Horizon Therapeutics plc
Fourth-Quarter and Full Year 2021 Conference Call
March 1, 2022

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Livia. 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. Aaron will be transitioning to CFO after our first-quarter call.

Tim will review the business, including our fourth-quarter and full-year 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.

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.

2021 was a milestone year for Horizon. We significantly expanded our pipeline – working to make a difference in the lives of people impacted by rare, autoimmune and severe inflammatory diseases. At the same time, we once again delivered top-tier financial performance. Our full-year total net sales of $3.2 billion increased nearly 50% and our full-year adjusted EBITDA of $1.3 billion increased 33%. We also generated more than $1 billion in operating cash flow.

This morning, we issued our full-year 2022 financial guidance that again represents very strong growth at the midpoint. Our full-year net sales guidance of $3.9 billion to $4 billion represents 22% growth. Our adjusted EBITDA guidance of $1.63 billion to $1.70 billion represents 30% growth and 230 basis points of margin expansion.

Importantly, we expect our commercial performance to drive significant margin accretion, which would more than offset the increased investments we continue to make in R&D. As we look across profitable large-cap and biotech peers, Horizon's growth profile is one of the best in the industry.

In 2021, we made tremendous progress on our strategic goals – building our pipeline, maximizing our commercial medicines and expanding globally.

- We acquired Viela, significantly expanding our pipeline, and deepening our R&D scientific expertise. Our pipeline now includes more than 20 programs, with the majority added in 2021.
- We worked to maximize the molecules in our portfolio; notably, we identified four new indications for daxdilimab that we plan to initiate trials in this year, beginning with our alopecia areata trial next quarter. We believe daxdilimab has the potential to be a true "pipeline in a product" with multi-billion-dollar potential.
- Commercially, we more than doubled net sales of TEPEZZA® in its second year post-launch, and increased KRYSTEXXA® net sales by nearly 40%, remarkable for a 12-year-old medicine. We also repositioned, rebranded and relaunched UPLIZNA® in just six months after acquiring it with Viela.
- We continued to build our global presence, including the required infrastructure in Europe to support a potential launch of UPLIZNA in the second quarter, assuming European Commission approval. And last week we announced the first patient enrolled in our clinical trial evaluating TEPEZZA in Japan. This is the first step in changing the treatment journey for people with TED (thyroid eye disease) outside the U.S. and puts us on the path for reaching our international peak TEPEZZA annual net sales expectations of more than $500 million.
- We also significantly expanded our global supply capacity to meet growing demand. We added a second TEPEZZA drug product manufacturer and acquired a new biologic drug product manufacturing facility in Waterford, Ireland.

Behind all of our efforts are the people of Horizon. Their dedication to executing on our strategy makes a difference in the lives of the patients we serve. Our employees continue to be highly engaged, as evidenced by the 15 workplace awards we received in 2021 – including ranking as the Number 1 biotech/pharmaceutical company in FORTUNE's 100 Best Companies to Work For®. We are also a company that values diversity and equity. In 2021, a second study conducted by Aon confirmed once again that Horizon demonstrates gender and ethnicity pay equity. This was an especially meaningful accomplishment as it was achieved while our workforce nearly doubled in size.

Moving on to our fourth-quarter and full-year results.

TEPEZZA

TEPEZZA fourth-quarter net sales were $590 million, representing year-over-year growth of 72%. Full-year net sales were $1.66 billion, exceeding our full-year expectations. We achieved this incredibly strong performance despite the continued impact of COVID-19 and a government-mandated supply disruption that took TEPEZZA out of the market from the end of 2020 through April of last year. We executed a strong commercial relaunch following this disruption, resuming patients on therapy quickly, converting new patients and driving new patient enrollment forms (PEFs). We also initiated a randomized, placebo-controlled trial in chronic TED to help drive further uptake in this patient population.

As we enter our third year on the market, we continue to drive strong PEF growth and adoption of TEPEZZA. We are focused on the next stage of our commercial strategy and see significant potential to help many more patients benefit from TEPEZZA.

First, we plan to more deeply penetrate our high-priority TED physician targets – oculoplastic surgeons, strabismus specialists and neuro-ophthalmologists. We've done an incredible job to date but, with only a third of those physicians prescribing TEPEZZA today, we see significant opportunity to build on our success and capture a higher proportion of those physicians and their patients.

We are improving our physician targeting and refining our messaging as we learn more about what resonates best with each specialty. For example, proptosis reduction is the main focus for oculoplastic surgeons, while neuro-ophthalmologists focus more on a broader set of signs and symptoms of TED, such as diplopia, or double-vision.

Second, we are broadening our reach to general ophthalmologists and endocrinologists in a targeted way. Endocrinologists typically treat patients with underlying Graves' disease and general ophthalmologists treat patients with the underlying symptoms of TED, but due to underdiagnosis and lack of awareness of TED, the majority of their patients do not find their way to a TEPEZZA prescriber today.

Remember, this was a market that just two years ago had no treatment options for patients, and therefore, there was no well-defined patient journey. We are educating these physicians and working to improve the patient journey to both accelerate the referral process and activate certain physicians as TEPEZZA prescribers. This is a longer-term, multi-year strategy that should help thousands of TED patients benefit from TEPEZZA.

Third, we are continuing our significant investment in DTC (direct-to-consumer), which has proven successful in reaching a broad spectrum of TED patients. We are evolving the focus of the campaign to expand the impact of TED symptoms, such as diplopia, and have launched a new unbranded awareness campaign as well. In addition to awareness creation, the main goal of our DTC campaign is to help patients find a TED treatment specialist. We've continued to generate strong results, and the use of our TED specialist finder more than doubled from when we launched the branded TV campaign in May of last year. Our primary commercial focus this year is to further penetrate the acute TED opportunity.

Additionally, in the fourth quarter of last year we began to educate physicians on the use of TEPEZZA in chronic patients. There are now seven published case series citing successful experiences with TEPEZZA in nearly 60 chronic TED patients. We expect the results from our randomized controlled clinical trial in chronic patients by year-end. Those trial results and subsequent publication in peer-reviewed journals next year could help remove barriers with payers as well as drive clinical conviction for many physicians who today will only prescribe TEPEZZA for their acute patients or patients with high inflammation.

We anticipate that 2022 will be another year of outstanding growth for TEPEZZA, where we estimate full-year net sales percentage growth in the mid-30s, driving toward our peak global annual net sales estimate of more than $3.5 billion.

KRYSTEXXA
With KRYSTEXXA, we reported fourth-quarter net sales of $170 million, representing year-over-year growth of 32%, and full-year net sales of $566 million.

2021 was a significant year for KRYSTEXXA as we continued to advance our immunomodulation strategy. Topline data from our MIRROR randomized controlled trial showed that 71% of patients on KRYSTEXXA plus the immunomodulator methotrexate showed a complete response. This was a more than 30-percentage-point improvement compared to patients on KRYSTEXXA plus placebo.

In January of this year, we submitted a supplemental biologics license application (sBLA) to the U.S. FDA to incorporate the MIRROR data into the KRYSTEXXA label. Approval would allow our commercial team to proactively promote KRYSTEXXA plus methotrexate to physicians. In the meantime, our medical affairs and clinical teams are working to present and publish the MIRROR trial results and additional analyses from the trial – including new safety data – at medical congresses throughout this year. Immunomodulation is driving higher clinical conviction among treating physicians – use is now approaching 50% of new patients, which is up from more than 30% at the start of 2021.

We continued to expand the prescriber base, with significant growth in new prescribers as well as physicians who hadn't prescribed KRYSTEXXA in over a year. That is strong evidence that our immunomodulation strategy is working.

Our nephrology segment has been growing rapidly with PEFs in 2021 nearly doubling compared to 2020. This reflects the continued growth we're seeing in nephrology prescribers, which increased 75% versus 2020. We attribute this successful progress to the dedicated nephrology sales team we put in place last year.

As we look to 2022, we expect another strong year, projecting net sales growth of more than 20%. We are on track to achieve our peak annual net sales estimate of more than $1 billion, which is supported by our strategy:

- to redefine KRYSTEXXA plus immunomodulation as the standard of care;
- to expand utilization in our core specialty areas of rheumatology and nephrology;
- to elevate the urgency to treat uncontrolled gout patients; and
- to invest to improve the patient experience, including our monthly dosing and shorter-infusion duration trials.

UPLIZNA
Moving to UPLIZNA, we generated fourth-quarter net sales of $26 million. Approximately $4 million of that was international revenue from our Japanese partner.

Following our acquisition of Viela and UPLIZNA, we worked quickly to build a team and develop our strategy to conduct a full relaunch of the medicine, leveraging the patient-centric approach we use for TEPEZZA, KRYSTEXXA and our rare disease medicines. We put the right infrastructure and team in place with deep neuroimmunology experience, relationships and market knowledge.

We successfully relaunched UPLIZNA in the fourth quarter, and we are beginning to see the results:

- This is evidenced by a market research survey we conducted earlier this year, where awareness of UPLIZNA among physicians and patients increased significantly compared to the period before our relaunch;
- In addition, our physician call activity in the fourth quarter more than doubled from the third, indicative of the extended reach of our expanded sales force;
- We significantly expanded our peer-to-peer speaker programs; and
- We generated a more than 30% increase in total prescribers in the fourth quarter compared to the third, with more than half of patient enrollment forms coming from new prescribers.

As a result of our efforts, we generated strong quarter-over-quarter PEF growth and new patient starts. Internationally, we made substantial progress in 2021, building the infrastructure and capabilities to support a potential launch of UPLIZNA in Europe this year, beginning with Germany in the second quarter, assuming European Commission approval.

We are increasingly confident in the prospects for this medicine in NMOSD and the other indications we are pursuing. We expect another year of very strong growth in 2022 as we progress towards our peak global annual net sales expectations of more than $1 billion across all indications for UPLIZNA.

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

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

Thank you, Tim, and good morning, everyone.

2021 was a transformational year for R&D, and I expect continued progress as we move through 2022.

- In 2021, we significantly expanded our pipeline through the acquisition of Viela, the five new internal programs we announced and the two preclinical programs we added through external collaborations.
- We made progress in three new therapeutic areas including neuroimmunology, dermatology and respiratory.
- We began building out our research organization and discovery engine to drive long-term growth. We plan to generate high-quality INDs (investigational new drug applications) over the coming years through our own internal efforts, as well as through partnerships and collaborations.
- And we announced our expansion into a new state-of-the-art facility in Maryland to further support the growth of our R&D function and serve as our primary East Coast hub.

This morning I'll update you on the progress of our key programs, starting with daxdilimab, or HZN-7734.

Daxdilimab (**HZN-7734)**
Daxdilimab is 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.

Our daxdilimab trial in systemic lupus erythematosus (SLE) is underway.

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. We estimate more than 600,000 patients in the United States suffer from this disease, of which approximately 40,000 would be appropriate candidates for biologics. There are currently no approved therapies, and most patients are treated with off-label medicines, often with significant side effects and variable efficacy. We are on track to initiate our Phase 2 open-label trial in alopecia areata in the second quarter in approximately 30 patients with moderate-to-severe disease. The primary endpoint of the trial is the percent change from baseline in the SALT score at Week 24. SALT, or the Severity of Alopecia Tool, is the commonly used score to measure the level of disease severity in patients.

We plan to initiate our discoid lupus erythematosus (DLE) trial by mid-year. DLE is a scarifying disease that can be significantly disfiguring; it can also result in hair loss.

We expect to initiate our trial in lupus nephritis, an autoimmune, inflammatory condition of the kidney, in the third quarter.

And finally, we expect to initiate our trial in dermatomyositis in the fourth quarter. This is a rare condition that manifests as severe skin rash and debilitating muscle weakness and can affect children in a very severe way.

Dazodalibep (HZN-4920)
Moving on to dazodalibep, or HZN-4920. This is our CD40-ligand antagonist designed to block a central pathway involved in many autoimmune and inflammatory diseases. Dazodalibep is currently in Phase 2 trials for Sjögren's syndrome, rheumatoid arthritis and kidney transplant rejection.

This year, we expect two Phase 2 trial readouts: for rheumatoid arthritis in the second quarter and kidney transplant rejection by year-end. Our rheumatoid arthritis trial gives us the opportunity to accelerate our learning about dazodalibep in a large and reasonably accessible population, using well-understood clinical endpoints. CD40 / CD40 ligand is a relevant pathway in rheumatoid arthritis and our initial Phase 1 results suggest that inhibiting this pathway can impact disease. In this trial, we can expand our understanding of the impact of the mechanism under various dosing regimens, which can also inform our decisions on a potential dosing profile in other indications.

We expect to initiate our dazodalibep trial in the progressive and rare kidney disease (FSGS, focal segmental glomerulosclerosis) 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 recently enrolled our first patients in our two pivotal Phase 2b trials for HZN-825: in diffuse cutaneous systemic sclerosis in November, and in idiopathic pulmonary fibrosis in January of this year.

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. We continue to contribute to the literature regarding the efficacy and safety profile of UPLIZNA. Most recently, in February, we presented new data at the North American Neuro-Ophthalmology Society meeting (NANOS). In addition to the benefit already demonstrated on increasing the time to first attack for patients living with NMOSD, this new analysis suggested that treatment with UPLIZNA also reduced the severity of attacks. We continue to advance our Phase 3 trials evaluating UPLIZNA for myasthenia gravis and IgG4-related disease.

TEPEZZA
Moving now to TEPEZZA, we are continuing to enroll patients in our Phase 4 randomized, placebo-controlled trial in chronic thyroid eye disease. The results of this trial will add to the emerging literature studying TEPEZZA in patients with chronic TED.

Meanwhile, we continue to see additional data and analyses regarding TEPEZZA and its role in the treatment of TED. For example, in a recently published meta-analysis and matching adjusted indirect comparison of TEPEZZA and intravenous methylprednisolone, or IV steroids, showed that for IV steroids, only small, not clinically relevant, changes were seen from baseline for proptosis and diplopia were seen. This is consistent with what we have known from some time, that steroids are not effective in treating some of the most impactful signs and symptoms of TED. In the same manuscript, cross-trial comparisons supported greater improvements on proptosis and diplopia with TEPEZZA compared with IV steroids.

We also continue to advance our TEPEZZA subcutaneous (subQ) administration program where we are exploring multiple options with a new, high-concentration formulation. Options under consideration include approaches with and without the Halozyme technology. We have completed a Phase 1 single dosing trial in healthy volunteers with our current formulation. In this trial, we assessed the safety, tolerability and pharmacokinetics of two different single subQ doses, and we were pleased with the results. Next, we are moving to test this formulation in TED patients and expect to initiate this Phase 1b

study mid-year. We expect to begin clinical work with the high-concentration formulation later this year. The results of this work will help define our dose and regimen, which we will then evaluate in a pivotal trial.

And, as we announced last week, we initiated our clinical trial in Japan. The trial was designed based on discussions with the Japanese regulatory authority and Japanese experts in TED, and informed by our experience in the OPTIC Phase 3 trial conducted in the United States and Europe. The trial will include approximately 50 patients with moderate-to-severe active TED. The primary endpoint is the proptosis responder rate at Week 24, measured by the percentage of participants with at least a two-millimeter reduction in proptosis from baseline in the study eye. We expect results in the second half of 2023.

KRYSTEXXA

We have made substantial progress with KRYSTEXXA, improving its efficacy and working to improve its profile for patients. Tim referenced our MIRROR trial, where we look forward to sharing additional details from the trial at key medical meetings such as EULAR mid-year and ACR in the fall. And we continue to explore ways to improve the KRYSTEXXA profile with our trials evaluating shorter infusion duration and monthly dosing. Beyond these efforts with KRYSTEXXA, we are investing in new approaches that target the underlying cause of gout, such as with our Arrowhead and HemoShear preclinical programs.

In summary, we expect another busy and productive year ahead. I will now turn the call over to Paul.

Paul Hoelscher
Executive Vice President, Chief Financial Officer

Thanks, Liz.

Fourth-Quarter 2021 Financial Results
My comments this morning will primarily focus on our non-GAAP results, unless otherwise noted. I will start with our fourth quarter results followed by our financial guidance for 2022.

Fourth-quarter net sales were $1 billion, representing year-over-year growth of 36%, driven by the strong performances of our key growth drivers, TEPEZZA and KRYSTEXXA. This closed out a record year, with full-year total net sales of $3.2 billion, nearly 50% growth compared to 2020.

Our orphan segment generated fourth-quarter net sales of $940 million, a year-over-year increase of 50%. Orphan segment operating income was $421 million.

Net sales for the inflammation segment were $74 million, with segment operating income of $33 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 gross profit ratio was 86.5% in the fourth quarter and 86.9% for the full year.

Fourth-quarter non-GAAP operating expenses were $460 million. This included non-GAAP R&D expense of $115 million, or 11% of net sales. As we noted in December, we no longer exclude upfront and milestone payments related to collaboration and license agreements from our non-GAAP financial measures. So R&D expense in the fourth quarter includes approximately $36 million of upfront and milestone payments. For the full year, our non-GAAP R&D expense was $373 million, which includes approximately $90 million of upfront and milestone payments.

Our non-GAAP SG&A expense was $345 million in the fourth quarter and $1.1 billion for the full year.

Fourth-quarter adjusted EBITDA was $416 million, or 41% of net sales, representing year-over-year growth of 22%. Our full-year adjusted EBITDA was $1.3 billion, or approximately 40% of net sales, representing growth of 33%.

The non-GAAP tax rate for the fourth quarter was 15.5%, bringing our full-year non-GAAP tax rate to 9.8%.

Non-GAAP net income for the fourth quarter was $334 million and non-GAAP diluted earnings per share were $1.41. Our full-year non-GAAP diluted earnings per share were $4.62.

The weighted average shares outstanding used to calculate fourth-quarter and full-year 2021 non-GAAP diluted EPS were 236 million shares and 236 million shares, respectively.

Fourth-quarter and full-year non-GAAP operating cash flows were $554 million and $1.19 billion, respectively.

As of December 31, cash and cash equivalents were $1.58 billion. With 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 debt outstanding is $2.6 billion, with the earliest maturity in 2026. As of December 31, our gross debt-to-last-12-months adjusted EBITDA leverage ratio was 2 times. Our net debt was $1 billion, resulting in a net-debt-to-last-12-months adjusted EBITDA leverage ratio of 0.8 times.

2022 Guidance

Moving on now to our outlook for 2022, this morning, we provided 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 expect full-year 2022 gross margin of approximately 87%. We expect our gross margin to be the highest in the first quarter. As we progress through the year, we expect gross margin to decrease as we reach higher-percentage tiers on the TEPEZZA royalties we pay.

Full-year adjusted EBITDA is expected to be $1.63 to $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 growth in net sales, 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. We expect our commercial performance to drive significant margin accretion, which would more than offset this increased investment.

As we think about our 2022 operating expense, we expect a steady increase over the course of the year. Excluding the R&D-related milestone payments from the fourth quarter of 2021, non-GAAP operating expenses were approximately $425 million. For 2022, we would expect a modest quarter-over-quarter increase from there, mainly driven by R&D.

We expect our full-year non-GAAP net interest expense to be approximately $80 million to $85 million.

We expect our full-year 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 estimate that our cash tax rate will be in the mid-to-high single digits. And 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 expect our full-year 2022 weighted average diluted share count to be approximately 238 million shares.

First-Quarter 2022

And finally, Now let me touch on the first quarter. As we see every year, our first quarter net sales are expected to be the lowest of the year, impacted by seasonality as patients experience co-pay and deductible resets and other changes in their healthcare coverage. We also saw an impact from the COVID-19 Omicron variant earlier this year due to delays in office visits and scheduled infusions for both TEPEZZA and KRYSTEXXA. We have seen a nice uptick in the trajectory since then and feel good about our full-year expectations. Therefore, we expect a typical step-down in net sales this year – in the mid-teens – from the fourth quarter of 2021 to the first quarter of 2022.

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

Tim Walbert
Chairman, President and Chief Executive Officer

Thank you, Paul.

- 2021 was another outstanding year for Horizon, with record financial results supported by strong commercial execution, as well as accelerated progress on our strategic goals – most importantly, the expansion of our pipeline.
- We expect to initiate seven new clinical trials this year – two of which have recently started.
- As we look to the future, we see a combined peak annual net sales potential of approximately $10 billion for our current growth drivers TEPEZZA, KRYSTEXXA and UPLIZNA along with our pipeline candidates.
- We expect another stand-out year of performance. Our full-year 2022 guidance represents one of the best growth profiles among our profitable large-cap and biotech peers.
- With more than $1.5 billion of cash, we have significant flexibility to support our business development activities to further expand our pipeline.

With that, we will now open the call up for questions.

Tina Ventura
Senior Vice President, Chief Investor Relations Officer

Thank you, Livia. 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.