Horizon Therapeutics plc
Second-Quarter 2021 Conference Call
August 4, 2021

Tina Ventura
Senior Vice President, Investor Relations

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

On the call with me today are:

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

Tim will provide a review of the business, including our second-quarter performance. 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'll 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 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 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 fantastic results this quarter with strong performance across the business, which sets us up for continued momentum in the second half of the year.

- The TEPEZZA® relaunch has outperformed our expectations, driven by rapid patient starts, strong new patient demand and an increasing prescriber base.

- KRYSTEXXA® generated year-over-year growth of 73 percent, driven by continued acceleration in the use of KRYSTEXXA plus immunomodulation, which is now at more than 40 percent, with growth driven by both rheumatologists and nephrologists.

- RAVICTI® and PROCYSBI® each delivered strong double-digit growth, as well.

- In total, our net sales increased 80 percent, and adjusted EBITDA increased 92 percent, underscoring our position as one of the fastest-growing biotech companies.

As a result of our outperformance, we are significantly increasing our guidance for full-year TEPEZZA net sales, full-year total company net sales and full-year adjusted EBITDA. Full-year TEPEZZA net sales guidance is now more than $1.55 billion, representing more than 89 percent growth year-over-year. Our increased full-year net sales and adjusted EBITDA guidance ranges represent strong year-over-year growth at the midpoints of 40 percent and 28 percent, respectively.

I'll now discuss key second-quarter and recent achievements:

- We continued to significantly expand our portfolio and pipeline, adding a new early-stage next-generation gout program through our collaboration with Arrowhead, as well as we initiated three new clinical trials.

- We continued to support our on-market medicines with many new data presentations and publications. This includes two new publications in June by independent physicians on the successful use of TEPEZZA in patients with chronic Thyroid Eye Disease (TED). There are now six publications with a total of more than 50 chronic TED patients in multiple case reports. In addition, we presented new data highlighting the efficacy, safety and differentiated benefits of UPLIZNA®.

- We were awarded four new best workplace recognitions, with the number of awards for the year now at seven. This is continued evidence that our performance and employee-focused culture is a key factor in our industry-leading growth.

- We acquired a new biologics drug product manufacturing facility in Waterford, Ireland. This is key to supporting the continued growth of TEPEZZA, KRYSTEXXA and UPLIZNA, as well as our development-stage biologics and represents an important step in our evolution as a leading biotech company.

- We continued our global expansion as we advance launch preparations in support of the potential approval for UPLIZNA in Europe and progress with clinical trial preparations for TEPEZZA in Japan.

- We also announced that we will be hosting a virtual R&D Day for investors and analysts on September 29 to discuss our pipeline and new programs planned, which significantly expanded this year with the acquisition of Viela Bio in March.

TEPEZZA

Looking at the second-quarter results, TEPEZZA second-quarter net sales were $453 million, with impressive year-over-year growth of 173 percent. The strong performance of the TEPEZZA relaunch was the result of excellent execution by the TEPEZZA team to resume treating patients impacted by the government-mandated first-quarter supply disruption. We converted new patients added during the disruption and drove new patient enrollment forms (PEFs) successfully.

The strong relaunch demonstrated the continued ability of our commercial team to execute. We were able to rapidly restart existing patients on therapy once we resumed supply of TEPEZZA. As we discussed last quarter, two groups of patients were involved: first, patients who were on therapy when the supply disruption began, or disrupted patients; and second, new patients enrolled during or prior to the disruption who had to wait until after supply resumed in April to start taking TEPEZZA. This second group were patients added based on our continued promotional efforts during the fourth and first quarters.

As expected, the vast majority of disrupted patients resumed therapy in the second quarter. New patients with PEFs generated prior to or during the disruption also started TEPEZZA very rapidly. The rapid access to therapy for both these new patients and the disrupted patients was driven by the execution of our field-based teams, who continued to remain in constant communication with physicians, patients and sites of care throughout the first quarter.

We were very pleased to see strong growth of PEFs during the disruption, a trend that continued post relaunch. We attribute this continued strong growth in patient demand due to the fact that our new and existing prescriber base continues to increase. We are also seeing increased conviction from these prescribers, with two-thirds of them writing more PEFs in the first half of 2021 than in the second half of 2020. Finally, given the rapid relaunch, we have accelerated and significantly increased our investment in direct-to-consumer marketing initiatives, with very positive results – notably from our branded and unbranded television campaigns, which have been increasing awareness about TED and TEPEZZA. Our goal for these national campaigns is to increase awareness of TEPEZZA and accelerate the speed to diagnosis and treatment.

We are enthusiastic about the prospects for TEPEZZA to help more patients address the serious, debilitating and sight-threatening aspects of TED. Given the second-quarter's better-than-expected results and continued strong new patient growth, we increased our full-year TEPEZZA net sales guidance to more than $1.55 billion, which is a near doubling of net sales in our second year of launch.

As we discussed last quarter, our guidance continues to assume that the third quarter is the highest net sales quarter in 2021. This is a function of the disrupted patients completing treatment, patients with PEFs generated in the fourth and first quarters starting treatment after the April resupply, and new patients starting treatment in the third quarter. The outperformance of the relaunch positions us for strong year-over-year growth of more than 50 percent in the fourth quarter this year, driven by continued strong PEF generation after the April relaunch.

TEPEZZA is one of the most successful rare disease medicine launches ever. There is still tremendous upside opportunity and we are focused on driving greater penetration, both in the acute patient population as well as the untapped chronic opportunity. We remain well on track for our peak global net sales estimate of more than $3.5 billion.

KRYSTEXXA
With KRYSTEXXA, we delivered outstanding results for the quarter, generating record net sales of $130 million, with year-over-year growth of 73 percent.

A key driver of this quarter's strong growth was the increasing adoption of KRYSTEXXA plus immunomodulation, the core part of our strategy to maximize the value of KRYSTEXXA and enable more patients with uncontrolled gout to benefit from the medicine. Use of KRYSTEXXA plus immunomodulation for new patients is now at more than 40 percent, which we attribute to the greater clinical conviction of physicians who use KRYSTEXXA plus immunomodulation. We look forward to the results of the MIRROR randomized control trial in the fourth quarter of this year, which is evaluating KRYSTEXXA plus methotrexate versus KRYSTEXXA alone.

Our strong execution is driving growth in KRYSTEXXA prescribing physicians – both rheumatologists and nephrologists. For nephrology in particular, we created a dedicated nephrology sales team early this year, and they have already driven more prescribing nephrologists in the first half of this year versus all of 2020. In addition, our messaging on the safety and efficacy of KRYSTEXXA is resonating with nephrologists – which has been reinforced by the positive interim results from our PROTECT trial for kidney transplant patients who have uncontrolled gout. We are encouraged by what we are seeing in nephrology, with significant upside opportunity ahead.

As a result of our execution, KRYSTEXXA PEFs and new patient starts both increased by strong double-digits in the second quarter, which sets us up well for the second half of the year.

UPLIZNA
With UPLIZNA, our humanized monoclonal antibody B-cell depleter, we generated second-quarter net sales of $14.5 million. UPLIZNA is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD), a severe, rare, relapsing, neuroinflammatory autoimmune disease that attacks the optic nerve, spinal cord and the brain stem. The timing of approval at almost the height of the pandemic last year proved to be very challenging for Viela Bio. We are planning and executing a relaunch of the medicine over the second half of this year, leveraging the patient-centric approach we use for both TEPEZZA and KRYSTEXXA.

Commercially, we are focused on rebuilding and expanding the sales team and establishing a robust commercial structure to support the complex aspects of the UPLIZNA patient journey. We made good progress on this in the second quarter and expect to complete the commercial expansion by the end of the third quarter. We are also leveraging support services we built for TEPEZZA. For example, as with TED specialists, many NMOSD specialists do not have infusion capabilities. We are leveraging our extensive TEPEZZA site-of-care network to support patient referral to infusion centers – which was a gap in the initial UPLIZNA launch.

On the clinical side, we are investing in medical and scientific engagement to develop our scientific leadership position in NMOSD. This includes conducting further analysis of the UPLIZNA clinical programs to expand the understanding by the prescribing community of its differentiation, as well as continuing to build a base of compelling real-world evidence supporting the use of UPLIZNA. In addition to presenting new data at several key medical meetings, which Liz will touch on, we have been actively reaching out to key NMOSD opinion leaders, who have welcomed our entry into the market and expressed enthusiasm for the differentiated approach UPLIZNA offers in treating NMOSD.

It takes time to establish infrastructure and educate stakeholders about a new medicine – in fact, we began our market preparation for TEPEZZA more than six months before we launched it. With UPLIZNA, we are off to a good start and expect to see the benefits of our new commercial organization and investments as we exit the year.

I'll 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 second quarter of 2021 marked another quarter of progress in R&D where we continue to focus on expanding our pipeline. We have 22 programs spanning the development life cycle from preclinical to post-marketing trials, which this quarter includes the addition of a new preclinical next-generation uncontrolled gout program through our collaboration with Arrowhead.

Today, I'll focus on the progress we've made on our key programs. In September, we'll be doing a deeper dive into our key programs at our investor R&D Day, which will incorporate our evaluation of the Viela programs we acquired in March along with new programs planned, as well as our portfolio and overall R&D strategy.

ARO-XDH
A highlight of our recent progress is our global collaboration and license agreement announced in June with Arrowhead for ARO-XDH, a discovery-stage investigational RNA interference (RNAi) therapeutic being developed as a potential treatment for people with uncontrolled gout.

RNAi is a natural cellular mechanism that uses a gene's own sequence to essentially turn that gene off, silencing gene expression and regulating the production of proteins. ARO-XDH leverages this natural pathway of gene silencing, which in this case can then be used to silence the XDH gene in the liver; XDH is the primary source of uric acid and represents a clinically validated target. As the leader in gout, we are uniquely positioned to successfully develop and commercialize the candidate that comes out of this program.

There remains a significant unmet need in treatment of uncontrolled gout. Roughly one-third of the nine million gout patients in the United States are treated with oral urate-lowering therapies, but a meaningful portion of these patients do not respond sufficiently to treatment and therefore continue to experience painful and debilitating gout symptoms. We expect to enter the clinic with ARO-XDH within the next two years.

HZN-7734
Moving to HZN-7734, in June we initiated our Phase 2 trial for the treatment of systemic lupus erythematosus (SLE). HZN-7734 is a plasmacytoid dendritic cell (pDC) depleter, an anti-ILT7 fully human monoclonal antibody with a differentiated mechanism of action. In healthy individuals, pDCs are present in low numbers, driving an appropriate immune response to fight infection. In individuals with certain autoimmune diseases, pDCs are found in high concentrations in diseased tissues, resulting in significant inflammation and tissue damage that are the hallmarks of autoimmune disease.

Our SLE trial is evaluating HZN-7734 in the treatment of people with moderate to severe forms of SLE, and we expect to enroll approximately 195 participants. The primary endpoint of the trial is the effect of HZN-7734 compared with placebo in reducing SLE disease activity using BICLA, a commonly used index that measures lupus outcomes. We anticipate results in 2023.

In addition, at the end of May, our work on this mechanism was published in the journal *Science Translational Medicine*, showing that pDC depletion may interrupt the cycle of inflammation that causes tissue damage in diseases such as lupus and other autoimmune and inflammatory conditions.

HZN-4920
Moving to HZN-4920, this is a CD40 ligand antagonist that blocks T-cell interaction with CD40-expressing B cells, thereby disrupting the overactivation of the CD40 / CD40 ligand co-stimulatory pathway.

HZN-4920 is currently in Phase 2 development for indications that involve immune overactivation. One such indication is Sjögren's syndrome, a chronic, systemic autoimmune condition that impacts exocrine glands. Patient enrollment in this trial continues. Our other two HZN-4920 trials, in rheumatoid arthritis and kidney transplant rejection, are ongoing.

In June, we presented results of an observational follow-up of the Phase 1b study conducted in patients with active rheumatoid arthritis. The purpose of this assessment was to estimate the duration of clinical improvement in trial subjects beyond the 3-month safety follow-up period following the last administered dose of HZN-4920. While the interpretation of this study is limited, and the duration of benefit could not be defined in these studies, these early data suggest a possible longer-term benefit of HZN-4920: of those patients with long-term follow-up, most remained better than baseline for more than two years after the last administered dose.

HZN-825
HZN-825, our oral selective $LPAR_1$ antagonist, has shown early signs of clinical impact in fibrotic disease. We have two development programs for HZN-825 – one in diffuse cutaneous systemic sclerosis and one in idiopathic pulmonary fibrosis (IPF). The sclerosis trial is screening now, with enrollment for both trials expected to begin in the third quarter.

TEPEZZA
Moving to TEPEZZA, we continue to see information accumulate in the literature about the successful use of TEPEZZA in chronic TED. At this point, there are six published patient case reports or case series that detail successful treatment with TEPEZZA in 52 patients with chronic TED, which is compared to the 41 acute TED patients treated with TEPEZZA in the Phase 3 clinical trial.

We are also progressing with our Phase 4 placebo-controlled trial, evaluating TEPEZZA for use in patients with chronic Thyroid Eye Disease. In this trial, we will be looking at chronic TED patients who are three to eight years post their TED diagnosis. As a reminder, TEPEZZA has a broad indication for all TED patients, and physicians can – and do – prescribe TEPEZZA for chronic patients today. The objective of our chronic trial is to generate clinical data to better inform payers and physicians about the performance of TEPEZZA in chronic patients.

Based on continued discussions with our principal investigators, we've decided to increase the target enrollment to approximately 60 patients to increase the robustness of the trial. We expect enrollment to begin in the coming weeks and anticipate a data readout in the second half of 2022.

We continue to advance our TEPEZZA subcutaneous administration program, which could potentially offer additional flexibility for patients by shortening the administration time and time spent with healthcare practitioners. We hope to have initial discussions with the FDA later this year around our plans for bringing a subcutaneous version of TEPEZZA to the market.

Regarding our clinical program for TEPEZZA in Japan, we are on track to submit our trial design to the Pharmaceuticals and Medical Devices Agency later this year.

UPLIZNA
For UPLIZNA, our anti-CD19 humanized monoclonal antibody B-cell depleter, enrollment continues in our two Phase 3 randomized controlled trials – one evaluating UPLIZNA in myasthenia gravis (MG), and the other in IgG4-related disease. MG is a chronic, rare autoimmune neuromuscular disorder that affects the voluntary muscles of the body, especially those that control the eyes, mouth, throat and limbs. IgG4-related disease refers to a group of disorders marked by tumor-like swelling and fibrosis of affected organs, such as the pancreas, salivary glands and kidneys.

For the NMOSD indication, we aim to maximize UPLIZNA for patients by educating physicians and the medical community about its benefits, a key component of our UPLIZNA relaunch. One of our priorities is to continue to build a robust body of evidence supporting the efficacy and safety of UPLIZNA in NMOSD. We've participated in numerous medical meetings this year and continued to highlight key UPLIZNA clinical data in medical journals. These presentations and publications highlight three key findings:

- First, the analysis of long-term data from the UPLIZNA Phase 3 NMOSD trials showing that UPLIZNA provided sustained reduction of NMOSD attacks for 87 percent of UPLIZNA patients for up to four years.

- Second, additional data demonstrate that UPLIZNA improved disability outcomes, regardless of baseline status, attack history or disease duration.

- A third set of data showed that patients on UPLIZNA with prior rituximab exposure experienced a meaningful reduction in NMOSD attacks.

KRYSTEXXA
Regarding KRYSTEXXA, in the second quarter we initiated our trial evaluating the concomitant use of KRYSTEXXA plus methotrexate for people with uncontrolled gout who did not achieve a complete response when previously treated with KRYSTEXXA alone. We continue to advance our five KRYSTEXXA clinical trials to increase the benefits and convenience of this medicine for patients.

Upcoming Milestones
So, to recap our upcoming milestones, we currently expect our TEPEZZA chronic TED trial to begin enrollment in the coming weeks, and we expect to begin enrollment in our two HZN-825 trials in the third quarter.

We expect topline data for both our KRYSTEXXA MIRROR randomized controlled trial and PROTECT trial by the end of the year, and TEPEZZA chronic data in the second half of next year. In 2023, we expect data from our UPLIZNA trials in myasthenia gravis and IgG4-Related Disease, our HZN-7734 SLE trial, and our HZN-4920 trial in Sjögren's syndrome.

Conclusion
I look forward to providing additional details on our key pipeline programs during our R&D Day in September, as well as updating you on our continued progress on our next earnings call. I will now turn the call over to Paul.

Paul Hoelscher
Executive Vice President, Chief Financial Officer

Thanks, Liz.

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

Second-Quarter 2021 Financial Results
Second-quarter net sales were $833 million, representing year-over-year growth of 80 percent. Our significant outperformance this quarter was driven by the successful relaunch of TEPEZZA and the continued strong growth of KRYSTEXXA, as well as our other rare disease medicines.

Our orphan segment generated net sales of $747 million, a year-over-year increase of 97 percent. Orphan segment operating income was $321 million.

Net sales for the inflammation segment were $86 million, and segment operating income was $47 million. We continue to focus on maximizing the cash flow generated from this segment to reinvest in our growth drivers and our expanding pipeline.

Our non-GAAP second-quarter gross profit ratio was 88 percent of net sales.

Non-GAAP operating expenses were $362 million. This included non-GAAP R&D expense of $81 million, or 10 percent of sales, and non-GAAP SG&A expense of $281 million.

Second-quarter adjusted EBITDA was $367 million, representing year-over-year growth of 92 percent.

Non-GAAP income tax benefit for the second quarter was $36 million. As we have seen in prior years, there can be variability in our tax rate across quarters. We expect the tax rate in the second half of the year to be in the mid-teens, which offsets the low tax rate in the first-half of the year and brings our full-year tax rate in line with our projected low double-digit rate.

The non-GAAP net income in the quarter was $381 million, and non-GAAP diluted earnings per share were $1.62. The weighted average shares outstanding, used to calculate second-quarter 2021 non-GAAP diluted EPS, were 235 million shares.

Second-quarter non-GAAP operating cash flow was $147 million.

As of June 30, cash and cash equivalents were $812 million, giving us significant flexibility to invest in our growing operations. This includes additional strategic transactions to further expand our pipeline. The total principal amount of our outstanding debt is $2.6 billion, with the earliest maturity in 2026. As of June 30, our gross debt-to-last-12-months adjusted EBITDA leverage ratio is 2.3 times, which is an improvement from the March 31 ratio of 2.8 times. We still expect to be at our gross leverage target of 2 times by year-end 2021.

2021 Guidance
Turning now to our guidance, this morning we announced that we are increasing our full-year 2021 net sales guidance range to $3.025 billion to $3.125 billion, from $2.75 billion to $2.85 billion. This reflects an increase in the full-year 2021 TEPEZZA net sales guidance to more than $1.55 billion, representing year-over-year growth of more than 89 percent. As Tim noted, we expect the third quarter to be TEPEZZA's highest net sales quarter of 2021, and we expect net sales year-over-year growth of more than 50 percent for TEPEZZA in the fourth quarter.

With KRYSTEXXA, we continue to expect net sales of more than $500 million for the year, representing strong year-over-year growth of more than 20 percent.

We are also increasing our adjusted EBITDA guidance range to $1.26 billion to $1.30 billion from $1.02 billion to $1.06 billion.

We continue to expect our non-GAAP gross profit ratio for the full year to be between 86 and 87 percent.

We expect 2021 R&D expense to be in the low double digits as a percent of sales.

We expect non-GAAP net interest expense for the full year to be approximately $75 million.

We continue to expect a full-year non-GAAP tax rate in the low double digits. We estimate that our cash tax rate will be in the high single digits in 2021. As always, our tax rates could change significantly as a result of any acquisitions or divestitures we may make, or any changes in tax laws.

We continue to expect our full-year 2021 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

Thank you, Paul.

We continued to execute on our strategy to expand our pipeline for future growth and maximize our key on-market medicines.

We added a next-generation gout program to our pipeline with the Arrowhead program and we initiated three new clinical programs.

And we generated record financial results, driven by TEPEZZA, KRYSTEXXA and our other rare disease medicines, where we see continued strong underlying demand. As a result, we increased our guidance for full-year TEPEZZA net sales, total Company net sales and adjusted EBITDA.

Two weeks ago we rang the opening bell at Nasdaq celebrating the 10th anniversary of our initial public offering. We have accomplished so much since then, when we just had two on-market medicines. Today we are a leading, high-growth, profitable biotech with a market cap of more than $20 billion, a portfolio of rare disease medicines that make a difference for thousands of patients and a robust pipeline of 22 programs spanning the development life cycle – and a path for much future growth to come. It speaks to the value of having the right strategy, remaining focused on executing and having an excellent team of people driving it. We look forward to reporting on our progress again next quarter.

We will now open the call up for questions.

Tina Ventura
Senior Vice President, Investor Relations

Thank you, Justin. 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.