The top 15 best-selling cancer drugs in 2022

by Phil Taylor

If there was any doubt that the oncology market is set to reach unprecedented heights, FiercePharma's top 15 list of cancer drugs in 2022 should eliminate it.

All told, by 2022, the top 15 cancer drugs are expected to collectively make almost $90 billion in sales. To put that in perspective, that represents about one-fourth of the entire U.S. pharma market in 2014, according to QuintilesIMS data. It's also bigger than pharma's haul in Japan or China that year.

It will likely be no revelation that three drugs among the top six on our list—provided courtesy of EvaluatePharma and Chempetitive—come from the highly touted PD-1/PD-L1 or checkpoint inhibitor class.

This brand-new category of cancer drugs works by activating the immune system, enabling it to recognize cancer cells and destroy them. The class has achieved unprecedented efficacy in a broad range of cancers and provides a much-needed new treatment approach alongside chemotherapy and targeted cancer drugs, which tend to lose efficacy over time.

But with that efficacy advance comes the thorny issue of pricing. The cost of medicines is under scrutiny by lawmakers around the world, and market watchers can't rule out some sort of clampdown by payers, both public and private. Drugmakers must now carefully select a price point for new meds—one that won't encourage payers to restrict their use.

That's even more important as immuno-oncology moves toward combination cocktails. Using combinations of drugs is nothing new in oncology, but it's particularly pertinent now as checkpoint inhibitors are tested alongside just about every other possible treatment, old and new. As clinical data on those cocktails emerge in the coming years, the relative importance of individual drugs could fundamentally change, and their prices along with it.

To illustrate the fast pace of change in oncology, take a look at the big names that have disappeared since our last top cancer drug list just three years ago. Among the missing are Takeda's multiple myeloma drug Velcade and Johnson & Johnson's oral prostate cancer med Zytiga, both of which are expected to be superseded by newer drugs and could potentially face generics if patent suits don't go their way. Others, notably Novartis' Gleevec and Eli Lilly's Alimta, will certainly see sales hit by generic rivals.

Even as the immuno-oncology meds have ascended, nine of the top-selling 15 drugs in 2022 will still be monoclonal antibodies. First approved in the late 1990s, these therapies quickly

became the preferred option for various cancers, and particularly blood cancer. Three of these—all from Roche—are first-generation cancer antibodies due to face biosimilar competition within the next couple of years. At the moment, it's tough to predict just how much biosimilar copies will eat into their sales. But the fact that the three are predicted to remain in the top flight after decades on the market indicates that brand strength will still play a major role.

Do you have thoughts about the top-selling cancer drugs in 2022? Will the list change much as that date approaches? As always, let us know.

1. Revlimid

Product: Revlimid
Generic name: lenalidomide
Company: Celgene
2015 sales: $5.80 billion
2022 sales: $13.44 billion
Current indications: multiple myeloma; myelodysplastic syndromes; mantle cell lymphoma

Revlimid has been on the market for a decade, and it's been the powerhouse behind Celgene's growth since its launch. Already a megablockbuster, the drug is the linchpin of a hematology franchise that Celgene expects to exceed $15 billion in annual sales by 2020, with Revlimid sales forecast to more than double by 2022.

The drug's compound annual growth through 2022 is expected to come in part from new indications, such as newly diagnosed multiple myeloma and non-Hodgkin lymphoma (NHL). A potential rival in newly diagnosed multiple myeloma—Amgen's Kyprolis—suffered a setback in September after flunking its first trial in this setting, setting up Revlimid to remain part of a go-to regimen for first-line use.

But not all of Celgene's extension efforts for Revlimid have panned out. Hopes of a $1 billion expansion into maintenance therapy for a subtype of NHL—and diffuse large B-cell lymphoma—were undermined after Revlimid failed the phase 3 REMARC trial, but the drug remains in testing for another form of the disease called follicular lymphoma. The company remains confident about Revlimid's role in lymphoma, with Hematology and Oncology President Michael Pehl saying that lymphoma "will be a major growth driver by 2020 and beyond."

With plenty of clinical trials looking at Revlimid's use as a backbone of combination therapies, as well as patent protection in place out to 2022 in Europe and 2027 in the U.S., the drug should have plenty of years of growth in the tank—unless it ends up on the losing side of a patent challenge. Celgene has already settled patent litigation with India's Natco Pharma, agreeing to a deal that will allow the rollout of a volume-limited authorized generic from 2022.

2. Opdivo

Product: Opdivo
Generic name: nivolumab
Companies: Bristol-Myers Squibb; Ono Pharmaceutical
2015 sales: $1.12 billion
2022 sales: $12.62 billion
Current indications: non-small cell lung cancer; metastatic melanoma; renal cell carcinoma; classical Hodgkin lymphoma

Opdivo was the first drug in the PD-1/PD-L1 inhibitor class to reach the market after its approval in Japan in 2014, but then followed Merck & Co.'s Keytruda by several months in winning an FDA approval. The two drugs have seesawed for dominance ever since.

Though Keytruda's new approval in first-line lung cancer could prove a spoiler for Opdivo's 2022 sales, the med has been the favorite to rule the roost among this new generation of immuno-oncology drugs.

Prospects for Opdivo took a knock after it failed to meet its objectives in the CheckMate-026 trial in first-line non-small cell lung cancer (NSCLC), largely because it did not confine its study population to patients whose tumors tested positive for high-level PD-L1 expression.

For now, that means Opdivo has probably ceded control of that territory to other drugs in the class, most notably Keytruda, which won its first-line approval in the U.S. in October. Roche's newer Tecentriq will be going for a first-line approval, too. But for that setback, Opdivo would have been at the head of the cancer drug pack in 2022 with sales of a $14.6 billion, according to EvaluatePharma's analysis.

A $2 billion deficit is clearly huge, but Opdivo's second-place position in this list goes some way to put the first-line failure into perspective. A massive clinical trial program for the drug, both as a monotherapy and in combination with other cancer drugs, could unlock new uses in other solid tumors such as breast, colorectal, small cell lung and gastric cancers, as well as hematological malignancies including follicular lymphoma and diffuse large B-cell lymphoma.

All is not necessarily lost in first-line NSCLC either, and it is worth noting that three-quarters of first-line NSCLC patients are PD-L1-negative and so still have to be treated with chemotherapy. A lot is therefore riding on the outcome of the CheckMate-227 trial that will look at the combination of Opdivo with another BMS immuno-oncology asset—Yervoy—and is due to report results in 2018. If positive, that data could return Opdivo to a position of strength in lung cancer.

3. Imbruvica

Product: Imbruvica
Generic name: ibrutinib
Companies: AbbVie (Pharmacyclics); ohnson & Johnson
2015 sales: $1.23 billion
2022 sales: $8.29 billion
Current indications: chronic lymphocytic leukemia; mantle cell lymphoma; Waldenström macroglobulinemia

Since its first launch in 2013, first-in-class BTK inhibitor Imbruvica has grown quickly to cross the blockbuster sales threshold, showing that targeting rarer cancers is no impediment. The drug now leads the market in the second-line chronic lymphocytic leukemia (CLL) market, backed up by use in previously treated mantle cell lymphoma and Waldenström macroglobulinemia.

In March, Imbruvica got the green light from the FDA as a first-line CLL therapy, opening up a much larger eligible patient population who will stay on therapy longer. Moving earlier in the treatment sequence is a key strategy for AbbVie and Johnson & Johnson, with AbbVie CEO Richard Gonzalez indicating the shift will drive a third of Imbruvica's growth in future. Add in potential new indications in non-Hodgkin lymphoma, solid tumors like pancreatic cancer and acute leukemias and—barring accidents—its 2022 prediction seems very achievable.

Imbruvica is facing some stiff competition in the coming years, however. Celgene's ambitions for Revlimid in lymphoma put it in opposition to AbbVie and J&J's drug. Meanwhile, Imbruvica is also heading for an encroachment on Celgene's patch with a trials program in multiple myeloma, so it looks like a fierce marketing battle is in the cards.

4. Keytruda

Product: Keytruda
Generic name: pembrolizumab
Company: Merck & Co.
2015 sales: $566 million
2022 sales: $6.56 billion
Current indications: advanced melanoma; non-small cell lung cancer; head and neck squamous cell cancer

Keytruda was the first PD-1/PD-L1 inhibitor to be approved for marketing in the U.S., ahead of Bristol-Myers Squibb's Opdivo, but has lagged behind its rival in sales pretty much from the get-go. That could change, given some trial results for the BMS med last fall—and that, in turn, could push Keytruda higher on this list by the time 2022 rolls around.

While Keytruda remains in direct competition with Opdivo in melanoma, second-line non-small cell lung cancer, and head and neck cancer, it got a chance to strike out on its own when it won an FDA approval to treat first-line NSCLC, while competitor Opdivo failed to meet its primary endpoint in that lucrative area.

Use of the drug is expected to ramp up quickly in previously untreated NSCLC patients whose tumors express high levels of PD-L1, a group which represents around 25% of the total population. That puts a greater emphasis on PD-L1 testing and in turn could boost use of the drug in patients who've failed on prior regimens.

Keytruda has been losing out to Opdivo in that second-line setting because its use depends on PD-L1 testing, while the BMS drug can be given to all comers. Roche's Tecentriq has now won a lung cancer approval for second-line use, too. But as Keytruda picks up momentum in first-line patients, that could transmit to its other indications—and to its 2022 sales. The current revenue forecast of around $6.5 billion that year would be far from shabby, but still just over half the projection for its archrival at the time this list was generated.

Like BMS, Merck is studying its drug for a host of other uses, including multiple myeloma, Hodgkin lymphoma, and breast cancer, as well as looking at the drug's role in combination therapies, which is where immuno-oncology drugs are really expected to shine.

For example, Merck has reported the results of a first-line NSCLC study showing a 70% response rate with Keytruda given in tandem with Eli Lilly's Alimta (pemetrexed) and platinum doublet therapy, something that R&D head Roger Perlmutter called "an amazing result," albeit in a small number of patients.

5. Ibrance

Product: Ibrance
Generic name: palbociclib
Company: Pfizer
2015 sales: $723 million
2022 sales: $6.01 billion
Current indication: metastatic breast cancer

Ibrance—the first in a new class of CDK 4/6 inhibitors—has romped away since Pfizer launched it in the U.S. in February 2015 as a combination therapy with letrozole for hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer that has spread to another part of the body.

The product showed no sign of slowing down in 2016, with first-half sales approaching a whopping $950 million. That growth was fueled by a second approval, in combination with AstraZeneca's Faslodex (fulvestrant), in women whose disease has progressed after hormone therapy. It's a remarkably quick rollout, considering that, at last count, the drug was still only approved in 15 countries, with a regulatory decision in Europe not expected until later this year.

Ibrance has potential rivals hot on its heels, however, with Novartis' ribociclib on the FDA's priority review track toward approval. Eli Lilly is following behind with abemaciclib—claiming advantages in terms of its safety and dosing regimen—but had a setback in August when an interim data analysis in a phase 2 trial showed it had not yet hit its efficacy objectives. That could delay a launch of abemaciclib until 2018.

Meanwhile, Pfizer is spending big to stay ahead of the competition. It is testing Ibrance on no fewer than 38 other cancers as it tries to capitalize on its lead in the market.

6. Tecentriq

Product: Tecentriq
Generic name: atezolizumab
Company: Roche
2015 sales: N/A
2022 sales: $5.53 billion
Current indications: urothelial carcinoma; non-small cell lung cancer

Roche's Tecentriq took third place in the PD-1/PD-L1 inhibitor race, reaching the market more than a year behind Opdivo and Keytruda, but it got off to a strong start and looks set to gain ground quickly. Sales reached $19 million in just a few weeks on the market in the U.S. for bladder cancer, and it has since nabbed a new indication in lung cancer.

The fact that it was approved first in bladder cancer—ahead of both its rivals—gives Roche an opportunity to build its position in that field as it battles for share in lung cancer and prepares for a follow-up filing in colorectal cancer.

In October 2016, Roche garnered approval for Tecentriq as a second-line therapy for all NSCLC patients regardless of PD-L1 status, allowing it to compete head-to-head with Opdivo and separating it from Keytruda, which requires PD-L1 testing. Roche's trials also tested Tecentriq in a much larger group of patients—more than 1,200 people—than studies which backed Opdivo's and Keytruda's approvals in second-line NSCLC. The company expects to prove that Tecentriq has a more durable effect on cancer than its rivals, with a lower likelihood of toxicity.

Tecentriq will draw on Roche's long heritage and marketing muscle as the leading company worldwide in anticancer biologics such as Avastin, MabThera/Rituxan and Herceptin. But the drugmaker needs it to step up quickly—those blockbuster brands are now all facing biosimilar competition.

7. Darzalex

Product: Darzalex
Generic name: daratumumab
Company: Johnson & Johnson
2015 sales: $20 million
2022 sales: $4.91 billion
Current indication: multiple myeloma

When Johnson & Johnson launched its multiple myeloma drug Darzalex in 2015, it knew it had its work cut out to carve out market share. Its drug was reserved for fourth-line use, setting it behind its closest competitors, Celgene's Pomalyst (pomalidomide) and Amgen's Kyprolis (carfilzomib), in the treatment sequence.

That wasn't a disaster, as multiple myeloma patients generally go through multiple treatment rounds to try to keep their cancer at bay, and J&J has already started to move the drug to earlier use.

Phase 3 trial data reported at last year's American Society of Clinical Oncology annual meeting showed Darzalex could cut the risk of disease progression or death by 61% when added to treatment with Takeda's Velcade (bortezomib) and dexamethasone as a second-line therapy. J&J says that data differentiates its drug from its rivals.

In November 2016, it received FDA approval for the med to be used—in combination with dexamethasone and either Celgene's Revlimid or Takeda's Velcade—in patients who had received just one prior therapy, a good piece of news for the drugmaker after it had bagged breakthrough status from the FDA for use in multiple myeloma patients who've relapsed after just one or more prior therapies.

There has been much speculation as to whether the first-in-class anti-CD38 drug will displace Pomalyst, Kyprolis and other drugs such as Takeda's Ninlaro (ixazomib), Bristol-Myers Squibb/AbbVie's Empliciti (elotuzumab) and Novartis' Farydak (panobinostat) in the increasingly crowded multiple myeloma market.

EvaluatePharma's analysis suggests it will win the tussle for market share. It's the only one of that group to make it into the top 15, although Pomalyst lies just outside with predicted 2022 sales of $2.81 billion.

8. Perjeta

Product: Perjeta
Company: Roche
Generic name: pertuzumab
2015 sales: $1.50 billion
2022 sales: $4.73 billion
Current indication: HER2-positive breast cancer

When Roche's Perjeta first launched in 2012, the jury was out as to whether the med would grow quickly enough to compensate for the expected decline in its $7-billon-a-year stablemate Herceptin once biosimilar competition gathered pace.

Four years later, those doubts have been largely laid to rest. Perjeta is one of the fastest-growing new products in Roche's portfolio, thanks to approvals for use in early-stage HER2-positive breast cancer that expand its initial use in more advanced disease. In fact, by 2022 Perjeta is predicted to add $3.2 billion to its annual sales, more than offsetting an expected $2.8 billion decline for Herceptin.

Giving it a big boost was its 2013 FDA nod as the first cancer drug approved for use before surgery, opening up a huge new group of eligible patients. The drug is used as a dual regimen alongside Herceptin or docetaxel chemotherapy to reduce the volume of breast tumors. The drug also set a precedent by becoming the first cancer drug approved by the FDA on the back of tumor shrinkage rather than survival data.

9. Xtandi

Product: Xtandi
Generic name: enzalutamide
Companies: Astellas Pharma; Pfizer
2015 sales: $2.10 billion
2022 sales: $4.71 billion
Current indication: prostate cancer

Eyebrows were raised when Pfizer offered $14 billion to buy Medivation last year to get control of fast-growing prostate cancer drug Xtandi, which was sold by Astellas. With that deal done, Pfizer has a stake in a drug that is growing at an impressive lick despite staunch competition from Johnson & Johnson's incumbent blockbuster Zytiga (abiraterone).

Zytiga outsold Xtandi last year—just barely—with sales above $2.2 billion, but Xtandi has a few advantages that are helping it compete against its rival. Firstly, it is given as a monotherapy, while Zytiga needs to be dosed alongside the steroid prednisone to balance side effects. Generally, doctors like to avoid use of steroids if at all possible. Secondly, patients on Zytiga need regular monitoring for liver enzyme levels, and the FDA required stronger warnings of potential liver toxicity to be added to the drug's label in June.

Those differences are having an impact in the market. Medivation claims that Xtandi has now surpassed Zytiga in market share, helped by earlier use, which means patients are staying on the drug for longer. And in the U.K., cost-effectiveness agency NICE gave its blessing for the use of Xtandi as a prechemotherapy regimen last year but turned down Zytiga. The agency changed its tune this March, agreeing to fund Zytiga as long as J&J delivers some discounts.

Results of the 500-patient Plato trial on the Xtandi-plus-Zytiga combo came in December 2016, and the pair proved no better at keeping cancer at bay than the Zytiga-only regimen did. But Xtandi is predicted to have a healthy lead in the prostate cancer market in 2022. It could also pick up additional approvals in breast and ovarian cancers that will crack open some big new markets for the drug.

It likely won't all be smooth sailing for Xtandi, however. The drug has been facing pricing pressure in the U.S., while health insurer CVS Health banned the drug from its 2017 formulary on cost grounds. It could also face competition from Bayer Healthcare's fast-growing Xofigo and possibly a resurgent Provenge if Valeant can inject some momentum into the troubled prostate cancer vaccine.

10. Avastin

Product: Avastin
Company: Roche
Generic name: bevacizumab
2015 sales: $6.95 billion
2022 sales: $4.68 billion
Current indications: colorectal cancer; non-small cell lung cancer; ovarian cancer; cervical cancer; renal cell carcinoma; glioblastoma

Avastin has been the gift that just keeps on giving for Roche. The VEGF-targeting antibody claimed its first approval in colorectal cancer in 2004 and has steadily added new indications since then, most recently picking up a European approval for use alongside Tarceva for patients with EGFR-positive non-small cell lung cancer.

Despite its age, Avastin is currently Roche's second biggest-selling drug (routinely swapping places with breast cancer stalwart Herceptin), and the company is still not done trying to add to its label. A filing in mesothelioma is expected to take place in 2017, and if studies of Avastin plus Tecentriq in renal cell carcinoma and non-small cell lung cancer go according to plan, the combination could be submitted to regulators the following year.

Avastin sales rose 9% in 2015 due to rising demand in ovarian, colorectal, lung and cervical cancer, particularly in Europe and emerging markets. The franchise has had a few drawbacks—notably a failure to win approval for breast cancer in the U.S. in 2010 followed by restrictions on its use in breast cancer in Europe, where it was also rejected for brain cancer in 2014.

But Avastin's upward trajectory is likely to falter now that biosimilar versions of the drug are hitting the market. These are already on the market in emerging markets, notably India and Russia; Amgen and Allergan have announced plans for "global regulatory submissions" for their version in 2016; and Biocon and partner Mylan have a version under review in the EU. They will have a fight on their hands, with Roche reckoning it has patent protection for Avastin in the U.S. until 2019 and in Europe until 2022.

Several other manufacturers—including Samsung Bioepis, Boehringer Ingelheim, Pfizer, AryoGen Biopharma, Reliance Life Sciences and Fujifilm Kyowa Kirin Biologics—have Avastin biosims in phase 3. EvaluatePharma is only expecting the brand to lose a couple of billion dollars by 2022, though, keeping it among the top 10 cancer drugs.

11. Herceptin

Product: Herceptin
Generic name: trastuzumab
Company: Roche
2015 sales: $6.79 billion
2022 sales: $3.98 billion
Current indications: breast cancer; gastric cancer

Approximately 15% to 20% of all breast cancer patients have tumors that are HER2-positive, which tend to grow more quickly than those that are HER2-negative. Until 1998, the prospects for patients with this form of cancer were pretty bleak, but the launch of Roche's Herceptin in that year revolutionized the way these patients were treated. The drug was Roche's first targeted cancer drug, and it has dominated the HER2-positive market ever since, with market share still well above 90%.

But Herceptin's position at the top of the HER2 tree is under threat from biosimilars, as the main EU patent for the drug was lost in 2014 and is due to expire in the U.S. in 2019. Mylan and Biocon have already launched a biosimilar version of the drug as Canmab in India, while Celltrion has another on the market in South Korea as Herzuma. Meanwhile, Mylan and Biocon are also squaring up for a launch in the EU, along with Samsung Bioepis, which has filed for approval of its SB3 candidate.

Analysts at Sanford Bernstein have suggested that Mylan/Biocon's version could be on the market by 2017 in Europe and in the U.S. the following year, a view shared by Roche's chief operating officer for pharmaceuticals, Daniel O'Day. "At this stage the main exposure for our business would certainly be more in 2018 than 2017," he said during the company's second-quarter conference call in 2016. "I feel quite confident that [the HER2 franchise] will grow through the biosimilar erosion curve of Herceptin."

Once the patent matters are out of the way, no shortage of players will be queuing up for a slice of the opportunity. Amgen/Allergan and Pfizer are among the other companies with biosims in late-stage testing.

12. Gazyva

Product: Gazyva
Generic name: obinutuzumab
Company: Roche
2015 sales: $133 million
2022 sales: $3.43 billion
Current indications: chronic lymphocytic leukemia; follicular lymphoma

Roche is relying on Gazyva to defend its position in the treatment of several blood cancers when big-selling Rituxan begins to face competition from biosimilars, possibly as early as 2017. The drug is billed as a new-and-improved version of Rituxan, with the same anti-CD20 mechanism of action. Like its parent, it is being developed for an array of B cell malignancies.

First approved in 2013 to treat people with previously untreated chronic lymphocytic leukemia (CLL), Gazyva initially saw sluggish growth. After picking up a second approval in follicular lymphoma (FL), sales picked up, and Roche's plans started to look more secure. That is, until Gazyva failed to best Rituxan when added to chemotherapy in previously untreated patients with diffuse large B-cell lymphoma in the GOYA trial. That failure—admittedly in an aggressive form of non-Hodgkin lymphoma (NHL)—could make it harder for Gazyva to capture market share from its tried-and-tested predecessor.

As for FL—the most common form of slow-growing NHL—Gazyva is currently approved for second-line use after Rituxan relapse based on the results of the GADOLIN trial. Roche also says Gazyva performed better than Rituxan in the head-to-head GALLIUM trial, improving progression-free survival, setting it up to enter the far-larger first-line market.

All eyes were on the data presented at the American Society of Hematology congress in early December 2016. In that trial, Roche said Gazyva, when tested alongside chemotherapy, trumped Rituxan in FL patients who hadn't been treated previously. In the meantime, Roche reckons it has other opportunities to grow Gazyva. It has trials in progress in acute myeloid leukemia, multiple myeloma and mesothelioma, as well as combination trials with AbbVie-partnered Venclexta in CLL.

13. Jakafi

Product: Jakafi; Jakavi
Generic name: ruxolitinib
Companies: Incyte; Novartis
2015 sales: $1.01 billion
2022 sales: $3.10 billion
Current indications: polycythemia vera; myelofibrosis

Jakafi's inclusion in the top 15 list may be something of a surprise, given the news last year that Incyte was pulling the plug on the drug for solid tumors after two failed trials in prostate and colorectal cancer.

EvaluatePharma's data suggest there is still plenty of upside for the JAK inhibitor despite that setback—although a chunk of its predicted $2 billion in the next few years will likely come from graft-versus-host disease, a noncancer indication.

First approved by the FDA for the bone marrow disorder myelofibrosis (MF) in 2011, a follow-up green light in polycythemia vera (PV) in 2014 consolidated its position in rare blood cancers. Incyte saw sales rise more than 50% in the first half of the year, while Novartis—which has marketing rights outside the U.S.—reported a 44% increase.

Incyte CEO Hervé Hoppenot said in August that the company still has more than a decade of patent protection for Jakafi, with plenty of room for growth in MF and PV thanks to raised awareness of the two diseases and the benefit of starting treatment early. In November 2016, Gilead's potential rival to Jakafi, momelotinib, stumbled in phase 3 when used to treat patients with MF, giving Incyte more breathing room.

14. Venclexta

Product: Venclexta
Generic name: venetoclax
Company: AbbVie; Roche
2015 sales: N/A
2022 sales: $2.91 billion
Current indication: chronic lymphocytic leukemia

AbbVie and Roche's Venclexta is a first-in-class BCL-2 inhibitor that made its debut in 2016 in the U.S. for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) caused by a particular genetic mutation. The mutation—which results in the loss of a tumor suppressor gene called 17p—is seen in around 10% of all CLL cases and is associated with a particularly poor prognosis.

The Venclexta price tag of around $110,000 a year will help the drug overcome a small patient population, as will possible future indications such as combination therapy for CLL with Roche's MabThera/Rituxan (rituximab), non-Hodgkin lymphoma (NHL), acute myeloid leukemia and multiple myeloma.

It will face some tough competition, locking horns with other CLL treatments on our list, notably Celgene's Revlimid, as well as newer entrants such as Gilead's Zydelig (idelalisib) and of course AbbVie's own Imbruvica.

AbbVie CEO Richard Gonzalez is not worried about cannibalization in his company's portfolio, however, saying recently that in addition to making its own headway in the market, Venclexta helped to boost Imbruvica—and vice versa—and they could become the best-in-class combination for CLL. Meanwhile, Roche stands to gain in similar fashion from the use of the drug in tandem with its Gazyva, which also appears in the top 15.

15. Rituxan

Product: Rituxan; MabThera
Generic name: rituximab
Companies: Roche; Pharmstandard
2015 sales: $7.39 billion
2022 sales: $2.89 billion
Current indications: non-Hodgkin lymphoma; chronic lymphocytic leukemia

Roche's third-biggest product, Rituxan, celebrates its 20th anniversary this year after debuting in 1997 in Switzerland and reaching the U.S. market the following year. The majority of sales for Rituxan are thought to come from oncology indications, although it is also approved for rheumatoid arthritis and organ rejection.

For now, Rituxan is still growing nicely, up 6% in the first half of 2016, thanks in part to a subcutaneous formulation of the antibody that reduces the treatment time and is more patient-friendly than the original intravenous infusion.

Since its launch in 2014, the new version has given some renewed momentum to the franchise, and according to one Roche exec, has around 35% penetration "with more to grow between now and the entrance of biosimilars."

Roche is expecting to face Rituxan biosimilars by the end of 2017 in Europe and in the U.S. after 2019. Several clones of the drug are already available in emerging markets, including India, Russia and several countries in Latin America. Celltrion is in pole position among the companies developing biosimilars of Rituxan, with the European Medicines Agency (EMA) filing its CT-P10 version of Roche's drug in late 2015. Another candidate from Novartis' generics unit Sandoz was filed in the EU in May, and Polish company Mabion S.A. has indicated it will submit its version before the end of the year. In December 2016, Sanofi struck a deal with Taiwan's JHL Biotech that could be worth up to $236 million to back future commercialization of JHL's in-development Rituxan copycat in China, among other products.

EvaluatePharma sees Rituxan as the most vulnerable among Roche's current stable of big-selling cancer drugs, losing $4.5 billion of its annual sales by 2022.

