Horizon Therapeutics plc
Second-Quarter 2022 Conference Call
August 3, 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 second-quarter performance and our revised 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.

Before we move into the details of the quarter, I wanted to summarize a few key points today:

- Our orphan segment generated net sales growth of 13%, driven by our strong commercial execution.
- We delivered another quarter of outstanding KRYSTEXXA® performance – up nearly 30% driven by increased uptake of our immunomodulation strategy and strong momentum in nephrology.
- Our relaunch of UPLIZNA® is also tracking well, and our rare disease medicines business delivered another solid quarter.
- And as expected, TEPEZZA® net sales were impacted by Omicron-related effects in the second quarter.

Of course we are disappointed that TEPEZZA didn't rebound from Omicron as fast as we anticipated. We expected TEPEZZA trends to continue to show the positive progress we saw in the post-Omicron recovery, and that didn't happen.

We have a spent considerable amount of time to understand the reasons for this and identified what we need to do to accelerate growth. We are now executing on these plans to drive near-term results and realize the full potential of TEPEZZA, which is significant given our estimates of more than 100,000 addressable U.S. patients with thyroid eye disease (TED). Our revised full-year TEPEZZA net sales guidance this morning is for growth in the high teens - still significant growth off our 2021 net sales of $1.66 billion. And while our pace of growth to reach peak sales is different given the slower start to this year, we remain highly confident in our global peak annual net sales expectation of more than $3.5 billion, and we expect to drive at least mid-teens growth next year. We also see upside opportunity to our peak annual net sales expectations from a potential launch in Europe, which I'll touch on later.

With that, let me provide additional perspective on TEPEZZA and then move on to the rest of the business.

We launched TEPEZZA into an undeveloped and complex market in what turned out to be an unprecedented external environment with both COVID and the ensuing government-mandated TEPEZZA supply disruption. The journey since launch has been anything but typical – driven by the fact that TEPEZZA, with its impressive profile, has dramatically changed the TED treatment paradigm for both physicians and patients.

And we have learned a great deal – in fact, the first year of our launch we initially expected net sales of approximately $35 million, and we ended the year at $820 million.

We achieved this rapid success because we executed extremely well to prepare the market and drive adoption of TEPEZZA among our core prescriber base – ocular specialists such as oculoplastic surgeons, who are TED specialists and know the disease well. We generated particularly fast uptake with early adopters and their highly motivated patients who had symptoms aligned to our clinical trial data.

We have a clear commercial strategy, which as we shared on our last earnings call, has not changed. With ocular specialists, we are focused on increasing the breadth as well as the depth of our prescriber base, so that they identify more patients appropriate for TEPEZZA. With ophthalmologists, we are working to increase the breadth of prescribers while encouraging those who are not yet comfortable prescribing to diagnose and refer to a TED specialist. And, with endocrinologists, our focus is on driving an urgency for them to diagnose and refer their patients to a TED specialist as well.

What changed since we provided previous full-year guidance?

First, based on prior trends, we expected a faster pace of growth from ocular specialists as we moved from the early adopters and the most motivated patients to a broader set of physicians and patients. We realized that we underappreciated some of the challenges in further penetrating this segment and that it will take more time and effort to accomplish this.

Second, we also expected a faster pace of referrals from ophthalmologists and endocrinologists to our core TEPEZZA prescribers. We now realize that our sales force did not have adequate bandwidth to properly dedicate the time required not only to engage with ocular specialists but also educate physicians about TED to drive key referrals. This underscores the need to expand our sales force, which I will touch on shortly.

The timing and broad impact of Omicron complicated our ability to understand these dynamics more quickly to make the necessary adjustments. As we discussed on our first quarter call, TEPEZZA growth trends dipped with Omicron earlier this year. We expected that to persist into the second quarter, with growth accelerating in the second half of the year as the Omicron impact waned. However, the recovery didn't progress as fast as we expected, indicating to us that Omicron wasn't the only dynamic impacting the business. After digging deeper, we better understood those dynamics, we made several adjustments and are deploying more resources in a targeted manner to drive short- and long-term growth of TEPEZZA:

- First, we are adapting our commercial focus to these new learnings. This includes focusing our targeting, simplifying our messaging and increasing the accountability of our field organization. Accordingly, we have recently made several changes to the leadership of our TEPEZZA commercial and sales force organizations.
- Second, we are spending more time and focus on the reimbursement process, which as we've mentioned previously, is burdensome on physicians, especially with surgeons who are not accustomed to it. We have changed how the patient services team operates, combining our patient and reimbursement access teams to streamline the process to more effectively support physicians and patients in the patient access journey. These changes free up time for our sales force to focus on driving TEPEZZA prescriptions.
- Third, we are spending more time educating physicians as part of the medical management process for their patients. Unlike most diseases which are managed by one physician, TEPEZZA patients are typically co-managed by their surgeon and either their ophthalmologist or endocrinologist. We are educating physicians on monitoring requirements and best practice protocols through peer-to-peer education.
- Finally, based on recent learnings and findings from our market segmentation work, we realized the importance of expanding our sales force more significantly than we had initially planned. We are in the process of doing just that – we are adding about 60 field-based employees. This gives our sales representatives more time for engagement with ocular specialists and now ophthalmologists and endocrinologists. We will now cover a universe of approximately 12,000 total physicians. This broader effort will enable them to further educate ophthalmologists and endocrinologists about thyroid eye disease, driving urgency to diagnose and refer their patients to a TEPEZZA prescriber. These physician specialties see tens of thousands of potential TEPEZZA patients but are much less familiar with TED, the pathology of the disease and the relevance of the TEPEZZA mechanism of action as a key treatment approach. So currently we believe many patients never make it out of their ophthalmologist's or endocrinologist's office to find the care they need. And this is why our sales force expansion and our direct to consumer (DTC) investments are so critical. Over time, we expect more and more ophthalmologists to prescribe TEPEZZA. We recently completed a survey of ophthalmologists whose awareness of TED and TEPEZZA is very high. The survey showed over 60% intend to increase their TEPEZZA prescribing, underscoring the benefits of a larger sales force expansion.

I will conclude my comments on TEPEZZA with a brief review of the market – it is one of the key reasons we are so confident in the continued growth of TEPEZZA. We recently completed an exhaustive market analysis to better identify the types of TED patients and where they are being treated. It confirmed that patients' symptoms, regardless of the time since diagnosis, are what motivate them to seek treatment and drive physicians to prescribe TEPEZZA. This research also confirmed our estimates that there are more than 100,000 patients in the U.S. appropriate for treatment with TEPEZZA.

We have segmented these patients based on disease severity and clinical activity score (CAS). We estimate more than 20,000 have high CAS with key severity symptoms, such as high proptosis, diplopia, or both. It is also where we have currently the highest penetration, at less than 20%. These patients are more likely to be seen by an ocular specialist. We believe we have the highest penetration in this segment because it's where we conducted our pre-launch work, where we primarily focused our sales force and where we have shown impressive efficacy in our randomized placebo-controlled trials.

We estimate the more than 80,000 patients in the next segment are also appropriate for TEPEZZA – they have a low clinical activity score with high proptosis, diplopia or both, and we have low-single-digit penetration of this segment today. These patients are primarily treated by ophthalmologists or endocrinologists, where, as I mentioned before, there is relatively low awareness of the disease. It's also where we are focusing our sales force expansion.

In addition to our sales and marketing efforts, we are generating additional clinical evidence intended to drive adoption in low CAS patients. Today, most TEPEZZA use is in high CAS patients, so our chronic trial, the trial in low CAS patients, will be important because it will round out the picture of the efficacy of TEPEZZA in *all* CAS types. We have already seen good efficacy from TEPEZZA in this patient population through various physician-driven case reports. We expect to release topline data from this randomized placebo-controlled trial in the first half of next year. We also anticipate presenting the data at key medical conferences and publishing it in peer-reviewed medical journals beginning in the second half of next year. As a result, we have the potential for more meaningful uptake in the market from this data beginning in 2024.

Our continued significant investment in DTC will amplify all of our actions discussed today, and our campaigns continue to generate above-average returns.

Beyond the significant opportunity in the U.S., we expect our global expansion to contribute meaningfully outside of the U.S. beginning in 2025. While our current TEPEZZA peak annual net sales estimate does not assume a launch in Europe, we are finalizing our assessment of that opportunity and expect to be in a position to provide an update later this year. We expect this will provide upside to our peak annual net sales expectations for TEPEZZA.

We have learned a great deal over the last two and a half years, first in creating the market for TEPEZZA and then as the market has evolved. Our track record of commercial execution gives us confidence in building toward our long-term growth expectation to help thousands more TED patients with this life-changing medicine.

KRYSTEXXA

Moving on to KRYSTEXXA, second-quarter net sales were $168 million, representing strong year-over-year growth of nearly 30%. This continued strong performance was driven by the growing adoption in both rheumatology and nephrology market segments, as well as uptake of KRYSTEXXA with immunomodulation, which is now running at more than 50% of new patients.

Following the recent FDA approval of our supplemental biologics license application (sBLA) for the co-administration of KRYSTEXXA with methotrexate, the team was well prepared to execute the launch. In less than 24 hours we launched our new promotional campaign, trained the field force and launched new websites for both physicians and patients. We also hosted a live national launch broadcast which included physician and patient speakers to educate more than 750 physicians across the country.

Since acquiring KRYSTEXXA, we have dramatically transformed the growth trajectory of this life-changing treatment for patients with uncontrolled gout, through our efforts to educate the physician community on the benefits of KRYSTEXXA as well as investing in clinical data to show its efficacy and safety. This sBLA approval is the culmination of our efforts. With an expanded label, our commercial team is now promoting the benefits of KRYSTEXXA with methotrexate for the first time. We expect this to drive higher clinical conviction, broadening our reach to more physicians and increasing patient penetration among current treating physicians.

In fact, we are already seeing this happen. Physicians who have never prescribed KRYSTEXXA before or have not prescribed in a long time are changing their opinion. One of the physicians who had not prescribed KRYSTEXXA in over a decade said the new data shifted the way he viewed KRYSTEXXA, and he already had a patient in mind who would be a good candidate for treatment. Building on the momentum we are seeing in this launch and to leverage the current nephrology progress, we are expanding the KRYSTEXXA sales force by approximately 20% over the coming months.

We are driving significant momentum with this medicine, giving us continued confidence in our peak annual net sales expectation of more than $1 billion.

UPLIZNA

With UPLIZNA, we delivered another strong quarter, generating net sales of $39 million, where we doubled our U.S. sales compared to last year. We continue to make progress on our relaunch in the U.S. and are encouraged by the steady and consistent growth in new prescribers and new patient starts. As part of our global expansion strategy, our commercial launch is now underway in Germany. We are increasingly confident in the prospects for UPLIZNA in neuromyelitis optica spectrum disorder (NMOSD) and are progressing towards our global peak annual net sales expectation of more than $1 billion across all potential 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.

We continued to make progress on our R&D strategy in the second quarter and advanced our pipeline programs.

KRYSTEXXA
Starting with KRYSTEXXA, as Tim just mentioned, the FDA label expansion was the result of a successful priority review by FDA and was based on the data from our MIRROR trial. As you know, the 6-month primary endpoint showed a 30-percentage-point improvement in the response rate using KRYSTEXXA with methotrexate compared with KRYSTEXXA alone. New 12-month data from the trial are also now included in the expanded label and also show a nearly 30-percentage-point improvement in the KRYSTEXXA with methotrexate arm. From a safety perspective, infusion reactions were meaningfully reduced in the KRYSTEXXA with methotrexate arm. Only 4% of patients randomized to receive KRYSTEXXA with methotrexate experienced an infusion reaction, compared to 31% in the KRYSTEXXA monotherapy group. Taken together, the data around co-administration with methotrexate are a significant change to the original label that was used to launch this medicine, the only one for uncontrolled gout, 12 years ago.

Daxdilimab
Moving to daxdilimab which is the first and only plasmacytoid dendritic cell depleter in clinical development. We are studying daxdilimab in several indications and made notable progress this quarter.

First, we completed enrollment in our Phase 2 trial evaluating daxdilimab in patients with systemic lupus erythematosus (SLE), in the second quarter. We expect to announce topline results in the second half of 2023.

We also initiated a Phase 2 clinical trial in the second quarter in alopecia areata, an autoimmune disorder characterized by nonscarring hair loss. This open-label trial is expected to enroll approximately 30 patients with moderate-to-severe disease and we expect to announce topline data in 2023.

Looking forward, we expect to initiate three additional clinical trials with daxdilimab:

- First, our Phase 2 randomized controlled trial in patients with discoid lupus erythematosus (DLE). DLE is a chronic inflammatory skin condition characterized by lesions.
- Second, our Phase 2 randomized controlled trial in lupus nephritis (LN). LN is an autoimmune, inflammatory condition of the kidney and is the most common major organ manifestation of SLE. Current treatment regimens include intensive immunosuppressive therapy that can be associated with several adverse events, supporting the need for a more specific medicine to address the unmet need in those with proliferative LN.
- And third, our Phase 2 trial in dermatomyositis, an autoimmune, inflammatory disorder characterized by rashes that often burn as well as by debilitating muscle weakness.

Dazodalibep
Moving on to dazodalibep, our CD40-ligand antagonist designed to block a central pathway involved in many autoimmune and inflammatory diseases.

- We completed enrollment in the Phase 2 trial evaluating dazodalibep for Sjögren's syndrome in the second quarter, and we expect results in 2023.
- We also announced topline results from our Phase 2 double-blind, placebo-controlled trial of dazodalibep in rheumatoid arthritis patients, demonstrating that the primary endpoint was met in all four dazodalibep dosing arms and showing that it was well tolerated. We expect to present the full results at an upcoming medical meeting.
- We are also working with regulatory agencies to finalize the details of our trial design for focal segmental glomerulosclerosis (FSGS), a rare kidney disorder.

TEPEZZA
As for TEPEZZA, we are continuing to enroll patients in our Phase 4 randomized controlled trial in TED patients with a low clinical activity score, otherwise referred to as our chronic TED trial, with topline data expected in the first half of 2023.

We continue to advance our TEPEZZA subcutaneous administration program, recently initiating enrollment in a Phase 1b trial in TED patients, and we continue to progress our work on our high-concentration formulation as well. We also continue to enroll patients in the OPTIC-J trial in Japan.

UPLIZNA
UPLIZNA is our anti-CD19 humanized monoclonal antibody, currently indicated for NMOSD, a rare and devastating neuroinflammatory autoimmune disease that attacks the optic nerve, spinal cord and brain stem.

We continue to enroll patients in our myasthenia gravis trial; however, the complex geopolitical situation in the Russian and Ukrainian regions, along with the COVID lockdowns in China, have impacted enrollment and site availability. As a result, we now expect the topline data readout for this trial in 2024. We continue to work diligently with patients and sites across the impacted regions and are putting the appropriate measures in place to meet enrollment targets. Enrollment is also advancing in our IgG4-related disease Phase 3 clinical trial.

And with that I will now turn the call over to Aaron.

Aaron Cox
Executive Vice President, Chief Financial Officer

Thanks Liz.

My comments this morning will primarily focus on our non-GAAP results, unless otherwise noted. I will review our second quarter results followed by our revised 2022 financial guidance.

Our orphan segment generated second-quarter net sales of $841 million representing year-over-year growth of 13%. Our orphan segment operating income was $315 million.

Net sales for the inflammation segment were $35 million, and segment operating loss was $7 million, primarily due to the impact of the at-risk launch of a generic PENNSAID 2%® entrant on May 6th. As a result of the subsequent market erosion, we are in the process of winding down the inflammation segment which we expect to conclude by the end of the year.

Our second-quarter gross profit ratio was 86% of net sales, somewhat below our expectations driven by the inflammation segment.

Second-quarter operating expenses were $448 million. This included R&D expense of $95 million, or 11% of net sales, and SG&A expense of $352 million.

Second-quarter adjusted EBITDA was $307 million.

The tax rate for the second quarter was 11.7%. As we have seen in prior years, there can be variability in our tax rate across quarters.

Net income in the quarter was $254 million, and diluted earnings per share were $1.07. The weighted average shares outstanding used to calculate second-quarter 2022 diluted EPS were 236 million shares.

Second-quarter operating cash flow was $251 million.

As of June 30, cash and cash equivalents were $1.89 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 1.6 times as of June 30 and our net leverage ratio was well under 1.0 times.

2022 Guidance

I will now turn to our revised outlook for 2022 and how we see the rest of the year playing out. We are revising our full-year 2022 net sales guidance to $3.53 billion to $3.60 billion, representing year-over-year growth of 10% at the midpoint.

- We now expect TEPEZZA full-year 2022 net sales growth in the high teens, with quarter-over-quarter sequential growth expected over the third and fourth quarters.
- For KRYSTEXXA, we continue to expect full-year 2022 net sales growth of more than 20%.
- For the inflammation segment, we expect net sales of less than $30 million in the second half of the year due to the market erosion caused by the generic PENNSAID 2% entrant. As we wind down the business, we expect our net sales for this segment to be immaterial beginning next year.

We continue to expect full-year 2022 gross margin of approximately 87%.

We expect full year adjusted EBITDA to be between $1.30 billion and $1.35 billion.

As it relates to operating expenses, we expect third and fourth quarter expenses to be in a similar range as the second quarter. We expect a modest benefit in the fourth quarter from the wind down of the inflammation business unit, which will be mostly offset by the expansions of the TEPEZZA and KRYSTEXXA field forces.

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

We continue to expect our full-year 2022 tax rate to approach 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 continue to expect our full-year 2022 weighted average diluted share count to be approximately 238 million shares.

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

Tim Walbert
Chairman, President and Chief Executive Officer

Thank you, Aaron.

A few thoughts this morning. We delivered strong growth this quarter with KRYSTEXXA, UPLIZNA and our rare disease medicines, as well as the continued advances we are making with our pipeline. With TEPEZZA, we are expanding our presence and putting in place the actions we believe are needed to accelerate growth. We are revising our growth this year to high teens and expect at least mid-teens growth next year. While the expected pace of growth is different than our original expectations, we remain highly confident in our TEPEZZA global peak annual net sales expectations of more than $3.5 billion, which does not include our potential entry into Europe.

We have also updated our full-year guidance for the recent and unexpected at-risk launch of a generic PENNSAID 2%. We will be winding down the inflammation business by the end of the year. It is our legacy business that launched Horizon 12 years ago and which provided the investment to allow our rapid and successful diversification into rare diseases. Five years ago the inflammation segment represented roughly 60% of our net sales, and it's a reminder of how quickly we have executed to transform Horizon to the rare disease-focused biotech company we are today.

Part of executing on our business is recognizing the changes that need to be made in the short term to drive long-term growth. We have demonstrated this strategic agility throughout our history – we have leveraged our commercial and R&D expertise to breathe new life into underutilized medicines; we have built new markets; we have made some of the highest returning acquisitions in the healthcare sector and we have completely transformed our company in an incredibly short period of time.

As we look ahead, the medicines that are driving our future growth are truly remarkable medicines with impressive efficacy, significant opportunity for increased penetration and they address important patient needs. We continue to expand our pipeline to support our future growth and look forward to several key read-outs beginning in the first half of next year. With nearly $2 billion in cash at the end of the quarter, we are in a strong position to continue to build and diversify our company through our business development activity and pipeline programs. We remain as committed as ever to continue to make a difference in the lives of patients and build long-term value for shareholders.

We will now open the call up for questions.

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.