UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 14A

PROXY STATEMENT PURSUANT TO SECTION 14(a) OF THE SECURITIES EXCHANGE ACT OF 1934
(Amendment No.)

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GW PHARMACEUTICALS PLC
(Name of Registrant as Specified In Its Charter)

JAZZ PHARMACEUTICALS PUBLIC LIMITED COMPANY
(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

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(2) Form, Schedule or Registration Statement No.:

(3) Filing Party:

(4) Date Filed:

The following is a transcript of a conference call held on February 23, 2021 in connection with Jazz Pharmaceuticals' Full Year and Fourth Quarter 2020 Financial Results.

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PRESENTATION

Operator

Hello, and welcome to the Jazz Pharmaceuticals Full Year and Fourth Quarter 2020 Financial Results Earnings Conference Call.

Following an introduction from the company, we will open the call for questions. I will now turn the call over to Andrea Flynn, Head of Investor Relations at Jazz Pharmaceuticals. You may begin.

Andrea N. Flynn - *Jazz Pharmaceuticals plc - VP & Head of IR*

Thank you. And thanks, everyone, joining the call. Today, we reported our fourth quarter and full year 2020 financial results and provided our financial guidance for 2021.

The press release and the slide presentation accompanying this call are available on the Investors section of our website. On the call today are Bruce Cozadd, CEO; Renee Gala, CFO; Dan Swisher, President; and Rob Iannone, Executive Vice President, R&D and Chief Medical Officer. Joining the Q&A are Kim Sablich, Executive Vice President and General Manager of North America; Phil Jochelson, Neuroscience Therapeutic Head; Anne Borgman, Hematology and Oncology therapeutic Head; Sam Pearce, Senior Vice President, Europe and International; and Shawn Mindus, Senior Vice President, Strategy and Finance.

I'd like to remind you that today's call includes forward-looking statements, such as those related to our future financial and operating results and which involve risks and uncertainties that could cause actual events, performance and results to differ materially. We encourage you to review statements contained in today's press release and our latest SEC disclosure documents, which identify certain factors that may cause the company's actual results to differ materially from those projected. We undertake no duty or obligation to update our forward-looking statements. On this call, we discuss non-GAAP financial measures. Reconciliations of GAAP to non-GAAP financial measures discussed on this call are included in today's press release and slide presentation available on our website. This communication is not intended to constitute an offer to buy or sell or the solicitation of an offer to buy any securities or solicitation of any vote or approval. GW intends to file a proxy statement with the SEC regarding the proposed transaction that will be mailed to GW shareholders. You should review material thought with the SEC carefully as they will include important information regarding the proposed transaction, including information about Jazz and GW, their respective directors, executive officers and certain other members of management and employees who may be deemed to be participants in the solicitation of proxies from GW Pharmaceuticals security holders in connection with the proposed transaction. Please also review Slides 2 through 5 of today's presentation for other important information, including where you can find more information on the proposed transaction and on the directors and executive officers of Jazz and GW.

With that, I'll now turn the call over to Bruce.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Thanks, Andrea. Good afternoon, everyone, and thank you for joining us today. 2020 was an exceptionally productive year for Jazz, driven by the expertise, commitment and capabilities of our organization and defined by operational excellence across commercial and R&D.

We enter 2021 in a position of strength. We plan to execute on significant milestones that we expect will further enhance the growth and durability of our business and to accelerate our transformation as an innovative biopharma company. I'm very proud that from this position of strength and readiness, we announced earlier this month that we signed a definitive agreement for the acquisition of GW Pharmaceuticals. We're excited about the potential to add epilepsies, a third high-growth commercial franchise to our business with Epidiolex, a potential near-term blockbuster as well as GW's robust neuroscience pipeline. The combined company would be a leader in neuroscience with a global commercial and operational footprint, and we expect this transaction to deliver substantial shareholder value.

We are excited to be joining 2 companies with a shared culture built around the same mission: innovating to transform the lives of patients.

In 2020, we demonstrated the resilience of our business and our agility, innovation and execution capabilities across the company despite the pandemic. We launched important new treatment options for patients, including Zepzelca and Xywav in the U.S. and Sunosi in Europe, delivered robust revenue growth and generated significant value for shareholders, successfully advanced early and late-stage clinical trials and added multiple new innovative products and targets to our expanding pipeline.

Our R&D organization initiated regulatory submissions to FDA through JZP-458 in acute lymphoblastic leukemia under the real-time oncology review in December and completed the rolling sNDA submission for JZP-258 in idiopathic hypersomnia this month, which positions us for 2 more potential product launches in 2021.

Last year, we also continued the expansion of our innovative oncology and neuroscience pipeline through internal and external collaborations with a focus on highly differentiated products that are durable and can be effectively commercialized, positioning us to transform patient lives and continue to deliver long-term growth.

Highlights of our successful execution on key 2020 objectives include: the successful launch of Zepzelca in the U.S. in July 2020, just 6 months after we acquired U.S. licensing rights. The launch of Xywav in November 2020 for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. I couldn't be more pleased with our early progress on this launch.

The initiation of the European rolling launch for Sunosi in May 2020, the initiation of a new drug submission for Zepzelca in Canada in December, the announcement of compelling top line results in the JZP-258 Phase III study in idiopathic hypersomnia in October 2020, followed by the completion of the rolling supplemental NDA submission to FDA in February 2021, positioning us for a potential launch in the fourth quarter of this year.

The initiation of the BLA submission to FDA for JZP-458 in ALL in December 2020 with a potential launch in mid-2021. And deployment of capital through multiple corporate development deals to grow and diversify revenues with innovative, new, early to late-stage product candidates, such as JZP-150 and post-traumatic stress syndrome and Zepzelca for the treatment of small cell lung cancer.

As we think about our key objectives for 2021, we are excited about the potential GW transaction and maintaining the significant momentum of GW's Epidiolex and our Xywav and Zepzelca launches. We also remain on track to execute and deliver on 2 more important product approvals and launches in 2021 with JZP-458 in ALL and JZP-258 in idiopathic hypersomnia while strategically diversifying our pipeline and revenues.

As a reminder, both JZP-458 and JZP-258 are products we've taken from concept to commercial readiness, underscoring the strength of our portfolio and development capabilities. Finally, the foundation we have built across our operations has resulted in a highly productive period of consistent execution and robust financial results and has prepared us for this transformative transaction.

I'll now turn the call over to Dan to give an overview of our commercial performance, after which, Rob will provide an update on progress across our R&D programs before Renée closes out with a financial overview. Over to you, Dan.

Daniel N. Swisher - *Jazz Pharmaceuticals plc - President & COO*

Yes. Thanks, Bruce. I'm also very excited about the progress of the launches of Zepzelca and Xywav in the U.S. and Sunosi in Europe. The strong execution across our commercial, R&D and operating teams during the pandemic continued to demonstrate our resilience and our agility to advance key corporate priorities while fully supporting our customers and our patients.

We're also excited about the prospect of 2 U.S. product launches in 2021 of JZP-458 in ALL and JZP-258 in idiopathic hypersomnia.

Now starting with Xyrem and Xywav. The successful initial launch of Xywav in November last year, which is the first asset we have taken from concept to approval and onto the market demonstrates our execution excellence across our R&D and commercial teams. Beginning now with the fourth quarter 2020 results, we will be providing you with metrics around the combined oxybate franchise, including Xyrem and Xywav. In addition, we will provide you with a number of patients adopting Xywav therapy. This information is intended to help you understand the growth and the durability of our entire oxybate franchise.

In the fourth quarter, oxybate net product sales were $455 million, 4% higher than the same period in 2019. For full year 2020, oxybate net product sales were $1.76 billion, an increase of 7% over 2019. Total oxybate revenue bottle volume growth was 2% for the quarter and 4% for the year compared to the same periods in the prior year. Through the fourth quarter, despite the ongoing negative impact of COVID-19 on new patient diagnosis and enrollment, average active oxybate patients increased to 15,300, a 2% increase over the same period last year.

We are pleased that our initial Xywav launch efforts have resonated well with both HCPs and patients. In the first 2 months of launch, Xywav generated net product sales of $15 million, and we ended 2020 with approximately 1,900 active Xywav patients. We are confident that Xywav will

become the preferred oxybate therapy over time through strong adoption by existing Xyrem patients, reaching patients who have been unable to take Xyrem due to sodium sensitivity and expanding opportunities with our planned fourth quarter launch this year in idiopathic hypersomnia, which would be the first FDA-approved treatment for this serious hyper somnolence disorder.

We remain on track for broad commercial payer coverage of Xywav within the first 6 to 9 months of launch. We've entered into agreements that provide coverage for 2 of the 3 largest PBMs in the U.S. with total commercial coverage now exceeding 60% of lives. We continued discussions with other major payers and PBMs.

So while we continue to secure additional commercial payer coverage, we do have robust patient access programs in place to help reduce barriers to access or initiation of Xywav treatment. Our market research indicates that the significant majority of HCPs recognize the ease associated with transitioning patients over to Xywav. In November and December, our field sales team engaged with the large majority of the top HCP prescribers. And in December, we also started our direct-to-patient education, most notably with Xywav leaflets added to all Xyrem shipments. We also have begun our Xywav webinar series and have had significant interest in both our KOL-led HCP and patient education programs. So we look forward to continuing the strong launch of Xywav, a very important step forward in oxybate treatment for narcolepsy patients to support their total health and well-being.

Additionally, we are excited to be preparing for the planned JZP-258 launch in IH in the fourth quarter this year and the opportunity for continued growth of our oxybate franchise. We are confident in, and we are on track for our goal of having the majority of all oxybate patients benefit from Xywav treatment in 2023.

We set this goal taking into account that patients may have multiple oxybate treatment options to choose from in that time frame. We believe that as we educate patients and physicians on the lifelong impact of high sodium intake, Xywav will be the oxybate therapy of choice.

So before I turn to Sunosi, I'd also like to mention that we are currently expanding and realigning our neuroscience sales force into 2 teams to focus exclusively on either Xywav or Sunosi, allowing us to provide dedicated product support and invest in the unique growth opportunities ahead for each product. For Xywav, we will continue our outreach to the top narcolepsy prescribers with a dedicated sales force and reimbursement team to support the adoption of Xywav as a preferred oxybate treatment. And for Sunosi, we will continue to increase our reach and frequency of calls among the top OSA treating physicians with the goal of driving significant awareness and uptake among these prescribers.

So now turning to Sunosi. During the fourth quarter, Sunosi net product sales were $9 million, approximately in line with third quarter, with full year net revenue for 2020 at $28 million. Prescriptions in the fourth quarter increased 9% in the U.S. compared to the third quarter of 2020. COVID-19 disproportionately affected our Sunosi launch, impairing our ability to build new relationships, especially with pulmonologists, the main OSA treating group who were also at the forefront in the initial battle against the pandemic.

As we move into 2021, we're excited about the investments we're making in Sunosi, with our expanded and dedicated sales force and our recent initiation of our TV DTC campaign. We remain focused on driving the next phase of Sunosi growth which will build on our broad commercial payer coverage at over 90%, the positive feedback and perception of Sunosi among existing prescribers and the large opportunity of undertreatment of excessive daytime sleepiness in the OSA patient population.

And lastly, we're pleased with the progression of our rolling launches in Europe, including the encouraging use of Sunosi in Germany for narcolepsy, which is ahead of our OSA launch expected later this year.

Turning now to Zepzelca. We were pleased with our fourth quarter Zepzelca net product sales of $53 million, and this is just the second quarter of product launch, an increase of $16 million over Q3. We continue to see significant patient growth and uptake across the community. And the academic settings with use in the second-line setting in both platinum-sensitive and platinum-resistant patients.

Our education and promotional campaigns remain focused toward the top small cell lung cancer treating physicians. We are seeing considerable interest, positive feedback and increased awareness across the academic and community cancer centers, reflecting the significant unmet need, the favorable Zepzelca product profile as well. So thanks to our team's outstanding execution. This launch continues to exceed expectations.

We were pleased in the U.S. hemopoetic stem cell transplants rebounded through third quarter and into fourth quarter. And we also observed robust growth in Europe, where our field teams have shared that physicians in select regions are treating the serious complications of bone marrow transplants, including VOD, earlier in order to minimize the risk of patients having to go to ICU.

This resulted in fourth quarter Defitelio net product sales of $55 million, 16% higher than the same period in 2019. 2020 Defitelio net product sales were $196 million, an increase of 13% over 2019. While intensive therapies have been affected by COVID, and the entrance of new therapies, we continue to believe in the growth opportunity for Vyxeos, both in terms of our ongoing development activities and continued expansion into new markets internationally as well as our ability to return to in-person promotional activity and continuation of our education on the importance of this clinically meaningful improvements seen, as highlighted, in the recently presented 5-year survival data from the pivotal study.

In the fourth quarter, Vyxeos net product sales were $31 million, 2% below the same period in 2019. 2020 Vyxeos net product sales were $121 million, approximately in line with 2019.

So turning now to asparaginase. In the fourth quarter, Erwinaze net product sales were $57 million, 3% above the same period in 2019. 2020 Erwinaze net product sales were $147 million or 17% below 2019. Our agreement with PBL terminated at the end of 2020. We have the right to sell certain Erwinaze inventory post termination, and we expect to distribute this inventory during the first half of this year.

Given the urgent need for a reliable and high-quality recombinant asparaginase, we remain focused on bringing JZP-458 to market as quickly as possible. Our commercial team is currently preparing for U.S. launch, which is targeted for mid-year.

In summary, I'm extremely pleased with our overall fourth quarter and 2020 performance. Last year was highly productive for Jazz. We clearly demonstrated our expanded capabilities and the ability to execute across our operating teams. Highlights include the successful launches of both Zepzelca and Xywav. I'm proud of the agility and resilience of our teams have shown to support the programs, the products and patients throughout this very challenging past year. We look forward to continuing to execute and meaningfully advance our pipeline and commercial programs through 2021, with a particular focus on our ongoing launches and following FDA approval are 2 planned launches for JZP-258 and JZP-458.

I'm now going to turn the call over to Rob for an update on our development programs. Rob?

Robert Iannone - *Jazz Pharmaceuticals plc - Executive VP of Research & Development and Chief Medical Officer*

Thank you, Dan. In the fourth quarter, we continued to make significant progress across R&D, including initiating the BLA submission of JZP-458 under real-time oncology review for patients with acute lymphoblastic leukemia and lymphoblastic lymphoma, initiating the rolling submission, sNDA submission of JZP-258 in patients with hepatic hypersomnia in December, with completion of this submission this month.

We have also continued our efforts in geographic expansion for key products, including Defitelio, Vyxeos, Sunosi and Zepzelca. I'll start with an update on the progress in our neuroscience portfolio.

Starting with JZP-258, we are looking forward to the presentation of our Phase III study results in adult patients with idiopathic hypersomnia at an upcoming medical conference in second quarter 2021. We're excited by the compelling study results we observed and look forward to sharing this data. Under Fast Track designation, we prioritized the rapid initiation and completion of the rolling sNDA submission to FDA within approximately 4 months of announcing our top line data as we work to bring JZP-258 to patients with IH as soon as possible, a debilitating disorder, for which there are no approved treatment options.

Turning to JZP-385, for the treatment of patients with essential tremor, a progressive, irreversible and chronic debilitating disorder that profoundly impacts quality of life. In 2020, we completed our healthy volunteer study and we anticipate initiating our Phase IIb trial in mid-2021.

Moving now to JZP-150, an irreversible FAAH inhibitor, which we are initially investigating in post-traumatic stress disorder. We plan to initiate our Phase II study in late 2021. I'm excited to get both JZP-150 and JZP-385 into important clinical trials this year and move a step closer to helping these patients who suffer significant impacts to their quality of life and for whom there are limited parent treatment options.

Now turning to our oncology development programs and starting with Zepzelca. We are continuing to work on the development program for Zepzelca in combination with — in collaboration with PharmaMar to support robust data generation in combination with other therapies in small cell lung cancer as well as in other tumor types. We are working toward the 2021 initiation of a Phase III study, evaluating immunotherapy plus lurbinectedin as maintenance therapy compared to immunotherapy alone in patients with extensive stage small cell lung cancer after induction chemotherapy.

Following the results of the Atlanta study, we and our partner, PharmaMar, met with the FDA and shared the top line results. We and PharmaMar agree that Atlantis would not serve as the confirmatory study and are actively engaging with FDA to determine the required confirmatory study package. We're also working with PharmaMar to continue evidence generation on Zepzelca. We anticipate initiating a Phase IV study with Zepzelca in mid-2021 with an objective to provide additional data and information on treatment practices, patient characteristics and real-world efficacy and safety.

Finally, we submitted the new drug application to Health Canada in December 2020.

Now moving to JZP-458, our recombinant urine asparaginase for the treatment of patients with ALL and LBL who have hypersensitivity to E. coli derived asparaginase. In December, we initiated the BLA submission to FDA under real-time oncology review. We are on track and working closely with FDA to complete the BLA submission and remain focused on bringing JZP-458 to patients as quickly as possible. We are targeting a mid-2021 launch in the U.S.

We are also working on our regulatory strategy in Europe and Canada and working with our partner on the approach in Japan. We anticipate the data from our current development program for JZP-458 will support our efforts to seek approval in Europe and Canada, and we will be confirming these plans with regulators later in the year.

Turning now to Vyxeos. We have submitted data to health authorities in the U.S. and in Europe for Vyxeos in relapsed/refractory pediatric AML. We anticipate a potential approval in Europe and a label update in the U.S. in 2021. While pediatric patients represent a relatively small percentage of total AML patients as the average age of an AML patient is 67, there is a critical need for more effective therapies in this setting.

I will now turn the call over to Renée.

Renée D. Galá - *Jazz Pharmaceuticals plc - Executive VP & CFO*

Thanks, Rob. I'm very pleased to share our financial results for fourth quarter and full year 2020, which reflect considerable top line revenue growth, including a meaningful contribution from our recent launch of Zepzelca. With our strong financial and operational performance in 2020 and our planned acquisition of GW Pharma in second quarter 2021, we are poised for substantial future growth.

In addition, the transaction will accelerate and enhance our revenue diversification goal, positioning us to deliver more than 65% of our total 2022 revenues from products launched or acquired since 2019.

2020 was a great year for Jazz. Total revenues for the fourth quarter increased 14% to $666 million and for the full year increased 9% to $2.6 billion — $2.36 billion over the same period last year. Our full year 2020 revenue growth was driven by robust double-digit growth in our oncology portfolio and high single-digit growth in our neuroscience portfolio.

Neuroscience net sales for the fourth quarter increased 6% to $463 million, and full year revenues increased 8% to $1.79 billion compared to the same periods in 2019. Full year 2020 growth in neuroscience was driven by continued notable performance of Xyrem despite the pandemic, growth of Sunosi prescriptions and the initial launch of Xywav in November.

Oncology net sales for the fourth quarter of 2020 increased 46% to $196 million and for the full year increased 18% to $554 million compared to the same periods in 2019. 2020 oncology sales growth was driven by the robust launch of Zepzelca in July 2020, which generated net sales of $90

million in its first 2 quarters on the market. And the continued growth of Defitelio, partially offset by the decrease of Erwinaze sales due to ongoing supply disruptions.

Turning to operating expenses. As we move through 2020 and assessed the impact of the pandemic, we balanced our investments in the business and focused on key value drivers. Our 2020 adjusted SG&A expense was 33% of total revenues, an increase compared to 2019 of 2 percentage points or $112 million driven by targeted investments to support our multiple new and planned 2021 commercial launches. We increased our 2020 adjusted R&D expense by $32 million compared to 2019 as we expanded our robust and productive R&D pipeline, with new innovative product candidates and targets.

As a ratio of total revenues, spend was in line with 2019 at approximately 13%. We are pleased with the business progress made in 2020 as a result of our disciplined approach to capital allocation and strong operational and financial performance. And we remain excited about the opportunity to deliver continued growth through our innovative and expanding neuroscience and oncology portfolios in the future.

Turning to guidance. For our 2021 guidance, I'll provide Jazz's stand alone guidance, and we will update this to include the previously announced GW transaction after it closes. Starting with top line financial guidance. Our total revenue guidance is in the range of $2.55 billion to $2.7 billion, which represents a double-digit 11% increase at the midpoint over our 2020 total revenues.

In neuroscience, we are providing net sales guidance in a range of $1.785 million to $1.885 billion, which reflects an increase of 3% at the midpoint of the range compared to 2020 and reflects our expectations of the robust adoption of Xywav and for 2021 Sunosi performance supported by our investments to accelerate growth and adoption of both products.

With regards to Xywav, as mentioned previously, we are pleased with the strong initial adoption. As we work towards broad payer coverage over the first 6 to 9 months post launch, our investment in patient access and bridging programs is helping to enable seamless access to Xywav by patients. The temporary impacts of these programs, which are important to the long-term durability and growth of the oxybate franchise are reflected in our 2021 neuroscience guidance.

For our oncology portfolio, we are providing 2021 net sales guidance in a range of $715 million to $835 million which represents an increase of 40% or $221 million at the midpoint compared to 2020 and reinforces the confidence we have in this growing product portfolio. Our oncology sales guidance reflects the impact of the first full year of sales for Zepzelca and our expectations for continued momentum in that launch, anticipated Erwinaze supply for the first half of 2021 and the planned launch of JZP-458 in mid-2021.

Now turning to our expense guidance. We were pleased with our operational excellence in 2020 and our ability to navigate the impacts of COVID-19 while still making investments for future growth. As we move into 2021, we will continue to prioritize our investments to drive our key objectives of growth and diversification.

Our 2021 adjusted SG&A guidance range is $905 million to $945 million, which represents 35% of total revenues at the midpoint. This increased investment reflects our continued prioritization of the launches of Zepzelca, Sunosi and Xywav and the planned launches of JZP-458 in mid-2021 and JZP-258 in IH in the fourth quarter of 2021.

On the adjusted R&D front, our 2021 guidance is in the range of $330 million to $370 million or 13% of projected revenues at the midpoint, which is consistent with 2020. With our exciting and differentiated R&D pipeline, we believe these investments will continue to fuel sustainable long-term growth for our expanding and innovative portfolio.

Our guidance for non-GAAP adjusted net income and EPS are in the ranges of $915 million to $985 million and $15.65 to $16.85, respectively. Our adjusted net income as a percentage of total revenues will increase to 36% at the midpoint, up 6 percentage points compared to 2020.

Turning to our balance sheet. In 2020, we generated $900 million in cash from operations and ended the year with cash and investments of $2.1 billion. We are excited about the potential GW Pharma transaction and see this as a transformative deal that is consistent with both our overall business and capital allocation strategy and effectively leverages our strong financial and operational position. As we've mentioned, the transaction

is expected to accelerate our double-digit top line revenue growth and be EPS accretive in the first full year of combined operations and substantially accretive thereafter.

At close, we expect the pro forma company net debt-to-EBITDA leverage ratio to be approximately 5.4x. And given our significant cash flows, we expect to reduce this to below 3.5x by the end of 2022. We view this investment as a disciplined and productive use of our capital to significantly expand our growing neuroscience portfolio and drive substantial value for our shareholders.

Finally, we set out an ambitious range of transformative objectives for 2020 and 2021. We are well on our way to executing on 5 important product launches and diversifying our portfolio and revenue base with products to address significant unmet medical needs and transform patient lives. We are looking forward to the planned close of the GW Pharma transaction in the second quarter and leveraging the combined talents and expertise of the Jazz and GW Global teams to develop and launch differentiated therapies to support often overlooked patient populations.

Upon close, we look forward to creating an innovative, high-growth global biopharma leader with an enhanced product portfolio, providing the scale and expertise to reach and transform the lives of more patients around the globe with unmet needs. Thank you for joining us today, and I'll now turn the call over to Andrea.

Andrea N. Flynn - *Jazz Pharmaceuticals plc - VP & Head of IR*

Thanks, Renée. (Operator Instructions) We will gladly address any additional questions after the call or you can reenter the queue. So with that said, please go ahead and open the line for Q&A.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from the line of Jessica Fye with JPMorgan.

Jessica Macomber Fye - *JPMorgan Chase & Co, Research Division - Analyst*

I was wondering if you could say how many active patients around Xywav currently.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Jess, this is Bruce. We're not going to give intra-quarter data like that. We'll obviously update again on our next call. But our body language here is we're really pleased with the way launch is going, not just during the first couple of months, but as we continue through today.

Operator

Our next question comes from the line of Ami Fadia with SVB Leerink.

Ami Fadia - *SVB Leerink LLC, Research Division - MD of Biopharma & Generics and Senior Analyst*

Can you talk about — out of the patients that are on Xywav, can you talk about what peers have been requiring as a requirement for switch? Are — most of these patients are patients that have comorbidities or are you seeing a fair mix of patients that may or may not have comorbidity?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes, maybe I'll ask Kim to weigh in on this one.

Kim Sablich - Jazz Pharmaceuticals plc - Executive VP & GM of North America

Sure. So we're very pleased, obviously, with the progress that we're making here on the launch. Our focus here on the launch is on transitioning Xyrem patients to Xywav, we really are seeing that the vast majority of those patients are experienced on Xyrem in terms of the patients that are on Xywav. But both in terms of having just taken Xyrem or have taken Xyrem in the past. But we also see a portion of patients who are new to oxybate overall and new to Xywav. So I'm very pleased that it's been consistent with our strategy. And I think — did you have a question about payer coverage, I'm just trying to clarify that.

Ami Fadia - *SVB Leerink LLC, Research Division - MD of Biopharma & Generics and Senior Analyst*

Yes. So with regards to the payer coverage, I'm trying to understand how you're placed on the plan. And what might be certain criteria that payers are requiring physicians to address before allowing patients to switch from Xyrem to Xywav or a de novo patient being allowed to go in Xywav.

Kim Sablich - *Jazz Pharmaceuticals plc - Executive VP & GM of North America*

Yes. So I think, as you know, we've stated, we've had basically a parity strategy between Xyrem and Xywav both in terms of our pricing strategy and our goal of pricing not only at the gross level, but also at the net level, the 2 products at parity. But also in terms of how the 2 products are treated ultimately on the on formulary, we're looking for Xywav to be placed on formulary in a comparable position to that Xyrem enjoys today. And within that means also not just where it sits in terms of the tier, but how it's treated in terms of utilization management. And so far to date, we're very pleased to say that with the contracts we've signed, we are achieving that goal of parity treatment.

Ami Fadia - *SVB Leerink LLC, Research Division - MD of Biopharma & Generics and Senior Analyst*

Okay. And if you don't mind, just a final point on that. Out of the patients that have been switched to Xywav up until the end of the year, can you talk about whether or not the mix of patients from that subset that may have other cardiovascular comorbidities or not.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Dan, maybe I'll ask you to weigh in on that one.

Daniel N. Swisher - *Jazz Pharmaceuticals plc - President & COO*

Yes. Thanks, Ami. Yes, just — we're positioned, and we're actually pleased with the uptake. In the offices that are adopting that really all patients who are on oxybate therapy, lifelong treatment, modifiable risk factor whether or not they have current comorbidities, they're at risk of it. And so we're seeing kind of a broad cross-section of patients. We're also seeing some new patients, obviously, coming on where the suite of access services enables and the rising payer coverage with more than 60% of commercial lives covered, coming on to Xywav initially for oxybate therapy versus Xyrem. And we also think over time, we're going to find patients who had previously not been candidates for Xyrem coming into therapy as well in addition to growing into the IH indication. So very pleased with the uptake. Certain physicians were further along in the journey at the time of launch and understanding the risk factors and the amount of sodium. In Xyrem, some physicians were not, and also the patients become an active part of this dialogue as well.

Operator

Our next question comes from the line of Jason Gerberry with Bank of America.

Jason Matthew Gerberry - *BofA Securities, Research Division - MD in US Equity Research*

So Bruce, appreciate the commentary about favorable body language on the Xywav switch. What I was wondering is, is the switch trending ahead of your expectation? I know you put out some metrics for where you expect it to be in 2023. But just curious if you're operating ahead of expectation or if we should consider there to be a pent-up bolus. I would assume maybe only 20% of patients have seen probably their doctors since the switch occurred. So I'm a little surprised how high the number was. So just curious if you can provide any commentary there because I think that will help us think about the progression over the course of the year.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. I mean we're — Jason, we're still early in the launch. But to directly answer your question, we are ahead of the expectations we had set internally for the first couple of months. And I think as you heard Kim and Dan comment, our messaging is resonating with people about the benefit of this therapy and excitement about it. And so I don't think of this as just a bolus that adopted early. We see continued interest and look forward to continue our educational efforts over the balance of this year. And next and continuing to work toward our goal of this being the primary brand in the oxybate space even out in 2023.

Operator

Our next question comes from the line of Ken Cacciatore with Cowen.

Kenneth Charles Cacciatore - *Cowen and Company, LLC, Research Division - MD & Senior Research Analyst*

Bruce, as we stare at the Xyrem and Xywav franchise, it's kind of a really fascinating modeling exercise as we kind of look at 2023. Obviously, you have Xywav, which could be taking a vast majority of the franchise. And then you have information about the settlements and who can come and the kind of the volume they can supply. And you also know the royalties that they owe back to you. So as we look at 2023, and we try to take all these individual pieces of kind of significant conversion to the franchise, and then your knowledge of what could be the generic supply for Xyrem, and again, what they owe you, can you help qualitatively maybe talk through a little bit of either any enthusiasm you have or how we can start thinking about maybe a preservation that some of us have modeled a little bit too negatively? And then I just wanted to follow-up on the commentary you made on Erwinaze in 458. I would assume that you all understand the supply that you're not able to put into the marketplace. I would think that information is almost perfect. So can you maybe give us a sense of what we are unable to supply and therefore, what we may be able to supply with 458?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Thanks, Ken, and maybe I'll take the first part of the question around oxybate and ask Dan to weigh in on asparaginase. In terms of oxybate, the way we're thinking about this is we've got a great growth opportunity in front of us. We're seeing continuing growth in diagnosis and initiation of therapy on oxybate. That's a continuing trend we've had for a number of years now. We see an opportunity with Xywav to address some patients whose physicians were unwilling to start them on therapy historically due to the high sodium load. We see an opportunity, obviously, with idiopathic hypersomnia. Upon the approval and launch of that product later this year, and that's a substantial opportunity relative to the size of the narcolepsy population. So we see growth opportunity in front of us. In — as you go out a few years, we do expect there will be authorized generic competition beginning in 2023 or potentially earlier in some circumstances. And as we've disclosed, we have economics, in some cases, substantial economics in those authorized generics, which we distributed through our REMS. But to be clear, we think that most patients in this lifelong therapy in this

group known to have high cardiovascular risk will benefit from the advantage of Xywav therapy. So we see the opportunity to expand the product and then really to be a continued preferred treatment far out into the future. Dan, do you want to take asparaginase?

Daniel N. Swisher - *Jazz Pharmaceuticals plc - President & COO*

Sure. Yes, Ken, on your question about asparaginase. I mean, we don't have perfect information in the sense that we've been supply-constrained for 4 years. And probably last year was our worst year in terms of supply capacity to the U.S. market. And so as that happened, we've cut back completely on promotion and ISTs and clinical work. We've also put in sort of patient-by-patient verification for product supply. So no inventory sits on the shelves at the hospitals. And we haven't sort of penetrated into certain new geographies like Japan or really helped with the promotion of asparaginase containing regimens for adolescent and young adults. So before we were supply constrained, we were moving above $200 million in product sales, that was several years ago. We believe there's substantial room for expansion with a high-quality, fully recombinant product that physicians can count on that when they start the course of therapy, they can get to the end of therapy and ensure the really successful treatment outcomes that they currently have with asparaginase.

Operator

Our next question comes from the line of Balaji Prasad with Barclays.

Balaji V. Prasad - *Barclays Bank PLC, Research Division - Director*

Maybe just on Xyrem. With the pace of conversion that we are seeing, Xyrem has soon become a moot point, but want to get an update on Avadel. It's been 2 months since they've filed. What is your strategy now? And if FDA accepts their filing, is there any way for you to still mandate that they be a para IV, considered a para IV? How do we think about the impact of this, especially next year?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Thanks for the questions. We're not going to do any disclosure on behalf of Avadel. We'll keep people posted on where they are with FDA. We'll remind you that we do believe they should need to paragraph or certify against Orange Book listed patents on Xyrem that have to do with the safe distribution of the drug, both as regards our distribution system, which ensures safe use of the product and limits abuse, misuse and diversion as well as helping patients understand an important drug-drug interaction. That paragraph or certification can happen on submission, but it can be required at any point during the review process as well. And then, of course, we have what we believe is relevant intellectual property and we'll defend that in the best way possible for Jazz.

Operator

Our next question comes from the line of Randall Stanicky with RBC Capital Markets.

Randall S. Stanicky - *RBC Capital Markets, Research Division - MD of Global Equity Research & Lead Analyst*

Bruce, how are you guys thinking about total oxybate volume growth for 2021? And specifically, we're hearing from physicians that there's an expectation of a big pickup going forward in oxybate patient volumes. And I'm trying to understand if that's consistent with what you're expecting. And then how much of that would be related to the lifting of COVID headwinds versus the onboarding of new high-risk patients coming into the patient pool? Or even just you being out there more aggressively educating physicians around Xywav and detailing the product?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Maybe I'll start, and then I'll ask Dan if he wants to add. In general, Randall, I'd say this is a really exciting period for narcolepsy patients with the additions to Xyrem as a standard of care. The addition of Sunosi as a new way of promoting agent, pitolisant coming to market. Now Xywav coming to market. There are treatment options that weren't available before. There are more people out talking to doctors about appropriate diagnosis and treatment options, and that's good for patients. And if that leads to either more diagnosis or more treatment, that would be really helpful since narcolepsy is still an underdiagnosed and undertreated disease. In terms of our growth expectations, we know that COVID-19 had an impact. We think that impact is lessening as we move through 2020. And we, like the rest of the world, are hopeful that 2021 will turn out to be a better year in terms of patients being able to access medical care and get appropriate treatments. We're excited to be promoting a new product. And as we head toward the end of the year, look forward to a launch in an indication with no currently approved therapy. Dan, any color you want to add?

Daniel N. Swisher - *Jazz Pharmaceuticals plc - President & COO*

Yes. I just add on to what you said, say, persistence and compliance is something we did see pickup during COVID, but headwind was, of course, the diagnosis of patients. And that's been definitely impacted again in the fourth quarter with COVID. So — and narcolepsy still remains pretty underdiagnosed. The other thing in terms of growth will be just patients as they're becoming aware of the treatment option, whether they had tried Xyrem and come off or hadn't tried it before knowing there's sort of a longer term, healthier treatment option. I think the patient will play part of the journey and reaching the patient is going to be important to us. And then lastly, I would say there's patients who clearly were salt sensitive and not candidates who now Xywav provides a therapy for them. And also significant expansion into the idiopathic hypersomnia market where there's no FDA-approved drugs and managed care has made sure that oxybate has not been widely available for those patients.

Randall S. Stanicky - *RBC Capital Markets, Research Division - MD of Global Equity Research & Lead Analyst*

Bruce, are you able to share a volume growth number?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

No. So we provided a neuroscience net sales guidance for the year, which has the puts and takes of Xyrem, Xywav and continued Sunosi growth both in the U.S. and ex U.S., but we're not giving a specific volume growth expectation. Obviously, as we move out into the very end of the year and next year with a successful IH launch, we expect that there's opportunity for the kind of volume growth we haven't seen in recent years.

Operator

Our next question comes from the line of Gary Nachman with BMO Capital Markets.

Gary Jay Nachman - *BMO Capital Markets Equity Research - Analyst*

Just follow-up on last question (inaudible).

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

So Gary. Unfortunately, that was garbled. I was trying to pick out enough words that I could answer a question that was related to what you asked, but I'm not sure what you asked. So I don't know if you can get a better connection.

Gary Jay Nachman - *BMO Capital Markets Equity Research - Analyst*

Could you hear me now?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

That's better.

Gary Jay Nachman - *BMO Capital Markets Equity Research - Analyst*

I was just (inaudible) anything potentially this year in the guidance and just how you're preparing to launch the indication into the market. So now that you've had a lot more time to think about the overall opportunity, just give us a better sense of how you're going to be going after that once it's (inaudible)

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

I know you were asking about the launch. Was that idiopathic hypersomnia or JZP-458?

Gary Jay Nachman - *BMO Capital Markets Equity Research - Analyst*

No, it was idiopathic hypersomnia. I don't know why — I'm sorry for the connection, bad connection. Yes. Just — yes, do you have more time to think about it, the overall opportunity. And if it's in the guidance for this year, if there's anything baked into the latter part of this year once it's approved.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Maybe I'll start with the last piece, which is there would be very little in our guidance for 2021 because the launch would be happening towards the very back-end of the year. It will take a little while to build awareness, as you know, as you're seeing with the launches of Sunosi and Xywav, you don't necessarily have perfect coverage day 1. So I wouldn't think of it as a major revenue contributor this year. Although we'd love to get some patients on therapy. Maybe we could just ask Rob to jump in for a minute and just talk about — Rob or Phil, just talk about idiopathic hypersomnia as an opportunity from a medical standpoint. And then, Kim, maybe a few reflections on launch.

Robert Iannone - *Jazz Pharmaceuticals plc - Executive VP of Research & Development and Chief Medical Officer*

Why don't I have you go first, and I'll join in as needed.

Philip Jochelson - *Jazz Pharmaceuticals plc - VP of Therapeutic Area Head, Sleep & CNS*

Great. Thank you, Rob. Yes. So I think as we've understood this population more and more, we clearly understand that this is a chronic disabling disease and these patients have a lot of not only excessive daytime sleepiness, but also a lot of dysfunction as a result of that excessive daytime sleepiness have a lot of sleep inertia. And I think we've talked to you about that before. They have a lot of difficulty waking up and have very long sleep periods, in many cases. As we've understood this more and more, and we see the benefits from our [ODE] study, we recognize that we can treat many of the symptoms associated with this chronic disabling disease. From our team's databases, we're aware as I think we've shared before that we have about 37,000 patients from data basis. But we've also heard reports from a number of key opinion leaders who are also prescribers of the narcolepsy population that they see a large number of these patients that have ranged from anywhere from up to a similar number from anywhere, I think, from 10% up to 80% to 90% of a similar population in size to the narcolepsy. So we haven't completed all the Epi data around this. I think we'll continue to do that. We just know what's in the health claims databases. We think it's going to be a sizable opportunity. And I think

when we have a chance to share all of the data at the upcoming meeting that Rob alluded to in the second quarter of this year. The data is really compelling, and I think will be — resonate very well with the prescribing population for this target population.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

And just to pivot quickly over to launch planning. We've got a team ready to go. Obviously, significant overlap with the physician audience we've already got relationships with and are educating about Xywav therapy. We think there's a significant number of under diagnosis, but the current diagnosed patients from a chart poll was 37,000. So that's a big opportunity to start with. And then very importantly, we do have our clinical data from the Phase III that has been accepted at an upcoming medical conference in Q2. Really pleased to not only having statistical significance, but really clinically meaningful data in terms of the endpoints. And that will be shared 6 months ahead, and that's great as part of the medical education in advance of the fourth quarter launch.

Operator

Our next question comes from the line of David Amsellem with Piper Sandler.

David A. Amsellem - *Piper Sandler & Co., Research Division - MD & Senior Research Analyst*

So just another question on IH. So the contracting that you have in place right now, is that going to apply to IH patients? I mean, just maybe give us some clarification on how broadly applicable those contracts are as you think about the IH launch. And then a longer-term question is, with the orexin agonist in development, how do you think about the potential impact on the footprint of oxybate in general, to the extent that one or more orexins get commercialized?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes, David, on the first part of the question on contracting, we've certainly done our contracting with a view toward the evolving narcolepsy treatment landscape. But to your question narrowly, we do need an approved label and have conversations with payers about that before we're done. So no, it's not a pay to complete.

And then on orexin, maybe I'll ask Jed or Phil to just weigh in a little bit about the potential of orexin vis-à-vis oxybate.

Jed Black - *Jazz Pharmaceuticals plc - SVP of Sleep & CNS Medicine*

This is Jed. I'll jump in. I think it's fair to say that everyone is excited about the potential for orexin agonist to be helpful in the treatment of narcolepsy. The mechanism of an ex agonist is substantially different from the mechanism of oxybate. And we anticipate the orexin agonist will likely have an impact — a pharmacodynamic impact that's similar to what we see with weight promoting agents and stimulants. And so we expect that long term, those agents would be complementary to those potential orexin agonists would be complementary to oxybate in treating narcolepsy.

Operator

Our next question comes from the line of Greg Gilbert with Truist Securities.

Gregory B. Gilbert - *Truist Securities, Inc., Research Division - Analyst*

I hadn't thought to ask Jed a question, but since he's got the mic, maybe you could offer any thoughts you have on cannabinoids and sleep. I'm guessing you have some thoughts there. But my other question was for Renee. When you closed the GW deal, do you provide updated guidance right on the back of that or the next scheduled quarterly conference call, maybe you could just set the stage first on what and how you will guide.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes, I think in interest — in the interest of time, I'm going to suggest we not take the cannabinoid and sleep question right now. We'll have more to say about the combined neuroscience pipeline at closing, but I'll let Renee take your guidance question.

Renée D. Galá - *Jazz Pharmaceuticals plc - Executive VP & CFO*

Yes. Thank you. And as you can appreciate, we're still working through getting to close of the transaction. And so once we actually close the transaction and are actually running the business, then we'll have a much better feel for the timing of the guidance that we'll provide for the combined company. We will certainly provide updated guidance to reflect Jazz combined with GW post close, but the exact timing of that is a little early to say.

Operator

Our next question comes from the line of David Risinger with Morgan Stanley.

David Reed Risinger - *Morgan Stanley, Research Division - MD in Equity Research and United States Pharmaceuticals Analyst*

So management had hosted a very compelling call on the risk of high salt intake last year, and it seems logical that most doctors and patients would opt for Xywav instead of Xyrem, and that should potentially drive a faster-than-expected switch. But my question is, how would you characterize the risk of potentially triggering an early Xyrem generic entry in 2022 before you have a full year to drive Xywav adoption in idiopathic hypersomnia? Obviously, the current assumption is the IH launch occurs at the end of 2021, I believe. And then the generic entry against Xyrem is in January of 2023. So if you could just provide some perspective on that, that would be helpful.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. Good question, Dave. And let's just say, we want to help as many narcolepsy patients as possible with Xywav. We are not holding back in any way. If we're so successful that we've triggered earlier AG entry, that is a success scenario from our standpoint in terms of our progress with Xywav. Specific to the IH launch, we did our studies with JZP-258 or what's on the market as Xywav. And the IH indication would be specific to that product.

Operator

Our next question comes from the line of Brandon Folkes with Cantor Fitzgerald.

Brandon Richard Folkes - *Cantor Fitzgerald & Co., Research Division - Analyst*

Congratulations on another good quarter. Maybe just changing gears a little bit here and focusing on Zepzelca. Another good quarter there. Can you provide some color in terms of how much pent-up demand are we still seeing in third and fourth-line versus pure second line? And I know you mentioned that both platinum incentive and platinum resistent are growing usage. Any way to parse that out a bit more just in terms of the uptake between sensitive and resistant?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. For Zepzelca color, maybe I could ask Kim to just talk a little bit about what you're seeing in terms of how the launch is progressing.

Kim Sablich - *Jazz Pharmaceuticals plc - Executive VP & GM of North America*

Yes, sure. So we remain very pleased with the response to the launch among the small cell lung cancer treating community feedback to the profile, and what they've seen in their patients has been quite positive. And as you see there, we're seeing nice growth in the product overall. What I can tell you is that we're seeing growth through December, the data that we have across all patient types, including second line, as you said, in both types of second-line patients in terms of platinum sensitive and platinum resistance. So I think we're still in a stage where physicians are getting experience with it and are seeing a tremendous unmet need, a strong profile and still using it across a broad spectrum of patient types.

Brandon Richard Folkes - *Cantor Fitzgerald & Co., Research Division - Analyst*

Okay. And are we still seeing usage from certain fourth line patients as we saw last quarter?

Kim Sablich - *Jazz Pharmaceuticals plc - Executive VP & GM of North America*

Yes, through the data that we have, we're still seeing strong usage there.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

I will say our goal is, over time, to have this become the standard for second-line small cell lung cancer treatment and to have patients get it at that point. Obviously, that hasn't been true in the first few months after launch, right, because we're establishing awareness. But over time, we'd expect that second-line share to go up and therefore, to see less usage later. Of course, in second line, we'd expect longer duration of therapy as well.

Operator

Our next question comes from the line of Esther Rajavelu with UBS.

Esther P. Rajavelu - *UBS Investment Bank, Research Division - Analyst & Executive Director*

So 2 for me. One on JZP-458. Dan, you mentioned that you've been somewhat out of the market with this product. So I'm wondering, as you're preparing to launch 458, if you can help us understand how we should be thinking about the launch trajectory compared with where Erwinaze sort of left off or leaves off in the middle of the year.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Dan, you want to take that?

Daniel N. Swisher - *Jazz Pharmaceuticals plc - President & COO*

Yes. I think I'm going to punt on that question. I mean, we're going to give more detail as we've got precise launch timing and launch label. And frankly, also know what's the asparaginase market look like in the U.S., but we do see opportunity for growth from where we've been clearly across all the categories I referenced. But I'd say stay tuned a little bit longer on anything more precise.

Esther P. Rajavelu - *UBS Investment Bank, Research Division - Analyst & Executive Director*

Okay. And then for 385, you talked about tremor, essential tremor as an attractive opportunity boost before. And I think you just mentioned on the call that you've had some Phase I healthy volunteer data. So can you give us some context of the data that you've produced for 385 versus what's been in the public realm in the past?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. So Phil or Rob, do you want to jump in on that?

Robert Iannone - *Jazz Pharmaceuticals plc - Executive VP of Research & Development and Chief Medical Officer*

Sure, I'm happy to, Bruce. This is Rob Iannone. The proof-of-concept Phase II study was conducted before the acquisition. It was done with a formulation that was fit for purpose. And so our initial steps was to develop a once daily formulation that could be commercialized, and that's what we refer to as the healthy volunteer study. And that will be taken forward into the pivotal Phase IIb study that we referenced earlier.

Operator

Our next question comes from the line of David Steinberg with Jefferies.

David Michael Steinberg - *Jefferies LLC, Research Division - Specialty Pharma Analyst & Equity Analyst*

I know you've taken several questions about the Xywav switch, but just want to see if we could get a little more granularity. So if you take the number of patients that were on oxybate therapy that you gave out at the end of the year as well as those you mentioned were active Xywav patients, you get about a 12% switch rate. And I know it's not that because you mentioned there were some newer patients who come in. I was just curious on the non most recent oxybate switches, how many — or what percent of those new patients were just natural evolution of newly diagnosed narcolepsy patients and which were patients who previously redeemed not being able to be on Xyrem simply because they had cardiovascular issues or comorbidities? And then related to the patients with severe cardio issues who previously could not be put on Xyrem. Some of the KOLs we've spoken to think there's a very small percent and others up to 20%. I'm just curious, from your own research, what would be that theoretical number of patients who have severe enough CV issues that previously could not be put on Xyrem?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes, Dave, a couple of good points there. You keep using the word switch. I would just remind you that we — as you said in your question, we've got patients coming to Xywav, in some cases, directly from Xyrem; in some cases, from prior Xyrem; in some cases, new diagnosis; in some cases, their physicians may have not felt they were good oxybate candidates with the high sodium product in the past, even though they were diagnosed. And so it's a variety at the beginning as we would have expected prior to launch. We are seeing a majority of the Xywav starts come from patients with Xyrem experience. That's not a surprise to us. On the exact size of the opportunity of patients who didn't receive Xyrem historically because of those concerns, I'm not sure we have any better hard data to give you other than it's a significant population. But we see, like you do, varied estimates on that, and there's no precise way to track that.

Operator

Our next question comes from the line of Annabel Samimy with Stifel.

Annabel Eva Samimy - *Stifel, Nicolaus & Company, Incorporated, Research Division - MD*

So I just want to ask about Zepzelca for a minute. I know that you have to do a confirmatory trial and that you're still in discussions with FDA. Is there any color that you can provide on a type of trial that you might consider for Zepzelca, whether it be combination or anything else? And then on the sodium oxybate franchise. Obviously, the pricing parity has helped, I guess, accelerate contracting a bit, and you're already a pretty — at 60%, so pretty good. Do you expect this to continue to proceed rapidly or faster than average? And what can we assume for timing of, I guess, net price normalization where you're not providing as much patient assistance as these payers get the drug on board and start reimbursing regularly?

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

So I'll take the second question first and then maybe ask Rob to talk about where we're going with Zepzelca additional study. On the contracting, when we say we've got contracts in place for 60%, that doesn't necessarily mean all the rest are not revenue bottles. I know I used a double negative there. But that doesn't mean we aren't getting paid for some of the others. It's just we don't have contracts in place. And our goal at the time of launch was we said within 6 to 9 months of launch. Launch was in November. We still feel comfortable with that. Sooner is better, but we want to put in place sensible contracts. So it's quality over speed to make sure we've got good access for patients going forward. Rob, you want to talk about Zepzelca?

Robert Iannone - *Jazz Pharmaceuticals plc - Executive VP of Research & Development and Chief Medical Officer*

Yes. I would just mention that we, so far, have only had a very preliminary discussion with FDA where we presented the ATLANTIS data, and we expect to have a more meaningful discussion on what's — what would constitute a confirmatory data package sometime in 2Q. So no further details really to offer on that. I would say that we have disclosed that we're very interested in evaluating Zepzelca in first-line extensive stage small cell lung cancer, and that would be a switch maintenance design, where we'd be adding on to existing therapy. So in the maintenance setting, it would be an immunotherapy, plus or minus the Zepzelca versus immunotherapy plus placebo, for example. Also would mention that we are — we do have an observational Phase IV study that's intentionally designed to gather additional useful information in the second line indicated setting.

Operator

Our next question comes from the line of Graig Suvannavejh with Goldman Sachs.

Graig Suvannavejh - *Goldman Sachs Group, Inc., Research Division - Executive Director & Senior Equity Research Analyst*

Congrats on a really nice quarter. Maybe I'll ask a different question that has to do with your BD strategies going forward. Clearly, the last 12-plus months or so, you've executed on a number of nice deals and it's kind of changed the trajectory of the top line. And with that in mind, given the size of the GW acquisition, what should we be thinking about in terms of BD and whether it's a priority over the next 12 to 24 months? You have a quite robust pipeline and you're integrating a fairly significant acquisition, so we'd love to get any color there.

Renée D. Galá - *Jazz Pharmaceuticals plc - Executive VP & CFO*

Sure. Greg, this is Renée. I'll take that one. So granted, the GW transaction is a meaningful transaction for us that we're very excited about. We've talked for a while about the potential opportunity to do a transformative transaction to be able to accelerate our strategy. And we've lined up financing that we think still gives us adequate flexibility to both invest in our important product launches, invest in our pipeline and then invest in additional business development transaction for the right assets. We still see plenty of opportunities to continue to add to expand the pipeline, both in neuroscience as well as in oncology because you see we have quite a few things we brought into the pipeline, and we want to continue to focus on bringing in both differentiated assets and then building a durable business.

Operator

Our next question comes from the line of Akash Tewari with Wolfe Research.

Akash Tewari - *Wolfe Research, LLC - Director of Equity Research & Senior Research Analyst*

On Xywav, have you heard anything back from the FDA on your application for orphan drug exclusivity for narcolepsy? And additionally, if you do get the ODE, what would that mean theoretically for the Avadel product? Additionally, do you have any updates on your once-nightly program? I know it looks like your Phase I trial should have read out by now.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. So no particular updates on either. As you know, FDA does not have a particular clock there on when it comes to ODE. So we're waiting to hear on that. That should become public once it's decided, and I won't speculate on impact on Avadel, you can ask them that question. And I forget the second part of your question. Once-nightly, yes. So we're — we have not said more about our once-nightly development program, although it continues.

Operator

Our next question comes from the line of Ronny Gal with Bernstein.

Aaron Gal - *Sanford C. Bernstein & Co., LLC., Research Division - Senior Research Analyst*

Bruce, I wonder if you can share with us whether the payer equipment that you have on Xywav and Xyrem give you a preferred position versus other oxybate drugs. And then to the extent you chose not to take that one, I was wondering if I can ask you about the share of prescribers who have not used Zepzelca yet.

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Yes. So on the first one, we're trying to ensure patients have good access to what we believe is a really important treatment option in Xywav. In general, that means we want them to have reasonable ways to get treatment with appropriate diagnosis and in some cases, having tried other therapies. But essentially, it's not different from what we've had with Xyrem for a long time. And then on Zepzelca, happy to have any of my colleagues jump in on — for those docs who have not yet used Zepzelca in second line, what your expectations are there.

Operator

I'm show no further questions in the queue. I will now turn the call back over to Andrea for closing remarks.

Andrea N. Flynn - *Jazz Pharmaceuticals plc - VP & Head of IR*

Thank you...

Bruce C. Cozadd - *Jazz Pharmaceuticals plc - Co-Founder, Chairman & CEO*

Maybe just before I flip it back to Andrea, just to say thanks to the team at Jazz for really an incredibly productive 2020. And I hope all of you on this call take away that 2021 looks like another exciting year with lots of product launches, lots of clinical progress, excitement about the GW

transaction and what that can mean for Jazz, for patients, for employees and for our shareholders. We've got a lot ahead of us, and hope to continue executing exceptionally well. Andrea?

Andrea N. Flynn - *Jazz Pharmaceuticals plc - VP & Head of IR*

Thanks, Bruce. Thanks, everyone, for joining us today. We'll be participating in the upcoming Leerink and Cowen virtual conferences, and we hope to speak with many of you then. This concludes our call.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for your participation. You may now disconnect.

Forward Looking Statements

This communication contains forward-looking statements regarding Jazz Pharmaceuticals and GW Pharmaceuticals, including, but not limited to, statements related to the proposed acquisition of GW Pharmaceuticals and the anticipated timing, results and benefits thereof, including the potential for Jazz Pharmaceuticals to accelerate its growth and neuroscience leadership, and for the acquisition to provide long-term growth opportunities to create shareholder value; Jazz Pharmaceuticals' expected financing for the transaction; and other statements that are not historical facts. You can generally identify forward-looking statements by the use of forward-looking terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "explore," "evaluate," "intend," "may," "might," "plan," "potential," "predict," "project," "seek," "should," or "will," or the negative thereof or other variations thereon or comparable terminology. These forward-looking statements are based on each of the companies' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties, many of which are beyond Jazz Pharmaceuticals' or GW Pharmaceuticals' control. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: Jazz Pharmaceuticals' and GW Pharmaceuticals' ability to complete the acquisition on the proposed terms or on the anticipated timeline, or at all, including risks and uncertainties related to securing the necessary regulatory and shareholder approvals, the sanction of the High Court of Justice of England and Wales and satisfaction of other closing conditions to consummate the acquisition; the occurrence of any event, change or other circumstance that could give rise to the termination of the definitive transaction agreement relating to the proposed transaction; risks related to diverting the attention of GW Pharmaceuticals and Jazz Pharmaceuticals management from ongoing business operations; failure to realize the expected benefits of the acquisition; significant transaction costs and/or unknown or inestimable liabilities; the risk of shareholder litigation in connection with the proposed transaction, including resulting expense or delay; the risk that GW Pharmaceuticals' business will not be integrated successfully or that such integration may be more difficult, time-consuming or costly than expected; Jazz Pharmaceuticals' ability to obtain the expected financing to consummate the acquisition; risks related to future opportunities and plans for the combined company, including the uncertainty of expected future regulatory filings, financial performance and results of the combined company following completion of the acquisition; GW Pharmaceuticals' dependence on the successful commercialization of Epidiolex/Epidyolex and the uncertain market potential of Epidiolex; pharmaceutical product development and the uncertainty of clinical success; the regulatory approval process, including the risks that GW Pharmaceuticals may be unable to submit anticipated regulatory filings on the timeframe anticipated, or at all, or that GW Pharmaceuticals may be unable to obtain regulatory approvals of any of its product candidates, including nabiximols and Epidiolex for additional indications, in a timely manner or at all; disruption from the proposed acquisition, making it more difficult to conduct business as usual or maintain relationships with customers, employees or suppliers; effects relating to the announcement of the acquisition or any further announcements or the consummation of the acquisition on the market price of Jazz Pharmaceuticals' ordinary shares or GW Pharmaceuticals' American depositary shares or ordinary shares; the possibility that, if Jazz Pharmaceuticals does not achieve the perceived benefits of the acquisition as rapidly or to the extent anticipated by financial analysts or investors, the market price of Jazz Pharmaceuticals' ordinary shares could decline; potential litigation associated with the possible acquisition; regulatory initiatives and changes in tax laws;

market volatility; and other risks and uncertainties affecting Jazz Pharmaceuticals and GW Pharmaceuticals, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals' and GW Pharmaceuticals' Securities and Exchange Commission (SEC) filings and reports, including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2019 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, GW Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2019 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and future filings and reports by either company. In addition, while Jazz Pharmaceuticals and GW Pharmaceuticals expect the COVID-19 pandemic to continue to adversely affect their respective business operations and financial results, the extent of the impact on the combined company's ability to generate sales of and revenues from its approved products, execute on new product launches, its clinical development and regulatory efforts, its corporate development objectives and the value of and market for its ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time. Moreover, other risks and uncertainties of which Jazz Pharmaceuticals or GW Pharmaceuticals are not currently aware may also affect each of the companies' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. Investors are cautioned that forward-looking statements are not guarantees of future performance. The forward-looking statements made in this communication are made only as of the date hereof or as of the dates indicated in the forward-looking statements and reflect the views stated therein with respect to future events as at such dates, even if they are subsequently made available by Jazz Pharmaceuticals or GW Pharmaceuticals on their respective websites or otherwise. Neither Jazz Pharmaceuticals nor GW Pharmaceuticals undertakes any obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

Additional Information and Where to Find It

In connection with the proposed transaction, GW Pharmaceuticals intends to file a proxy statement with the SEC. Each of Jazz Pharmaceuticals and GW Pharmaceuticals may also file other relevant documents with the SEC regarding the proposed transaction. The definitive proxy statement (if and when available) will be mailed to shareholders of GW Pharmaceuticals. INVESTORS AND SECURITY HOLDERS ARE URGED TO READ THE PROXY STATEMENT (WHICH WILL INCLUDE AN EXPLANATORY STATEMENT IN RESPECT OF THE SCHEME OF ARRANGEMENT OF GW PHARMACEUTICALS, IN ACCORDANCE WITH THE REQUIREMENTS OF THE U.K. COMPANIES ACT 2006) AND ANY OTHER RELEVANT DOCUMENTS THAT MAY BE FILED WITH THE SEC, AS WELL AS ANY AMENDMENTS OR SUPPLEMENTS TO THESE DOCUMENTS, CAREFULLY AND IN THEIR ENTIRETY IF AND WHEN THEY BECOME AVAILABLE BECAUSE THEY CONTAIN OR WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTION.

Investors and security holders will be able to obtain free copies of the proxy statement (if and when available) and other documents containing important information about Jazz Pharmaceuticals, GW Pharmaceuticals and the proposed transaction, once such documents are filed with the SEC through the website maintained by the SEC at http://www.sec.gov. Copies of the documents filed with the SEC by Jazz Pharmaceuticals will be available free of charge on Jazz Pharmaceuticals'

website at https://www.jazzpharma.com. Copies of the documents filed with the SEC by GW Pharmaceuticals will be available free of charge on GW Pharmaceuticals' website at https://www.gwpharm.com.

Participants in the Solicitation

Jazz Pharmaceuticals, GW Pharmaceuticals, their respective directors and certain of their executive officers and other employees may be deemed to be participants in the solicitation of proxies from GW Pharmaceuticals' security holders in connection with the proposed transaction. Information about GW Pharmaceuticals' directors and executive officers is set forth in GW Pharmaceuticals' proxy statement on Schedule 14A for its 2020 Annual General Meeting, which was filed with the SEC on April 7, 2020, and its Current Report on Form 8-K filed with the SEC on September 10, 2020 and subsequent statements of beneficial ownership on file with the SEC. Information about Jazz Pharmaceuticals' directors and executive officers is set forth in Jazz Pharmaceuticals' proxy statement on Schedule 14A for its 2020 Annual General Meeting, which was filed with the SEC on June 12, 2020 and subsequent statements of beneficial ownership on file with the SEC. Additional information regarding the persons who may, under the rules of the SEC, be deemed participants in the solicitation of GW Pharmaceuticals' security holders in connection with the proposed transaction, including a description of their direct or indirect interests, by security holdings or otherwise, will be set forth in the proxy statement when it is filed with the SEC.

No Offer Or Solicitation

This communication is not intended to and shall not constitute an offer to buy or sell or the solicitation of an offer to buy or sell any securities, or a solicitation of any vote or approval, nor shall there be any offer, solicitation or sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. No offer of securities shall be made in the United States absent registration under the U.S. Securities Act of 1933, as amended (Securities Act), or pursuant to an exemption from, or in a transaction not subject to, such registration requirements. The Jazz Pharmaceuticals securities delivered in the proposed transaction are anticipated to be delivered in reliance upon an available exemption from such registration requirements pursuant to Section 3(a)(10) of the Securities Act.