Horizon Therapeutics plc
Third-Quarter 2022 Conference Call
November 2, 2022

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Chris. 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.**, Executive Vice President, Research and Development;
- **Aaron Cox,** Executive Vice President, Chief Financial Officer; and
- **Andy Pasternak**, Executive Vice President, Chief Strategy Officer

Tim will provide a review of the business, including our third-quarter performance and full-year guidance. Liz will then review our R&D programs, followed by Aaron, who will discuss our financial performance and guidance in more detail. After closing remarks from Tim, we will take your questions. We posted our investor slide deck this morning as well.

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 from these forward-looking statements due to a number of factors, including the risk factors and other information outlined in our latest Forms 10-K, 10-Q and any 8-Ks filed with the Securities and Exchange Commission, and our earnings press release, which we issued this morning.

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, our slide presentation 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.

Our continued focus on clinical, commercial and operational execution drove progress across our portfolio this quarter. With our pipeline, we completed enrollment in our TEPEZZA® chronic/low clinical activity score (CAS) thyroid eye disease (TED) trial and expect to share topline results in the second quarter of next year. We also announced positive topline results from our Phase 2 trial evaluating dazodalibep in patients with Sjögren's syndrome – validation of the value we saw in the Viela pipeline we acquired last year.

Commercially, we have made a lot of progress executing on the actions we discussed on our second-quarter call to accelerate the growth of TEPEZZA in 2023, where our expectation is for at least mid-teens growth. And across the rest of the business, we exceeded expectations. Our launch of KRYSTEXXA® with methotrexate has gone exceptionally well and the team continues to drive strong performance with immunomodulation going from more than 50% to more than 60%. Generating 21% growth in the quarter, we now expect growth of 25% for the full year. The relaunch of UPLIZNA® continues to progress nicely, and again we doubled our U.S. net sales this quarter. Our rare disease medicines, which typically grow in the low-single digits, generated strong growth as well.

As a result, this morning we increased our full-year net sales and adjusted EBITDA guidance. We also increased our peak annual net sales expectations for both TEPEZZA and KRYSTEXXA – in aggregate, by an additional $1 billion. We feel very good across the board executing on our strategic goals. I'll now discuss our third-quarter performance.

TEPEZZA
First with TEPEZZA, it is on track with our expectations and generated third-quarter net sales of $491 million.

The most important of these actions we are taking to drive TEPEZZA growth is the expansion of our TEPEZZA sales force. It expands the reach of our effort across ophthalmologists and endocrinologists and gives our sales representatives more time to engage with ocular specialists. Ophthalmologists and endocrinologists see tens of thousands of potential TEPEZZA patients, but due to limited TED education or a lack of understanding on how to best refer their TED patients, many patients never find the care they need. So this expansion, along with our direct-to-consumer (DTC) efforts, are critical to helping patients get on TEPEZZA therapy. With this expanded sales force, we are now targeting 12,000 total physicians, including approximately 2,000 ocular specialists and approximately 10,000 ophthalmologists and endocrinologists.

We completed the hiring of this expanded team at the end of the third quarter, adding about 60 sales representatives to what was previously about an 80-person sales team. And so by the end of October, the majority of the expanded team had completed their training and were out in the field starting to build relationships and engage with the broader set of ophthalmologists and endocrinologists, many of whom we are calling on for the first time. We have enhanced our physician targeting based on new data sets and information from increased claims capture, which gives us even greater confidence we are engaging with the right physicians. While it is still early, we have heard positive feedback from the expanded team. Our sales representatives are getting into physician offices they haven't accessed before; the new physicians we are calling on are very willing to see us and showing high interest in learning about TED. We are very excited about the expanded team's potential to drive additional growth for TEPEZZA, and we expect to see the impact begin next year.

To further support the field team, we recently launched an updated marketing campaign highlighting the mechanistic rationale for TEPEZZA in the treatment of TED. Our new TV campaign also supports our efforts to drive broader patient and physician awareness. Both campaigns aim to highlight the unseen symptoms of TED and create an urgency to seek an eye exam or treatment by discussing the consequences of delaying diagnosis. Our continued investment in DTC has been effective at encouraging undiagnosed patients to visit a TED specialist.

In addition, we are continuing to focus on educating physicians by strengthening our advocacy network and driving clinical conviction through peer-to-peer education. Facilitating discussions on real-world experiences and best practices of managing patients is giving physicians increased confidence in the co-management of their patients. Our peer-to-peer program has more than doubled compared to the second quarter, and we expect to continue to increase it moving forward. As we have seen with both KRYSTEXXA and UPLIZNA, peer-to-peer education is one of the most effective ways to drive clinical conviction for physicians, and this is particularly critical for TED, which has a more complex co-management approach than other diseases.

In addition, our patient services and reimbursement team is spending more time and focus on the reimbursement process. While coverage is favorable overall, as we have discussed, the process can be burdensome for some physicians, especially for ocular specialists who are not accustomed to it. We have enhanced how our patient services team operates, and we have worked to reduce reimbursement hurdles by educating physician offices on how best to work through this process.

All of these actions, coupled with the very strong momentum coming out of the key fall medical meetings with our target physicians, gives us confidence that we are on the right track.

We continue to expect full-year 2022 TEPEZZA net sales growth in the high teens, which assumes modest sequential growth in the fourth quarter. With our expansion efforts beginning to have an impact as we move into next year, we continue to expect to drive net sales growth of at least mid-teens in 2023.

As we've discussed over the last several months, we have also been conducting further analysis on the opportunity for TEPEZZA outside of the United States. Our prior ex-U.S. peak annual net sales guidance of more than $500 million was primarily focused on Japan and other related markets. Since then, we have gone back and looked more closely at the European opportunity, as well as re-evaluated the international markets where we intend to launch TEPEZZA. We have confirmed there is a significant unmet need in these markets, with incidence and prevalence rates similar to the U.S. Including our updated expectations for TEPEZZA outside the U.S., and now incorporating plans to launch in Europe, we have increased our ex-U.S. peak annual net sales expectations to greater than $1 billion.

Our work to launch TEPEZZA outside of the U.S. is progressing well. We expect to complete enrollment in our clinical trial in Japan by year end. Market development and launch preparations there are well underway. In Europe, we expect our regulatory submissions to include data from both our Phase 3 OPTIC trial as well as our chronic/low CAS TED trial, which we believe will drive significant uptake for this medicine in Europe. We expect meaningful contribution from our global expansion beginning in 2025.

We estimate there are more than 100,000 addressable TED patients in the U.S., where we expect peak annual net sales of more than $3 billion. With our increased expectations outside the U.S., we now expect TEPEZZA global peak annual net sales to exceed $4 billion.

KRYSTEXXA

KRYSTEXXA was again a major driver of our third-quarter performance, with net sales increasing 21% year-over-year to $192 million. This continued momentum was driven by both the rheumatology and nephrology market segments, including increased adoption of KRYSTEXXA with immunomodulation, which now exceeds 60%. Putting this into perspective, it has been five years since we launched our immunomodulation strategy. In that time, through the early part of this year, we saw immunomodulation use increase from low-single-digits to more than 50%. In the few short months since our U.S. FDA approval, immunomodulation use increased to greater than 60%.

Our efforts in educating physicians on the new profile of KRYSTEXXA with methotrexate are working well. We are receiving positive feedback from the field that more physicians have high confidence in KRYSTEXXA after seeing the MIRROR data. In fact, following our immunomodulation relaunch in the third quarter, about half of all KRYSTEXXA patient enrollment forms have been submitted by new prescribers or physicians who had not prescribed KRYSTEXXA in at least a year. This is clear evidence of increasing clinical conviction.

Both our rheumatology and nephrology strategies continue to deliver results. In nephrology, momentum has been strong, and through the end of the third quarter, we have had more nephrology prescribers and patient starts than we had in the full year of 2021. This has led to a more than doubling of nephrology patients on therapy as of the third quarter compared to the same time last year. As we mentioned last quarter, we are expanding our KRYSTEXXA sales force by approximately 20% to allow for greater reach and continued growth within the nephrology space.

Given the strong momentum with KRYSTEXXA, we raised our full-year 2022 net sales growth guidance to approximately 25% and our U.S. peak annual net sales expectations to greater than $1.5 billion.

UPLIZNA

Moving on to UPLIZNA, we delivered another strong quarter, generating net sales of $44 million, with $41 million in the U.S. This is the second consecutive quarter we have more than doubled our year-over-year U.S. net sales.

UPLIZNA is another example of how we have taken an underperforming medicine and put it on a strong growth trajectory. We continue to see steady and consistent growth in new prescribers and new patient starts. Our team remains focused on disease education and drove a record number of peer-to-peer programs in the third quarter, increasing activity by more than 50% compared to the second quarter. We had a strong commercial and medical presence at the fall medical meeting ECTRIMS, European Committee for Treatment and Research in Multiple Sclerosis, presenting multiple new data analyses from our Phase 3 trial. Our launch in Europe is making good progress as well, and we are increasingly confident in the prospects for UPLIZNA in NMOSD. We are well on track toward our global peak annual net sales expectation of more than $1 billion across all potential UPLIZNA indications.

I will now turn the call over to Liz.

Elizabeth Thompson, Ph.D.
Executive Vice President, Research and Development

Thank you, Tim, and good morning everyone.

The goal of our R&D efforts is to bring more medicines to patients in need, particularly for patients in underserved communities. During the third quarter, we announced several important R&D milestones, including positive Phase 2 results from our dazodalibep trial in Sjögren's syndrome, enrollment completion in our TEPEZZA chronic/low CAS TED trial, and a new collaboration and option agreement with Q32 Bio.

Dazodalibep
I'll start with dazodalibep, which is our CD40-ligand antagonist designed to block a central pathway involved in many autoimmune and inflammatory diseases. As a reminder, this was one of several development-stage biologics that we brought on with our acquisition of Viela last year. As Tim referenced, the recent positive data from dazodalibep provide validation of the value we saw in the Viela pipeline. In fact, this is the second positive trial readout for this molecule, following positive topline results in rheumatoid arthritis patients.

In September, we shared topline results from the first of two patient populations we are studying in our Phase 2 Sjögren's syndrome trial. Sjögren's is a disease that affects 250,000 to 350,000 patients in the U.S. across two patient populations: patients with moderate-to-severe systemic disease activity, and patients with moderate-to-severe localized symptoms. Of the patients with systemic manifestations of the disease, the population for which we shared topline results, we believe approximately 50,000 patients would be appropriate for novel therapeutics like biologics. And today, no disease-modifying medicines are approved.

Sjögren's is a debilitating, chronic autoimmune disease that impacts exocrine glands, including the salivary and tear glands. Dryness is the most marked symptom – and while this could sound trivial, dryness across various systems in the body can greatly impact a patient's life. Dryness in the mouth can impact chewing, swallowing and lead to cavities. In the eyes, it can create a sensation of constant grittiness and irritation and can lead to corneal ulcers. Excessive dryness can also impact sexual function in women. Sjögren's is commonly associated with arthritis, pain, debilitating fatigue and can cause kidney impairment, neurological dysfunction, and in some cases, lymphoma.

We were very pleased with the topline results from this trial, meeting the primary endpoint with statistical significance in patients with moderate-to-severe systemic disease activity and achieving more than a six-point reduction in the ESSDAI disease activity score. ESSDAI measures all of the potential areas of systemic disease involvement. Evaluating the various levels of response on ESSDAI, including some high bars of improvement, we saw several important separations between patients on dazodalibep and patients on placebo. Other measures, such as the number of tender and swollen joints, fatigue, dryness and physical function, showed numerical improvements, suggesting dazodalibep could impact many aspects of the disease that affect a patient's quality of life. From a safety perspective, the profile was acceptable and supportive of continued development. The Phase 2 trial is also evaluating a second population of patients with moderate-to-severe localized symptoms, which is fully enrolled and continues to progress. So, as far as next steps, we look forward to sharing new data from our Sjögren's trial next year. We'll have the full results for patients with moderate-to-severe systemic disease activity, including results from patients who initially received placebo and then went on to receive treatment with dazodalibep. We'll also have results for patients with moderate-to-severe localized symptoms. And we look forward to working with regulatory authorities to design our Phase 3 clinical program, which we plan to initiate next year.

TEPEZZA
Moving to TEPEZZA, in September, we completed enrollment in our Phase 4 randomized, placebo-controlled trial in thyroid eye disease patients with a low clinical activity score, otherwise referred to as our chronic TED trial. While TEPEZZA has a broad indication for TED, these data will help define its profile in patients with low clinical activity scores for patients, physicians and for payers. We expect a topline data readout from this trial in the second quarter of 2023.

As Tim referenced, we had a strong presence at several key medical meetings this fall – each giving us the opportunity to connect with physicians who diagnose and refer their TED patients, as well as physicians who prescribe TEPEZZA. We presented additional data and analyses regarding TEPEZZA and its role in the treatment of TED. This includes new data at the American Academy of Ophthalmology Annual Meeting showing that insulin-like growth factor-1 and its related pathways are extensively upregulated throughout all stages of TED, including in patients with high and low clinical activity scores. This is important because it supports the relevance of TEPEZZA's mechanism of action, regardless of CAS. We also presented new data from a real-world analysis of TEPEZZA at the American Thyroid Association Annual Meeting, showing the percentage of patients being prescribed an additional course of TEPEZZA remains low.

We continue to advance our TEPEZZA subcutaneous administration program. Our Phase 1b trial in TED patients initiated earlier this year, and we are on track to begin enrolling our high concentration formulation cohort by the end of the year. Our OPTIC-J clinical trial is progressing well, with a lot of interest from our Japanese investigators. We are pleased with enrollment progress and anticipate completion of enrollment by the end of the year.

UPLIZNA

Moving beyond TEPEZZA, we also continue to contribute to the literature regarding our other on-market medicines. For UPLIZNA, this centered around new data analyses from the Phase 3 trial presented at the ECTRIMS medical conference. First was a presentation showing that UPLIZNA effectively depletes CD19+ B cells, including plasmablasts and plasma cells, which have been found to play a crucial role during a NMOSD attack. A separate analysis highlighted the efficacy of UPLIZNA among patients with fairly common genetic variations that have been associated with somewhat reduced response to other therapies, such as anti-CD20 B-cell-depleting therapies.

KRYSTEXXA

As we look to the fourth quarter, we will have several important presentations for KRYSTEXXA. We recently announced a series of data presentations at the American College of Rheumatology meeting (ACR), later this month, focusing on our continued efforts to advance the understanding and care of uncontrolled gout. Twelve-month results from the MIRROR trial will also be presented for the first time at ACR. These results showed 60% of patients who received KRYSTEXXA with methotrexate achieved a complete response, nearly twice that of those who received KRYSTEXXA with placebo. We also have presentations planned for the American Society of Nephrology conference later this week, including a study in kidney transplant patients showing that KRYSTEXXA with methotrexate did not negatively impact those with diminished kidney function.

Q32 Bio

Finally, we just announced an important milestone in our collaboration with Q32 Bio – the initiation of a Phase 2 trial in atopic dermatitis patients. We first announced the collaboration, focused on Q32's lead asset ADX-914, in August. ADX-914 is a fully human anti-IL7R-alpha antibody that inhibits the signaling of TSLP and IL-7. This program represents a novel approach to address allergic indications, as well as disorders with an imbalance of regulatory T cells to potentially restore healthy immune regulation. Q32 plans to start a Phase 2 trial in a second autoimmune disease next year.

I will now turn the call over to Aaron.

Aaron Cox
Executive Vice President, Chief Financial Officer

Thanks, Liz.

Before I cover this quarter's performance, let me start with a brief comment on capital allocation. As you are aware, we announced a $500 million share repurchase program in September. This program reinforces the confidence we have in both our strategy and our commitment to deliver long-term value to our shareholders. Our strong balance sheet and cash generation gives us the flexibility to opportunistically repurchase shares while maintaining ample capital to prioritize business development, which remains our top priority. To date, we have repurchased in aggregate of $250 million of shares under this program, a total of 3.9 million shares.

In addition, as we have noted previously, we no longer exclude upfront, milestones and other similar payments related to collaborations, licenses and asset acquisitions from our non-GAAP financial measures. Beginning with the third quarter of 2022, we are separating R&D expenses into two categories – R&D expenses, and a new category for acquired IPR&D and milestones expenses, which will isolate these amounts that are driven by business development transactions. Prior periods have also been revised to conform with the new classification.

Now, I will cover our performance in the third quarter and our updated guidance. My comments this morning will primarily focus on our non-GAAP results, unless otherwise noted.

Our orphan segment generated third-quarter net sales of $905 million, with strong contributions across our portfolio. Our orphan segment operating income was $367 million. Net sales for the inflammation segment were $21 million and operating loss was $11 million. We are winding down the inflammation segment following the market erosion caused by the generic PENNSAID 2%® entrant. We expect this wind-down to be substantially complete by year end, and as a result, we expect to operate and report as a single reporting segment starting in the fourth quarter of this year.

Our third-quarter gross profit ratio was 87.2% of net sales.

Third-quarter operating expenses were $470 million. R&D expenses were $108 million, or 11.7% of net sales. Acquired IPR&D and milestones expenses were $19 million, primarily related to our collaboration agreement with Q32 Bio; and SG&A expenses were $343 million.

Third-quarter adjusted EBITDA was $335 million, which also included the $19 million of acquired IPR&D and milestones expenses.

The tax rate for the third quarter was 6.9%. As we have seen in prior years, there can be variability in our tax rate across quarters.

Net income in the third quarter was $293 million.

Third-quarter diluted earnings per share were $1.25. The weighted average shares outstanding used to calculate third-quarter 2022 diluted EPS were 235 million shares.

Third-quarter operating cash flow was $368 million. In the last twelve months to September 30, we've generated more than $1 billion of operating cash flow.

As of September 30, cash and cash equivalents were $2.13 billion. Backed by this strong cash position and expected future cash flows, we expect business development to continue to play a critical role in expanding our pipeline and diversifying our business.

The total principal amount of our outstanding debt is $2.6 billion, with the earliest maturity in 2026. Our gross debt-to-last-12-months adjusted EBITDA leverage ratio was 1.8 times as of September 30, and our net leverage ratio was well under 1 times.

2022 Guidance

Turning now to our guidance, this morning we announced we are increasing our full-year 2022 net sales guidance range to $3.59 billion to $3.61 billion, up from $3.53 billion to $3.6 billion, representing year-over-year growth of more than 11% at the midpoint.

- We continue to expect TEPEZZA full-year 2022 net sales percentage growth in the high teens.
- For KRYSTEXXA, we are increasing our full-year 2022 net sales growth guidance to approximately 25%.
- For our inflammation business, we expect fourth-quarter net sales of less than $10 million and net sales next year to be immaterial.

We now expect full-year 2022 gross margin to be modestly higher than 87%.

We are increasing our full year adjusted EBITDA guidance range to $1.32 billion to $1.34 billion, up from $1.27 billion to $1.32 billion. Both the current and prior guidance ranges for the full-year 2022 include acquired IPR&D and milestones expenses of $53 million.

As it relates to operating expenses, we expect the fourth quarter to be in a similar range as the third quarter, including acquired IPR&D and milestones expenses, which are expected to be $34 million in the fourth quarter.

We continue to expect our full-year net interest expense to be approximately $85 million to $90 million.

We now expect our full-year 2022 tax rate to be modestly above 11%, versus our prior expectation of approaching 12%. As with every year, we anticipate variability in our tax rate on a quarterly basis. We continue to estimate that our 2022 cash tax rate will be in the mid-to-high single digits. As always, our tax rates could change significantly as a result of acquisitions or divestitures we may make, or any changes in tax laws.

We now expect our full-year 2022 weighted average diluted share count to be approximately 235 million shares, which incorporates the 3.9 million shares repurchased to date.

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

Tim Walbert
Chairman, President and Chief Executive Officer

Thank you, Aaron.

In closing, our continued focus on execution drove meaningful progress this quarter. We are taking the actions we discussed last quarter to accelerate the growth of TEPEZZA in 2023. And the rest of our business, KRYSTEXXA, UPLIZNA and our rare disease medicines, all had outstanding performance. As a result, we increased our full-year 2022 net sales and adjusted EBITDA guidance, as well as our KRYSTEXXA full-year 2022 guidance. In addition, based on the strong momentum we are seeing with KRYSTEXXA and the further analysis we have completed on TEPEZZA internationally, we have increased our peak annual net sales expectations for both medicines.

Importantly, in our pipeline, we completed enrollment in our TEPEZZA chronic/low CAS TED trial and announced positive topline results from our Phase 2 trial evaluating dazodalibep in patients with Sjögren's syndrome. We look forward to several key readouts next year from our growing pipeline. This includes data from our TEPEZZA chronic/low CAS trial; our TEPEZZA trial in Japan; additional readouts from our dazodalibep Sjögren's Phase 2 program; the first Phase 2 data read out for daxdilimab, which will be in systemic lupus; and potentially data from our UPLIZNA Phase 3 trial in IgG4-related disease.

There is a lot to look forward to over the next 12 months. We remain highly focused on executing on our strategy, and I look forward to updating you further on our next call.

We will now open the call up for questions. Thank you.

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Chris. 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.