Horizon Therapeutics plc
First-Quarter 2022 Conference Call
May 4, 2022

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Norma. 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;
- **Paul Hoelscher**, Executive Vice President, Chief Financial Officer;
- **Andy Pasternak**, Executive Vice President, Chief Strategy Officer; and
- **Aaron Cox**, Executive Vice President, Finance. As a reminder, Aaron will be transitioning to the role of CFO on May 16.

Tim will provide a review of the business, including our first-quarter performance. Liz will then review 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.

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 had a strong start to the year, with first-quarter net sales of $885 million and first-quarter adjusted EBITDA of $371 million. We also reiterated our full-year 2022 guidance this morning and are well positioned for another year of top-tier growth.

In addition to strong financial and operational performance, we made meaningful progress on our strategic priorities:

- We continued to advance our pipeline, initiating two of the seven clinical trials expected to start this year. We also advanced our dazodalibep clinical programs, announcing positive topline results from our Phase 2 trial in rheumatoid arthritis (RA), and completing enrollment in our Phase 2 trial in Sjögren's syndrome. The positive readout from our RA study serves as an important proof of concept validating the dazodalibep mechanism of action, as well as providing further validation of our acquisition of Viela last year. We look forward to the readout of the Phase 2 trial in Sjögren's syndrome next year.
- With KRYSTEXXA®, we were pleased to be granted FDA priority review of our supplemental biologics license application (sBLA) for KRYSTEXXA plus methotrexate. This marks an important milestone in establishing KRYSTEXXA plus immunomodulation as the standard of care.
- We are also making progress on our global expansion strategy. We recently received approval for UPLIZNA® in Europe for neuromyelitis optica spectrum disorder (NMOSD) and we are initiating its European launch starting with Germany. We also initiated the buildout of our infrastructure in Brazil to support the potential launches of UPLIZNA and TEPEZZA®.
- As we continue to advance our strategy to drive rapid growth over the coming years, we announced today that we have hired Jacopo Leonardi as president, global commercial operations, reporting to me. Jac is an accomplished life sciences executive with more than two decades of commercial experience, including driving growth of high-performing businesses in rare disease and immunology. Jac will oversee the U.S. and international commercial organizations, commercial development and global medical affairs.
- Finally, we continue to receive recognition as a best workplace, including ranking in Fortune's "100 Best Companies to Work For®" for the second consecutive year and retaining the highest-ranked position in the biotechnology/pharmaceutical category. This recognition underscores the strong engagement of our employees, which is very important in our highly competitive industry.

Before I move on to our results for the quarter, I want to thank Paul Hoelscher for the contributions he has made to Horizon during his time here. As many of you know, Paul is retiring this month. He has been a tremendous partner over his nearly eight years with us, and I am grateful for his leadership and dedication to Horizon, as well as his financial stewardship that has contributed significantly to our success and transformation during that time. We are pleased that Paul will be staying on in an advisory role through May of next year to ensure a smooth transition. As announced previously, Aaron Cox will assume the CFO role on May 16.

TEPEZZA

Moving on to our growth drivers, TEPEZZA first-quarter net sales of $501 million were in line with our expectations. As we mentioned last quarter, the omicron variant had an impact on our business beginning at the end of last year, as did typical seasonality. Despite that, we generated strong performance in the quarter.

As we discussed last quarter, we continue to drive the next stage of our commercial strategy. This includes more deeply penetrating our high-priority thyroid eye disease (TED) physician targets. Additionally, we are broadening our reach to general ophthalmologists and endocrinologists in order to further educate them on TED and accelerate the referral of their patients to TED treaters. As part of our plan, we are increasing our field force to accelerate referrals to existing treaters and expand the number of physicians prescribing TEPEZZA, as well as continuing our significant investment in direct to consumer and other key digital activities. We expect these activities to accelerate growth as we move further through the year, reaffirming our confidence in achieving our strong growth expectations for TEPEZZA this year, despite omicron-related impacts persisting into the second quarter.

The TED market has evolved considerably in the last two years since the approval of TEPEZZA, which has proved to be a paradigm-shifting medicine. As the TED market leader, we have continued to do a significant amount of work to further inform our understanding of the market – this includes additional market analysis, payer claims analysis, physician and patient market segmentation and commercial strategy work, which allsupport the growth of TEPEZZA over the long term. Initial readouts have been insightful and positive:

- First, we have continued to validate the size of the U.S. TED market and believe it is at least as large as what we have communicated in the past, if not larger. This gives us even greater confidence in the long-term potential for TEPEZZA and our global peak annual net sales expectation of more than $3.5 billion globally.
- Second, it is providing us with important information about the patient journey and therefore how we can further drive execution over the short and long term.
    - We are finding that patients' symptoms, such as diplopia and pain, regardless of the time from diagnosis, are what drive them to seek treatment and drive physicians to prescribe TEPEZZA. And contrary to earlier views suggesting the majority of TED patients experience less severe symptoms over time, we now know there is a significant cohort of patients who experience high inflammation and high proptosis more than two years after diagnosis. In fact, most of the chronic patients being treated with TEPEZZA today have high levels of inflammation along with their proptosis.
    - When you launch a transformative medicine into a market that has never had an adequate treatment, the treatment of the disease is continually being redefined. We see symptoms, versus time from diagnosis, as the key driver of patient uptake. As you have seen in our DTC commercials and other digital activities, we are expanding our messaging to cover a broader set of signs and symptoms beyond proptosis – symptoms such as diplopia, eye mobility, eyelid retraction, orbital pain and swelling around the eye.

We see significant potential to access many more patients with thyroid eye disease who are appropriate for TEPEZZA.

KRYSTEXXA
For KRYSTEXXA, first-quarter net sales were $141 million, representing year-over-year growth of 32%. We generated strong performance despite the impact of the omicron variant. This was driven by continued adoption in both rheumatology and nephrology market segments, as well as uptake of KRYSTEXXA plus immunomodulation, which is now running at approximately 50% of new patients. This is up from 35% just a year ago and remarkable considering the MIRROR data is not currently available for promotion by our commercial organization. We expect the rate of immunomodulation use to continue to increase over time.

We are preparing for the July 7 Prescription Drug User Fee Act (PDUFA) action date to modify the KRYSTEXXA label with the results of the MIRROR trial, which demonstrated that 71% of patients who received KRYSTEXXA plus methotrexate achieved a complete response, a more than 30-percentage point improvement compared to placebo patients who received KRYSTEXXA alone.

With an expanded label, our commercial team would be, for the first time, able to actively promote the benefits to physicians. We expect this to driver higher clinical conviction – broadening our reach to more physicians and deepening our penetration among current treating physicians. This will help to address the significant ongoing unmet need for the more than 100,000 patients living with the debilitating effects of uncontrolled gout.

The team is preparing for the potential approval and will be ready to launch a new promotional campaign early in July. Additionally, our clinical team continues to work on MIRROR data dissemination at medical meetings and through key publications. We will be conducting peer-to-peer education to continue to build a broader understanding of the MIRROR clinical data. We are also very pleased that the MIRROR trial was accepted as an oral presentation at the upcoming European rheumatology medical conference, EULAR, in June.

We have been significantly investing in KRYSTEXXA to change its perception since we acquired it in 2016. Rarely if ever has a company been able to completely transform the profile of a 12-year-old medicine as we have with KRYSTEXXA. And we are incredibly proud to be at this next step in its transformation to bring this medicine to so many more patients – which gives us increased confidence in our peak annual net sales expectation of more than $1 billion.

UPLIZNA
Moving on to UPLIZNA,which we began to relaunch in the fourth quarter last year, we delivered another strong quarter, generating first-quarter net sales of $31 million. Approximately $5 million was international revenue from our international partners.

We continue to make good progress with our relaunch, expanding the prescriber base and driving new patient starts. In the first quarter:

- More than half of the patient enrollment forms were generated by new prescribers, building a foundation for long-term growth.
- While the majority of new patients are switching from other therapies – which is in line with our commercial strategy – we are also seeing a good portion of new patients that are naïve to therapy. This speaks to the confidence physicians have in UPLIZNA as a next-generation B-cell-depleting therapy.
- We continue to see faster and higher patient pull-through, driven by the strong support provided by our patient services, reimbursement and site of care teams — which was a critical component of the UPLIZNA relaunch.

On the clinical side, we continue to invest in medical and scientific engagement to drive patient and physician preference for UPLIZNA based on its strong clinical data, its differentiated mechanism of action and clear patient benefits. We significantly expanded peer-to-peer speaker programs, with more programs held in the first quarter than all of last year. In addition, we presented new data at several key medical meetings, continuing to build on its long-term safety and efficacy data.

As part of our global expansion strategy, we will be launching UPLIZNA in Europe, starting with Germany, following the recent European Commission approval.

We are increasingly confident in the prospects for UPLIZNA in NMOSD as well as in the other indications we are pursuing for the medicine and are progressing towards our peak global annual net sales expectation of more than $1 billion across all 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.

On this call a year ago, we shared that we had completed the Viela acquisition and were in the process of integrating the two companies. We've come a long way since then and have a busy year ahead as we continue to drive our pipeline forward.

This morning I'll update you on the progress of our key programs, starting with our TEPEZZA trial in chronic thyroid eye disease.

TEPEZZA
We are continuing to enroll patients in our Phase 4 randomized, placebo-controlled trial in chronic TED. The results of this trial will add to the emerging literature studying TEPEZZA in patients with chronic TED. We now expect the topline data readout for this trial in the first half of 2023. This is somewhat later than we had originally expected and is due to a slower level of patient enrollment, which is primarily due to the impact from the omicron variant. We've since put in place a number of measures that are helping drive enrollment, and we are tracking to a topline readout in the first half of next year.

We continue to advance our TEPEZZA subcutaneous administration program, where we are on track to begin enrolling TED patients in a Phase 1b trial mid-year, and we continue to progress our work on our high-concentration formulation. We also continue to enroll patients in the OPTIC-J study in Japan.

We remain focused on developing scientific leadership in TED through attendance at key medical meetings during the year including endocrinology, ophthalmology, oculoplastic and optometry conferences. In the second quarter alone, we plan to attend seven key medical meetings.

Daxdilimab (HZN-7734)
Moving to daxdilimab (HZN-7734) the first and only plasmacytoid dendritic cell (pDC) depleter in clinical development. pDCs are found in high concentrations in diseased tissues of individuals with certain autoimmune and inflammatory diseases, and the activity of these cells can result in significant inflammation and tissue damage.

The Phase 2 trial for our first potential indication for daxdilimab in systemic lupus erythematosus (SLE) continues to enroll, and we continue to expect results for this trial in 2023.

We expect to begin clinical trials in four additional indications this year. The first, alopecia areata, is an autoimmune disorder characterized by nonscarring hair loss. As we discussed in significant detail on our last earnings call, we remain on track to initiate this Phase 2 open-label trial in the second quarter in approximately 30 patients with moderate-to-severe disease.

We expect to initiate our discoid lupus erythematosus (DLE) trial mid-year. DLE is a chronic, inflammatory skin condition characterized by lesions. It is a scarifying disease that can be significantly disfiguring and can also result in hair loss. One of the mischaracterizations of DLE is that it only affects systemic lupus patients. However, 80% of DLE patients do not have systemic disease and therefore have primary DLE. We estimate about 30 thousand patients with DLE are candidates for novel therapies, including biologics. The current standard of care is not uniformly effective and is associated with potential side effects. Our DLE clinical trial will be a Phase 2 randomized, placebo-controlled trial in patients with moderate-to-severe active primary disease. The primary endpoint will be the mean change

in the CLASI-A disease severity score from baseline to Week 24. We will also be looking at a variety of other measures of disease activity.

We also expect to initiate our trials in lupus nephritis and dermatomyositis later this year.

Dazodalibep (HZN-4920)
Moving on to dazodalibep, (HZN-4920), this is our CD40-ligand antagonist designed to block a central pathway involved in many autoimmune and inflammatory diseases.

We recently completed enrollment in the Phase 2 double-blind, placebo-controlled trial evaluating dazodalibep for Sjögren's syndrome, a chronic systemic autoimmune condition that impacts exocrine glands, including the salivary and tear glands. We expect results in 2023.

Yesterday, 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 dazodalibep was well tolerated. We expect to present the full results at an upcoming medical congress. This marks the first of what we hope will be many clinical validations of the value that we saw in the Viela pipeline. As a reminder, our rheumatoid arthritis trial gives us the opportunity to accelerate our learnings about dazodalibep in a large and reasonably accessible patient population, using well-understood clinical endpoints. This trial reinforced our understanding of the CD40 ligand pathway in immune mediated and autoimmune diseases and provides us with important insights as we consider dosing regimens for future trials in Sjögren's syndrome and the progressive and rare kidney disease, FSGS. We expect to initiate our dazodalibep trial in FSGS in the fourth quarter.

HZN-825
Moving to HZN-825, our oral selective $LPAR_1$ antagonist, which has shown early signs of clinical impact in fibrotic disease, we enrolled our first patient in our pivotal Phase 2b trial for HZN-825 in idiopathic pulmonary fibrosis in January of this year. This trial, and our trial in diffuse cutaneous systemic sclerosis, continue to enroll.

UPLIZNA
UPLIZNA is our anti-CD19 humanized monoclonal antibody indicated for NMOSD, a rare and devastating neuroinflammatory autoimmune disease that attacks the optic nerve, spinal cord and brain stem. As Tim mentioned, the European Commission recently approved UPLIZNA for the treatment of adult patients with NMOSD who are AQP4-autoantibody positive. This is a great accomplishment for the R&D team but an even more important step in our efforts to bring a new option to people impacted by this disease.

We also continue to contribute to the literature regarding the efficacy and safety profile of UPLIZNA. Most recently, in April, multiple new data from the Phase 3 trial were presented at the American Academy of Neurology meeting. The new data demonstrated that there were no significant differences in attacks or worsening of the Expanded Disability Status Scale between NMOSD patients treated with UPLIZNA who had experienced one pre-study attack and those who had experienced two or more pre-study attacks. A separate new analysis of the Phase 3 trial showed that long-term treatment with UPLIZNA improved pain and quality-of-life outcomes for at least three years.

We continue to advance our enrollment in our two Phase 3 clinical trials evaluating UPLIZNA for myasthenia gravis and IgG4-related disease.

KRYSTEXXA

Finally, as Tim mentioned, July 7 is the PDUFA action date for the sBLA that supports updating the KRYSTEXXA label to include co-administration with methotrexate. Data from the MIRROR randomized controlled trial will be presented at EULAR in early June, where all of our KRYSTEXXA and gout-related abstracts were accepted. We also hope to share additional details from the MIRROR trial at other key medical meetings.

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. I will start with our first-quarter results, followed by our 2022 financial guidance.

First-Quarter 2022 Financial Results
First-quarter net sales were $885 million, in line with our expectations.

Our orphan segment generated first-quarter net sales of $834 million, driven by the strong performance across the portfolio. Our orphan segment operating income was $352 million.

Net sales for the inflammation segment were $51 million, and segment operating income was $15 million.

Our non-GAAP first-quarter gross profit ratio was 88.9% of net sales.

First-quarter non-GAAP operating expenses were $420 million. This included non-GAAP R&D expense of $92 million, where we continue to invest in multiple clinical trials – many that we are initiating this year. Non-GAAP SG&A expense was $328 million.

First-quarter adjusted EBITDA was $371 million, or 41.9% of net sales.

The non-GAAP tax rate for the first quarter was 10.2%.

Non-GAAP net income in the quarter was $316 million, and non-GAAP diluted earnings per share were $1.34. The weighted average shares outstanding used to calculate first-quarter 2022 non-GAAP diluted EPS were 236 million shares.

First-quarter non-GAAP operating cash flow was $223 million.

As of March 31, cash and cash equivalents were $1.64 billion. Backed by this strong cash position and expected future cash flows, business development will continue to play a critical role in expanding our pipeline.

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 is 1.6 times as of March 31. Additionally, in March, Moody's upgraded our Corporate Family Rating to Ba1 from Ba2.

2022 Guidance
I will now turn to our outlook for 2022 and how we see the rest of the year playing out. We are maintaining our full-year 2022 net sales guidance of $3.9 billion to $4.0 billion, representing year-over-year growth of 22% at the midpoint. For TEPEZZA, we expect full-year 2022 net sales percentage growth in the mid-30s. For KRYSTEXXA, we expect full-year 2022 net sales growth of more than 20%.

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

We expect full-year adjusted EBITDA to be between $1.63 billion and $1.7 billion, representing a 42.1% margin at the midpoint, a 230-basis-point expansion compared to 2021.

Our adjusted EBITDA guidance reflects our expectations for strong net sales growth, partially offset by our increased investment in R&D, which we expect to be in the low double-digits as a percentage of net sales.

As we think about our 2022 operating expenses, we expect a steady increase over the course of the year, mainly driven by R&D.

As it relates to our net interest expense, we recently entered into an interest rate swap to move $800 million of our floating rate debt to a fixed interest rate. Given the expected rising interest rate environment, our new fixed versus floating debt mix, as along with our significant cash balance, positions us well to manage expected increases in interest rates. As a result of the swap transaction, $1.4 billion, or 54%, of our gross debt outstanding has fixed interest rates, which will provide more certainty to our interest expense over the next several years. We now expect our full-year non-GAAP net interest expense to be approximately $85 million to $90 million, a modest increase from our prior expectations of $80 million to $85 million.

We continue to expect our full-year 2022 non-GAAP tax rate to approach 12%. As with every year, we anticipate variability in our non-GAAP 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 any 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.

Finally, as Tim mentioned, Aaron Cox will assume the role of CFO when I retire in a couple of weeks, and I look forward to staying involved with Horizon in an advisory role for another year. I want to take this opportunity to say thank you – I have enjoyed the opportunity to work with all of you in the investment community during my time at Horizon. I also want to thank Tim and the Horizon team for the opportunity to have been a part of the incredible growth of Horizon over the past eight years.

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

Tim Walbert
Chairman, President and Chief Executive Officer

Thank you, Paul.

Again, I want to thank you again for your many years of service, for your partnership and for contributing to Horizon's tremendous success and transformation. It's pretty amazing to look back on the day you started with us – almost eight years ago today. We had three medicines, no rare disease business, and a market cap of about $1 billion. We have had an incredible transformation since that period, and you were a critical part of it. Paul, we appreciate everything you have done and that you will continue to be available, and we thank you for that.

In closing:

- We generated strong financial results for the quarter, positioning us for another year of top-tier growth.
- We made meaningful progress on our strategic priorities, including initiating two of the seven clinical trials planned for this year as well as advancing our dazodalibep program in two indications, evidence of our effort to aggressively maximize our pipeline.
- The positive readout of our dazodalibep study in rheumatoid arthritis is an important proof of concept, validating the dazodalibep mechanism of action, as well as providing further validation of the acquisition of Viela. We look forward to many more with multiple trial readouts as we move into 2023.
- We are preparing for a potential KRYSTEXXA sBLA approval in July after which we plan to launch a new promotional campaign to drive the use of KRYSTEXXA plus methotrexate; and
- Our international expansion efforts are taking shape, in support of recent and future potential approvals,such as the announcement of the EU approval made this week.

We are off to a good start and I look forward to continuing to deliver progress on our pipeline and strong commercial execution as we build on this foundation and drive increasing value for our shareholders.

With that, Tina, we will now turn it over for questions.

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Norma. 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.