Horizon Therapeutics plc
Third-Quarter 2020 Conference Call
November 2, 2020

Tina Ventura
Senior Vice President, Investor Relations

Thank you, Sara. Good morning everyone and thank you for joining us.

On the call with me today are:

- **Tim Walbert**, Chairman, President and Chief Executive Officer;
- **Liz Thompson, Ph.D.**, Group Vice President, Clinical Development and External Search;
- **Paul Hoelscher**, Executive Vice President, Chief Financial Officer; and
- **Andy Pasternak**, Executive Vice President, Chief Strategy Officer

Tim will provide a high-level review of the business, our third-quarter performance and our full-year guidance that we again increased this morning. Liz will then provide a review of our R&D programs, followed by Paul, who will discuss our financial performance and guidance in more detail. After closing remarks from Tim, we will take your questions.

As a reminder, during today's call we will be making certain forward-looking statements, including statements about financial projections, development activities, our business strategy and the expected timing and impact of future events. Our actual results could differ materially due to a number of factors, including the extent and duration of the effects of the COVID-19 pandemic; as well as other factors outlined in our latest Form 10-K, our 10-Q we filed this morning, and any 8-Ks filed with the Securities and Exchange Commission.

You are cautioned not to place undue reliance on these forward-looking statements and Horizon disclaims any obligation to update such statements.

In addition, on today's conference call, non-GAAP financial measures will be used. These non-GAAP financial measures are reconciled with the comparable GAAP financial measures in our earnings press release and other filings from today that are available on our investor website at www.horizontherapeutics.com.

I will now turn the call over to Tim.

Tim Walbert
Chairman, President and Chief Executive Officer

Thank you, Tina, and good morning, everyone.

We delivered record results this quarter driven by the continued outperformance of TEPEZZA®, our biologic medicine launched earlier this year for Thyroid Eye Disease (TED) as well as growth in the rest of the orphan segment, including a return to growth for KRYSTEXXA®, our biologic medicine for uncontrolled gout, and our second key growth driver.

We generated third-quarter net sales of $636 million, up 90 percent year over year, and adjusted EBITDA of $330 million, up 153 percent year over year. Given these exceptional results, we are increasing our full-year 2020 TEPEZZA net sales guidance to more than $800 million, a considerable increase from the previous guidance of more than $650 million we announced last quarter. TEPEZZA, already at an annual run rate of more than $1 billion in its second full quarter since launch, is turning out to be one of the most successful rare-disease-medicine launches ever. We are also announcing this morning a significant expansion of our TEPEZZA field-based organization; further investment in our direct-to-consumer TED awareness campaign; the initiation of our TEPEZZA global expansion; and the additional investment in our long-term manufacturing supply capacity to support our continued growth expectations.

Given the better-than-expected performance of TEPEZZA, KRYSTEXXA, and our orphan disease medicines overall, we are increasing our 2020 total company net sales guidance to $2.12 billion to $2.14 billion, which represents 64 percent year-over-year growth at the midpoint. We are also raising our adjusted EBITDA guidance to $920 million to $940 million, which represents 93 percent year-over-year growth at the midpoint. The adjusted EBITDA guidance midpoint represents 44 percent of net sales, a seven-percentage point increase over last year. Our margin expansion was significantly accelerated – a full year ahead of schedule – based on the very strong launch of TEPEZZA and despite the impact to our business from COVID-19.

We also continued to advance our clinical development strategy and expand our pipeline:

- With HZN-825, our $LPAR_1$ antagonist that we acquired earlier this year, we announced today that we are expanding the clinical program to now include interstitial lung diseases, including the idiopathic pulmonary fibrosis, or IPF, a rare progressive lung disease with a median survival rate of less than five years. We continue to expect our diffuse cutaneous scleroderma trial to start in the first half of 2021. If successful in these diseases, which have significant unmet need, we estimate that HZN-825 could generate more than $1 billion in peak net sales.

- For KRYSTEXXA, we continue to focus on improving its complete response rate in rheumatology, impacting the patient experience and increasing its use among nephrologists:
    - data will be presented from the KRYSTEXXA RECIPE trial at the American College of Rheumatology (ACR) annual meeting this week demonstrating an 86 percent complete response rate. This is the first randomized placebo-controlled trial using KRYSTEXXA plus immunomodulation and the fourth immunomodulator studied with successful results in combination with KRYSTEXXA;
    - We recently initiated our new KRYSTEXXA trial to explore a shorter infusion duration to w the patient experience; and
    - interim data was presented from our open-label KRYSTEXXA PROTECT trial at the American Society of Nephrology (ASN) meeting in October that showed KRYSTEXXA improved the management of uncontrolled gout in kidney transplant patients.

- With TEPEZZA, we continue to progress on our additional clinical programs, including our chronic TED trial, which we anticipate initiating shortly, and our subcutaneous dosing trial, which we recently initiated.

We also made considerable progress on our capital allocation strategy. We completed a public offering of 13.6 million shares, raising approximately $920 million in net proceeds, and we completed the extinguishment of all $400 million of our exchangeable senior notes. In less than two years, we have reduced our gross debt by almost $1 billion and transformed our balance sheet from a net debt position of $1 billion to a net cash position of more than $700 million at September 30. Our gross leverage ratio was 1.3 times at September 30, well below our target of 2 times. With our strong balance sheet, we are in an excellent position to take advantage of future opportunities that meet our disciplined M&A criteria.

Our extraordinary success in the third quarter and year to date is a testament to our incredible ability to execute – both commercially and clinically – driven by the talented people who make up Horizon. We continue to receive multiple recognitions as a "best workplace." This includes 11 workplace awards so far this year, including being selected as one of *PEOPLE* magazine's "50 Companies That Care" and as one of FORTUNE and Great Place to Work's Best Medium Workplaces. We have worked hard to preserve our company values and persevere through a challenging 2020 by listening to our employees, understanding their needs and developing solutions that help maintain a trusting, transparent culture. Based on these awards, our employees remain highly engaged and dedicated to making a powerful difference in the lives of the people and communities for which we serve.

Today we also named Karin Rosén as our executive vice president, research and development (R&D) and chief scientific officer. Karin comes to us with nearly three decades of experience, which includes clinical research and development of biologics, as well as building, leading and successfully launching multiple novel medicines in the United States and globally. We are very pleased to welcome Karin, and we are confident that her ability to build and lead cross-functional teams, along with her therapeutic area expertise, will contribute to solidifying our position as a leading rare disease biotech company.

Moving on now to our third-quarter results, in our Orphan segment, year-over-year net sales of $535 million, with growth of 131 percent was driven by the continued strong performance of TEPEZZA, the return to growth of KRYSTEXXA, and the durable growth of our rare disease medicines RAVICTI® and PROCYSBI®. Our orphan segment net sales now represent nearly 85 percent of our total company net sales, underscoring the rapid transformation we have made to a leading rare disease biotech company.

TEPEZZA

Third-quarter TEPEZZA net sales of $287 million significantly exceeded expectations. Our outperformance has been driven by the severity of TED leading to highly motivated patients seeking out therapy, the impressive efficacy and safety profile of TEPEZZA, our highly successful pre-launch efforts and our outstanding commercial execution. We are proud of that fact that in less than eight months, TEPEZZA has made such a dramatic difference in the lives of so many patients.

Ophthalmology continues to be one of the most impacted markets during COVID-19. As we have discussed since last March, it has impacted our launch and the growth of our patient enrollment forms, or PEFs, which are a leading indicator of demand. While ophthalmology has recovered from the acute impact of COVID that we experienced in the second quarter, today still only about a third of our sales calls are in person due to the pandemic. For perspective, we are back to roughly 75 percent in-person calls in our rheumatology and inflammation business units. Our significantly increased guidance to more than $800 million this year continues to incorporate this impact. Demand would have been substantially higher if it weren't for the impact of COVID-19. And while we are not yet back to our pre-COVID PEF volumes, we continued to see strong patient starts with more than 2,000 patients started on TEPEZZA through the third quarter.

We have only scratched the surface of the potential we see for TEPEZZA and its ability to help so many more patients suffering from TED. That's why we are announcing this morning our significant expansion efforts in multiple areas: our U.S. infrastructure and marketing activities, our long-term supply capacity, and our efforts to pursue TEPEZZA outside the United States.

First, with our U.S. expansion, our objectives are three-fold:

- to increase the penetration of TEPEZZA among our current prescriber base;
- to expand our reach to drive new prescribers; and
- to drive higher awareness of TED and TEPEZZA to reduce the time it takes for a patient to get diagnosed and ultimately treated.

Beginning in the fourth quarter, we are initiating a U.S. expansion to roughly double our ophthalmology commercial and field-based organization to approximately 200 employees. As we have discussed, this is a market that requires continued physician education on the importance of treatment, strengthening the co-management of the disease across key physician specialties, and establishing and reinforcing the treatment path, infrastructure and referral network. In line with that need, our field expansion includes our sales force, as well as our field-based teams across medical affairs, patient services, reimbursement services and sites of care.

We are taking this step sooner than originally anticipated given the significant progress we've made since launch and to support the continued demand from the 15 to 20 thousand new acute TED patients coming into the market each year, as well as the more than 70 thousand patients that have had chronic TED for five years or less. This expanded organization will support growth beyond 2020 by enabling us to reach more patients who are suffering from this rare and debilitating eye disease.

In fact, just like we have only treated a fraction of the TED patient population to date, we have also only reached a fraction of the total TED prescriber base. We penetrated the market quickly, driven by a highly successful pre-launch efforts and a launch effort that has driven a core base of prescribers, who are primarily oculoplastic surgeons and other ocular subspecialties, such as neuro-ophthalmologists. However, our ability to reach and educate new physicians based on our current commercial infrastructure has been limited by the impact of COVID-19.

To date, about 1,000 of our physician targets have prescribed TEPEZZA, with roughly 60 percent writing one or two prescriptions. By expanding our reach, increasing our call frequency through smaller territories and increasing the time spent with each physician to educate them on TED and TEPEZZA, we intend to drive uptake of TEPEZZA among these prescribers and increase the total prescriber base.

We are also significantly increasing our investment in marketing initiatives, including our direct-to-consumer disease awareness campaign we initiated last quarter. Our marketing efforts are driving results. For example, our TEPEZZA.com patient site has received more than 550,000 unique visits, with 80 percent of those happening in the third quarter following the initiation of the campaign. Similarly, our online TED specialist finder that connects patients with physicians has received 70,000 visits, with about one-third of those visits happening in the third quarter. We are now expanding our online, digital and broadcast DTC presence from select markets to a national campaign and will be adding a TEPEZZA brand awareness component. We are also targeting Graves' Disease sufferers to raise awareness of the connection between Graves' and TED and increase the speed to diagnosis and treatment. Our aim with these expanded marketing efforts is to drive more patients to identify TED sooner, seek treatment and connect with a TED specialist.

We are working to expand the long-term supply capacity for TEPEZZA as well and will be adding a third site in Boulder, Colorado, with our manufacturing partner AGC Biologics.

These expansion initiatives all support our expected near-term growth and long-term peak U.S. annual net sales for TEPEZZA of more than $3 billion.

In addition, we want patients in other parts of the world to also be able to benefit from TEPEZZA. We have conducted a preliminary analysis of the TED market opportunity outside the U.S. Based on our analysis to date, we project the overall peak annual international opportunity to be greater than $500 million. Europe is not yet included in this analysis.

One of the key countries we are pursuing is Japan, where we will be engaging with the Japanese regulatory authorities to discuss the potential regulatory pathway for TEPEZZA. We will also be engaging with the Japanese medical community to understand the TED patient journey in Japan. We are encouraged by the demonstrated commitment of the Japanese authorities to provide timely access to safe and effective treatments for unmet needs, and we look forward to our discussions with the key stakeholders there.

Finally, we are investing in our clinical programs for TEPEZZA to maximize the value it offers TED patients, including our TEPEZZA chronic TED trial, which we plan to initiate in the coming weeks. We also continue to expect to see more chronic TED case reports presented at future medical meetings. At the upcoming American Society of Ophthalmic Plastic and Reconstructive Surgery, or ASOPRS, Fall Symposium, the successful chronic TED case study that I discussed last quarter will be presented. In addition, another case study will be presented showing the successful use of TEPEZZA in the treatment of dysthyroid, or compressive, optic neuropathy, which is a severe manifestation of TED that can result in permanent vision loss. We also look forward to presenting additional TEPEZZA data that Liz will discuss in more detail shortly.

KRYSTEXXA

Moving on to KRYSTEXXA ... we returned to growth during the quarter sooner than expected, which is especially impressive given the challenges of COVID-19. KRYSTEXXA generated $108 million in net sales, resulting in year-over-year growth of 9 percent. As a result, we increased full-year 2020 net sales guidance to low double digits versus our prior expectation of similar net sales to 2019. Though we are continuing to monitor the impact of COVID-19 on KRYSTEXXA, we are encouraged by trends we are seeing of patients returning to their physicians' offices in recent months and many patients who had deferred treatment start to go back on KRYSTEXXA.

Most important, and key to our long-term success, is the continued execution of our KRYSTEXXA immunomodulation strategy. Since 2018, data has been published in well over 100 patients on concomitant treatment with several different immunomodulators. This represents more patients than studied in our Phase 3 trials using KRYSTEXXA alone. The data using KRYSTEXXA with immunomodulation points to a response rate that is double the response rate observed in our Phase 3 clinical programs. Our most recent internal data suggest that the use of immunomodulation with KRYSTEXXA for new patient starts is more than 25 percent, a significant increase from the approximately 15 percent we saw at the end of 2019. The approach of using immunomodulation with KRYSTEXXA is quickly becoming the preferred treatment option for patients with uncontrolled gout.

Data from the investigator-initiated RECIPE trial will be presented later this week at the American College of Rheumatology (ACR) annual meeting. As I mentioned earlier, RECIPE is the first randomized placebo-controlled trial to study KRYSTEXXA with an immunomodulator, in this case, mycophenolate mofetil (MMF). The primary endpoint at 12 weeks was achieved with 86 percent of patients in the immunomodulation arm achieving a complete response compared to 40 percent of patients in the placebo arm on KRYSTEXXA alone. The RECIPE results add to the growing body of evidence supporting the use of immunomodulation with KRYSTEXXA, and we look forward to seeing preliminary six-month results from our randomized controlled trial, MIRROR, in the first half of next year.

Given our return to growth and the continued increase in the use of KRYSTEXXA plus immunomodulation, we are highly confident in our peak U.S. annual net sales estimate for KRYSTEXXA of more than $1 billion.

Rare Disease Medicines

Our other rare disease medicines, RAVICTI, PROCYSBI and ACTIMMUNE®, continued to generate durable growth during the quarter. Combined active shipping patients increased mid-single digits year over year, and we continued to see high rates of compliance and adherence.

I will now turn the call over to Liz for an update on our R&D programs.

Elizabeth Thompson., Ph.D.
Group Vice President, Clinical Development and External Search

Thank you, Tim, and good morning, everyone.

As Tim mentioned, we've made considerable progress as we continue to advance multiple R&D programs. We've nearly doubled the number of pipeline programs this year, and this is despite the impact of COVID-19.

HZN-825
I will start today's update with HZN-825, our newest pipeline candidate. We acquired this oral selective $LPAR_1$ antagonist earlier this year, when we announced our HZN-825 clinical program in diffuse cutaneous systemic sclerosis. We are excited to announce today that we are expanding the HZN-825 program to include interstitial lung diseases, or ILD, starting with idiopathic pulmonary fibrosis, or IPF. IPF is a rare progressive lung disease with an estimated U.S. prevalence of 100,000 and high unmet need, despite the current available therapies. Given the potential impact that the $LPAR_1$ mechanism of action may have on fibrosis, we believe there is strong rationale to explore it further in IPF and potentially other ILDs. We will be sharing further information on the trial design as we finalize the trial protocol next year, and we anticipate initiating a Phase 2b pivotal trial in this indication in mid-2021.

Regarding our systemic sclerosis program, HZN-825 showed early clinical signals of benefit in this rare, chronic autoimmune disease, which has no FDA-approved therapies and a high unmet need, with an approximately 30,000 patient population in the U.S. We are working with the FDA and European regulators to finalize the Phase 2b pivotal trial protocol in the coming months and continue to expect to begin the trial in the first half of 2021.

TEPEZZA in Chronic TED
Moving to TEPEZZA and our trial in chronic TED patients ... chronic TED patients have disease that is no longer progressive or inflammatory, but they may continue to experience proptosis, diplopia, pain and other debilitating eye symptoms that can impair their quality of life. Signaling through IGF-1 receptor drives many of these symptoms. Given that IGF-1R is still present at heightened levels in orbital fibroblasts from chronic TED patient surgical samples, the TEPEZZA mechanism of action that inhibits IGF-1R appears to be relevant in chronic disease. And while the TEPEZZA prescribing information is broad and includes all TED patients, our objective is to generate data to better inform the physician community who may wish to use TEPEZZA in treating their chronic TED patients.

We expect to initiate the randomized, placebo-controlled trial in the coming weeks. Target enrollment is approximately 40 patients, with a two-to-one ratio of patients receiving infusions of TEPEZZA or placebo once every three weeks for a total of eight infusions. The primary endpoint is the change in proptosis in the study eye from baseline at Week 24. After the initial 24-week treatment period, proptosis non-responders may choose to enter an additional 24-week open-label treatment period. We expect topline data to be available in early 2022.

TEPEZZA OPTIC-X and OPTIC Follow-On Period Data; AAO/ASOPRS Medical Meetings
In July we were pleased to announce topline results of OPTIC-X, the open-label extension trial of the Phase 3 OPTIC trial for TEPEZZA, as well as results of the OPTIC 48-week off-treatment follow-up period. The results provide further data regarding the dramatic efficacy of TEPEZZA in patients with longer disease duration, its long-term durability and the potential for retreatment.

To briefly summarize the data: 89 percent of OPTIC placebo patients who participated in OPTIC-X achieved a clinically significant proptosis reduction of 2 millimeters or greater by Week 24. These patients had longer disease duration – an average of 12 months compared to six months for patients in the OPTIC trial. The 48-week follow-up data from OPTIC showed that the majority of TEPEZZA responders maintained their response at Week 72, nearly a year off treatment. And notably, of the small number of OPTIC TEPEZZA patients who relapsed during the 48-week follow-up period, more than 60 percent experienced at least a 2-millimeter reduction in proptosis with an additional course of TEPEZZA in OPTIC-X. Importantly, there were no new safety concerns in either the 48-week follow-up period, or OPTIC-X, during which patients received additional TEPEZZA treatment.

At upcoming medical conferences this fall, including the American Academy of Ophthalmology (AAO) meeting, we will present additional data on OPTIC-X and OPTIC 48-week off-treatment results, as well as data on the impact of TEPEZZA on less severe TED. There will also be a case report presented at AAO on the improvement of dysthyroid optic neuropathy as a result of treatment with TEPEZZA. Dysthyroid, or compressive, optic neuropathy is a severe manifestation of TED that can result in permanent vision loss. The ASOPRS Fall Symposium later in November will include a second discussion on TEPEZZA in the treatment of dysthyroid optic neuropathy, as well as a presentation on the recent case report published in the *American Journal of Ophthalmology* on the treatment of a patient with chronic TED.

Other TEPEZZA Trials

Work is well underway in our two other TEPEZZA trials. We have initiated a pharmacokinetic trial to explore the potential for subcutaneous dosing of TEPEZZA and we continue to expect to start our exploratory trial in diffuse cutaneous systemic sclerosis later this year.

KRYSTEXXA

RECIPE

Moving on now to KRYSTEXXA ... first, topline data in the investigator-initiated RECIPE trial will be presented this week at the virtual ACR annual meeting. RECIPE is the first randomized placebo-controlled trial evaluating the effect of co-administration of KRYSTEXXA with an immunomodulator to improve the complete response rate of KRYSTEXXA. Patients were randomized three-to-one and received a two-week run-in of either mycophenolate mofetil (MMF) or placebo, followed by daily dosing of MMF or placebo, and bi-weekly KRYSTEXXA infusions, for a total of 12 weeks. After this initial 12-week study period, patients continued on KRYSTEXXA therapy alone for a further 12 weeks.

The primary endpoint was the proportion of patients with serum uric acid less than 6 milligrams per deciliter at 12 weeks. 86 percent, or 19 out of 22 patients receiving KRYSTEXXA co-administered with MMF achieved this outcome, compared to 40 percent, or four out of 10 patients receiving KRYSTEXXA alone, with a p-value of 0.01. After 12 weeks off of MMF therapy but continuing on KRYSTEXXA therapy, 68 percent, or 15 out of 22 patients, achieved a complete response. This compares to 30 percent, or three of 10 patients, in the placebo arm. There were no new safety signals.

MIRROR RCT

We will be further adding to the clinical data for immunomodulation with our randomized placebo-controlled MIRROR trial, which is evaluating the efficacy and safety of the concomitant use of KRYSTEXXA with methotrexate. We have completed enrollment in the trial – the largest randomized controlled trial evaluating KRYSTEXXA with immunomodulation – with 145 patients in total. We continue to expect preliminary six-month results, including the primary endpoint, in the first half of 2021, with the full dataset, including the secondary endpoints, available after the trial completes in the second half of 2021.

Shorter Infusion Duration Trial
Regarding our KRYSTEXXA shorter infusion duration trial, we enrolled the first patient in this open-label trial last week. While KRYSTEXXA is currently infused over a two-hour or longer timeframe, this trial is assessing up to three new infusion durations – 60-minutes, 45-minutes and 30-minutes. A shorter infusion duration could meaningfully impact the experience and convenience for patients, physicians and sites of care.

PROTECT
In the PROTECT trial, we are studying the use of KRYSTEXXA for people who are living with uncontrolled gout and have undergone a kidney transplant. Evidence indicates that gout is more common and often more severe among those who have undergone kidney transplants, with data showing prevalence more than 10-fold higher than in non-transplant patients.

We were very pleased to announce encouraging interim data at this year's American Society of Nephrology Kidney Week in October that relate to KRYSTEXXA's ability to reduce serum uric acid levels in this very sensitive transplant population without compromising kidney function. To date, the estimated glomerular filtration rate, or eGFR, which is a measurement of kidney function, remained stable throughout KRYSTEXXA treatment. The data also showed reductions in pain and disability scores. We continue to expect enrollment to be completed by the end of the year.

Conclusion
In conclusion, it has been a busy quarter for R&D at Horizon. We continue to make significant progress on multiple trials across our portfolio. With that, I will turn the call over to Paul.

Paul Hoelscher
Executive Vice President, Chief Financial Officer

Thanks, Liz, and good morning.

My comments this morning will primarily focus on our non-GAAP results, unless otherwise noted.

Third-Quarter 2020 Financial Results
Third-quarter net sales were $636 million, a year-over-year increase of 90 percent.

Our orphan segment generated net sales of $535 million, a year-over-year increase of 131 percent, driven by the strong performance of our key growth drivers, TEPEZZA and KRYSTEXXA. Orphan segment operating income was $275 million, a year-over-year increase of 245 percent and representing a margin of 51 percent.

Net sales for the inflammation segment were $102 million, with segment operating income of $55 million. We continue to reinvest the cash flow generated from this segment into our key growth drivers, TEPEZZA and KRYSTEXXA, and our growing pipeline.

Our non-GAAP third-quarter gross profit ratio was 87 percent of net sales.

Non-GAAP operating expenses were $222 million. This included non-GAAP R&D expense of $28 million and non-GAAP SG&A expense of $194 million.

Third-quarter adjusted EBITDA was $330 million, an increase of 153 percent.

As we expected, the non-GAAP tax rate for the third quarter was negative 23 percent, resulting in a year-to-date tax rate of 5.5 percent. As we have seen in prior years, there can be variability in the tax rate across quarters.

Non-GAAP net income was $392 million and non-GAAP diluted earnings per share were $1.74. Weighted average shares outstanding used to calculate third-quarter 2020 non-GAAP diluted EPS was 225 million shares.

Cash Flow and Balance Sheet
As of September 30, cash and cash equivalents were $1.725 billion, which includes the net proceeds of approximately $920 million from our August equity offering of 13.6 million ordinary shares.

Our non-GAAP operating cash flow for the third quarter was $109 million. Although collections of TEPEZZA receivables increased significantly during the quarter, the benefit was offset by investments in TEPEZZA inventory and timing of payments for accounts payable and accrued expenses. We remain confident in our ability to generate considerable operating cash flow, allowing us to pursue acquisitions or licensing of further pipeline assets as a top priority.

Our total principal amount of debt is $1.018 billion, with the earliest maturity in 2026. We've reduced our gross leverage to 1.3 times at September 30 and significantly lowered our interest expense as a result of several capital structure improvements made since the beginning of 2019.

2020 Guidance
This morning, we announced that we are increasing our full-year net sales guidance range to $2.12 billion to $2.14 billion, from $1.85 billion to $1.9 billion. This reflects our significant outperformance across all business units in the third quarter, and increases in our full-year 2020 net sales guidance for both TEPEZZA and KRYSTEXXA.

For TEPEZZA, we are increasing our full-year 2020 net sales guidance to more than $800 million, compared to the previous guidance of greater than $650 million. For KRYSTEXXA, we are increasing our full-year 2020 net sales guidance to low double-digit growth, versus our prior expectation for similar net sales to 2019.

We are also increasing our adjusted EBITDA guidance range to $920 million to $940 million from $725 million to $775 million. At the midpoints, adjusted EBITDA is 44 percent of our net sales, reflecting a further significant acceleration of our margin expansion and a 700-basis-point increase over 2019 – a full year ahead of schedule. At the midpoints, our updated guidance represents year-over-year growth in net sales of 64 percent and a near doubling of adjusted EBITDA, which again was accomplished despite the challenges of COVID-19.

Moving on to the rest of the income statement, we now expect our non-GAAP gross profit ratio to be approximately 87 percent. This is primarily due to the impact of royalties associated with the significantly higher net sales expectations for TEPEZZA this year.

We expect full-year 2020 non-GAAP operating expenses to increase compared to our prior expectations. This is driven by additional SG&A expense to support the TEPEZZA launch outperformance. While we expect R&D spending to be in line with previous guidance on a dollar basis, given our significant increase in net sales guidance, we now expect our non-GAAP R&D expense as a percentage of net sales to be in the mid-single digits for 2020.

We continue to expect a full-year non-GAAP tax rate in the low double digits, with our fourth-quarter non-GAAP tax rate to be in the high teens to bring the full-year rate in line with our expectations.

We continue to expect our 2020 cash tax rate to be in the low-to-mid single digits.

We continue to expect full-year non-GAAP net interest expense to be approximately $45 million.

Given our August equity offering, we now expect our fourth-quarter weighted average diluted share count to be approximately 235 million shares.

With that, I will turn it over to Tim for his concluding remarks.

Tim Walbert
Chairman, President and Chief Executive Officer

Thanks, Paul.

The third quarter was another record quarter for Horizon and one of significant strategic progress:

- We again increased our full-year 2020 net sales and adjusted EBITDA guidance, driving robust year-over-year growth at the midpoint.
- TEPEZZA continues to generate outstanding results, already at a greater than $1-billion annual run-rate in just its second full quarter after launch.
- Importantly, we are also seeing positive trends with KRYSTEXXA as it returns to growth, and we now expect low double-digit year-over-year net sales growth.
- We made significant progress on our R&D programs, including on our two HZN-825 pivotal Phase 2b programs we intend to initiate next year and on development activities related to our international TEPEZZA expansion.
- And finally, we are in an incredibly strong financial position with a cash balance of over $1.7 billion at September 30, allowing us to execute on our M&A strategy.

We are one of the fastest growing, profitable biotech companies among our peers. With our continued progress and strong execution, we are well-positioned to continue to deliver increasing value to our shareholders now and over the coming years.

We will now open the call up for questions.

Tina Ventura
Senior Vice President, Investor Relations

Thank you, Sara. That concludes our call this morning. A replay of this call and webcast will be available in approximately two hours. Thank you for joining us.