 13% for patients in the placebo group

- Epidiolex treatment led to a 44% reduction in frequency of seizures at 14 weeks versus 22% for placebo

- However, if approved Epidiolex will likely encounter bureaucratic barriers to distribution and political hurdles associated with cannabis-derived medicines
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Lanadelumab for hereditary angioedema

Hereditary angioedema is a rare genetic disorder caused by excessive production of bradykinin, a vasodilatory mediator and enhancer of vascular permeability. The disorder is characterized by recurrent episodes of severe swelling (angioedema). The most common areas of the body to develop swelling are the limbs, face, intestinal tract and airway. Minor trauma or stress may trigger an attack but swelling often occurs without a known trigger. About one in 50,000 people is affected by the disease.
What is HAE?

- Hereditary angioedema (HAE) is an uncommon autosomal dominant disorder characterized by sudden and severe episodes of nonpruritic, localized subcutaneous and submucosal swelling that may affect any external or mucosal surface including the face, arms, legs, hands, feet, genitalia, gastrointestinal tract and larynx (Morgan, B.P., 2010; Lumry, W.R., 2013).

- HAE is most often caused by low plasma concentrations of antigenic and functional C1 esterase inhibitor (C1-INH), a naturally occurring molecule that inhibits plasma kallikrein and other serine proteases in the blood (Jolles, S. et al., 2014; Lumry, W.R., 2013; Craig, T. et al., 2012; Cicardi, M. et al., 2014)

Source: Clarivate Integrity Disease Briefings
Prevalence and Cost of HAE

- HAE has an estimated prevalence of 1:50,000 in the general population
- 80%-85% of patients have type 1 HAE; 15%-20% have type 2
- In the US the estimated number of HAE cases is on the order of 6000
- The average cost of treating acute attacks plus long-term disease management was estimated at approximately USD 42,000 per year in 2010, but ranged from USD 14,000 for patients with mild attacks to USD 96,000 for those with severe attacks (Wilson, D.A. et al., 2010; Bernstein, J.A., 2013).

Source: Clarivate Integrity Disease Briefings
Lanadelumab for hereditary angioedema

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Lanadelumab for HAE

- Lanadelumab could enter the market in late 2018 and is set to dominate the market for first-line prevention of angioedema attacks.

- Lanadelumab significantly reduced the mean frequency of angiodema attacks in patients with hereditary angiodema by 87% versus placebo.

- Lanadelumab is dosed once every two weeks with potential for once-monthly dosing.

- Lanadelumab is forecast to start out with modest sales of just $74 million in 2018, increasing to $1.153 billion in 2022.

<table>
<thead>
<tr>
<th>LANADELUMAB</th>
<th>HAEGARDA</th>
<th>CINRYZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>87%</td>
<td>84%</td>
<td>54%</td>
</tr>
</tbody>
</table>

Reduction in the mean frequency of angiodema attacks in patients with hereditary angiodema versus placebo.
What’s next?
Number of compounds with orphan drug designation by Phase 2013-2018

Source: Clarivate Cortellis for Clinical Trials Intelligence
What’s next?
Number of compounds with orphan drug designation by Year 2008-2018

Source: Clarivate Cortellis for Clinical Trials Intelligence
Most active companies in clinical trials with orphan drug designation

Source: Clarivate Cortellis for Clinical Trials Intelligence
Most active indications in clinical trials with orphan drug designation by Phase 2008-2018

Number of Compounds

Source: Clarivate Cortellis for Clinical Trials Intelligence
Clarivate Analytics Life Sciences

Clarivate Analytics is the global leader in providing trusted insights and analytics to accelerate the pace of innovation.

Building on a heritage going back more than a century and a half, we have built some of the most trusted brands across the innovation lifecycle, including Web of Science, Cortellis, Derwent, Techstreet, CompuMark, and MarkMonitor.

Today, Clarivate Analytics is a new and independent company on a bold entrepreneurial mission to help our clients radically reduce the time from new ideas to life-changing innovations.

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Cortellis Competitive Intelligence
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