First-Quarter 2022 Summary

Horizon Therapeutics plc

May 4, 2022

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Horizon's full-year 2022 net sales and adjusted EBITDA guidance; expected financial performance and operating results in future periods, including potential growth in net sales of certain of Horizon's medicines; development, manufacturing and commercialization plans; expected timing of clinical trials and regulatory submissions; potential market opportunity for and benefits of Horizon's medicines and medicine candidates; and business and other statements that are not historical facts. These forward-looking statements are based on Horizon's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks that Horizon's actual future financial and operating results may differ from its expectations or goals; Horizon's ability to grow net sales from existing medicines; impacts of the COVID-19 pandemic and actions taken to slow its spread, including impacts on supplies and net sales of Horizon's medicines and potential delays in clinical trials; impacts of the on-going war between Russia and Ukraine; the fact that Horizon's full-year 2022 net sales, adjusted EBITDA and TEPEZZA net sales guidance and the expected timing of certain TEPEZZA clinical trials assume that future committed manufacturing slots for TEPEZZA are not cancelled and are run successfully, which could be impacted by additional government-mandated COVID-19 vaccine production orders and other risks associated with the manufacture of biologic medicines; risks associated with acquisitions, such as the risk that the businesses will not be integrated successfully, that such integration may be more difficult, time-consuming or costly than expected or that the expected benefits of the transaction will not occur; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; risks relating to Horizon's ability to successfully implement its business strategies, including its manufacturing and global expansion strategy; risks inherent in developing novel medicine candidates and existing medicines for new indications; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information.

Presentation At A Glance

1. Horizon Overview, Differentiation and Strategy
2. First-Quarter 2022 Results and Full-Year Guidance
3. Our Pipeline
4. Our Key Growth Drivers: TEPEZZA®, KRYSTEXXA® and UPLIZNA®

What Sets Horizon Apart

Excellence in Commercial Execution

We accelerate the growth trajectory and maximize the potential of our medicines through best-in-class commercial execution

Proven and Disciplined Business Development

We acquire and license medicines through our strong in-house business development capability, focused on opportunities where we are uniquely positioned to drive value

Strong Research and Development Capability

We leverage deep drug development experience and an agile approach to continually innovate with our existing medicines and bring new ones to market

First-Quarter 2022 and Recent Company Highlights

Strong Financial Results and Significant Progress Executing on Our Strategy

Financial Highlights

- First-quarter 2022 net sales of **$885.2M**; adjusted EBITDA of **$371.2M**
- First-quarter 2022 TEPEZZA net sales of **$501.5M**; continue to expect full-year 2022 net sales percentage growth in **the mid-30s**
- First-quarter 2022 KRYSTEXXA net sales of **$140.7M**; continue to expect full-year 2022 net sales growth of **more than 20%**
- Maintaining full-year 2022 net sales guidance of **$3.9B to $4.0B** and adjusted EBITDA guidance of **$1.63B to $1.70B**
- Cash position of **$1.64B** and gross leverage ratio of **1.6 times**(1) at March 31, 2022

Executing on Our Strategy

- **U.S. FDA granted priority review of sBLA** for co-treatment of KRYSTEXXA plus methotrexate with PDUFA action date of July 7, 2022
- **European Commission approved UPLIZNA** for the treatment of NMOSD; initiating European launch strategy starting with Germany
- **Advancing global expansion strategy** with launch preparations to support potential approval of TEPEZZA and UPLIZNA in Brazil
- **Initiated 2 clinical trials:** HZN-825 in IPF and TEPEZZA OPTIC-J trial; 5 additional trials expected to initiate this year
- **Announced positive topline data** from Phase 2 trial evaluating dazodalibep (HZN-4920) in patients with rheumatoid arthritis; study met primary endpoint across all doses and dazodalibep was well tolerated; first proof-of-concept data for this mechanism of action
- Continued to be recognized as a top workplace: **one of Fortune's "100 Best Companies to Work For®"** and retaining the **highest ranked position in the biotechnology and pharmaceutical category**

(1) Gross Leverage Ratio: Principal amount of debt outstanding at March 31, 2022 to adjusted EBITDA over the preceding 12-month period. Principal amount of debt at March 31, 2022 was $2.602B.
EBITDA: Earnings before interest, taxes, depreciation and amortization. Adjusted EBITDA is a non-GAAP measure; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.
PDUFA: Prescription drug user fee act. | sBLA: Supplemental biologics license application. | NMOSD: neuromyelitis optica spectrum disorder. | IPF: idiopathic pulmonary fibrosis.

First-Quarter 2022 Financial Results

Cash Position More Than Doubled Driven By Continued Commercial Execution

($M, except for per share amounts and percentages)	Q1 2022	Q1 2021[1]	% Change
Net sales	**$885.2**	**$342.4**	**159**
Net income (loss)	204.3	(123.4)	NM
Non-GAAP net income	315.8	4.8	NM
Adjusted EBITDA	**371.2**	**42.8**	**767**
Earnings (loss) per share – diluted	0.87	(0.55)	NM
Non-GAAP earnings per share – diluted	**1.34**	**0.02**	**NM**
Cash and cash equivalents[2]	**1,643.1**	**811.6**	**102**

(1) First-quarter 2021 results were negatively impacted by a short-term TEPEZZA supply disruption due to U.S. government-mandated COVID 19-vaccine orders.
(2) Cash balance at March 31, 2022 and March 31, 2021, respectively.
Note: Non-GAAP net income, adjusted EBITDA and non-GAAP earnings per share diluted are non-GAAP measures; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

First-Quarter 2022 Orphan Segment Results

Net Sales Growth Driven by Strong Performance Across the Portfolio

($M)	Q1 2022	Q1 2021	% Change
TEPEZZA®(1)	$501.5	$2.1	NM
KRYSTEXXA®	140.7	106.7	32
RAVICTI®	78.3	72.8	7
PROCYSBI®	49.6	43.4	14
ACTIMMUNE®	31.3	28.8	9
UPLIZNA®(2)	30.5	1.8	NM
BUPHENYL®	2.2	1.7	30
QUINSAIR™	0.3	0.2	41
Orphan Net Sales	**$834.4**	**$257.5**	**224**
Orphan Segment Operating Income	**$351.5**	**$1.1**	**NM**

(1) First-quarter 2021 results were negatively impacted by a short-term TEPEZZA supply disruption due to U.S. government-mandated COVID 19-vaccine orders.
(2) UPLIZNA was acquired on March 15, 2021. First-quarter 2022 UPLIZNA net sales included $5.2 million in revenue and milestone payments from the Company's international partners.| NM: Not meaningful.

First-Quarter 2022 Inflammation Segment Results

Investing Cash Flows in Growth Drivers and Pipeline Expansion

($M)	Q1 2022	Q1 2021	% Change
PENNSAID 2%®	$35.4	$45.8	(23)
RAYOS®	13.5	15.3	(12)
DUEXIS®(1)	1.1	19.5	(94)
VIMOVO®	0.9	4.3	(79)
Inflammation Net Sales	**$50.9**	**$84.9**	**(40)**
Inflammation Segment Operating Income	**$15.3**	**$42.7**	**(64)**

(1) On Aug. 4, 2021, Alkem Laboratories, Inc. initiated an at-risk launch of generic DUEXIS in the U.S.

Maintaining Full-Year 2022 Guidance

	Guidance	Year-Over-Year Growth[1]
Net Sales	**$3.9B to $4.0B**	22%
Adjusted EBITDA	**$1.63B to $1.70B**	30% *230 basis points of margin expansion[2]*

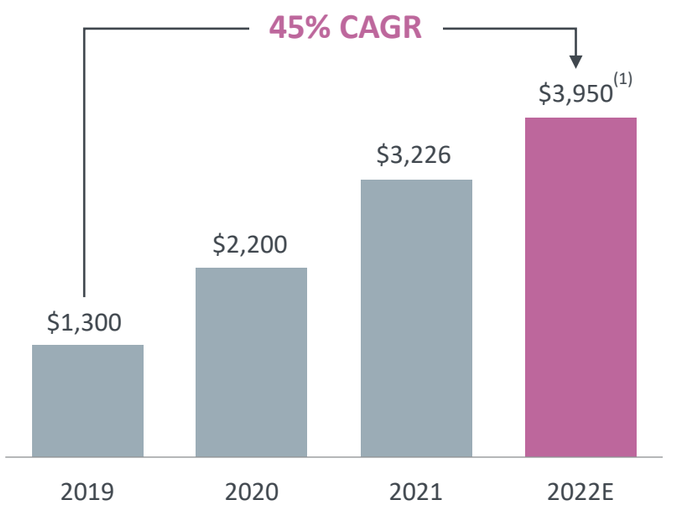
Key Highlights

- **TEPEZZA** full-year 2022 net sales percentage growth in the **mid-30s**
- **KRYSTEXXA** full-year 2022 net sales growth of **more than 20%**

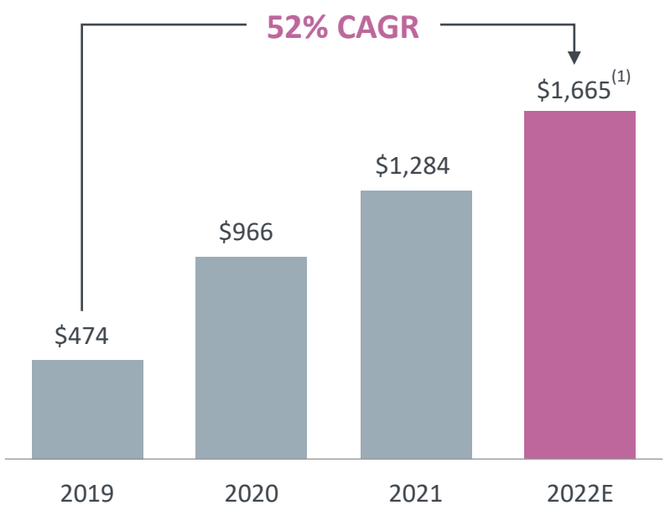
(1) Year-over-year growth at the midpoint of guidance. (2) Midpoint of net sales and adjusted EBITDA guidance implies 230 basis points of margin expansion. Margin is calculated as adjusted EBITDA divided by net sales for the respective time period.
EBITDA: Earnings before interest, taxes, depreciation and amortization. Adjusted EBITDA and adjusted EBITDA margin are non-GAAP measures; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

2022 Guidance Implies Continued Strong Execution While Increasing R&D Investment

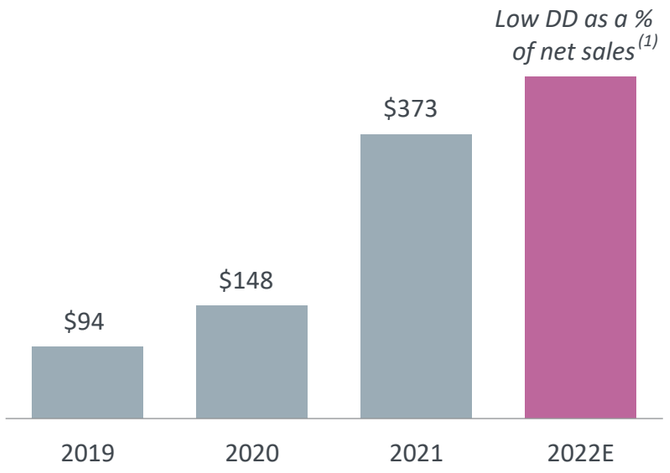
Net Sales Growth ($M)



Adj. EBITDA Growth ($M)



R&D Investment ($M)



Financial Goals

- **Generate strong double-digit net sales growth**
- **Generate strong double-digit adjusted EBITDA growth**
- **Generate meaningful adjusted EBITDA margin expansion**
- **Maintain R&D investment at double-digits as a % of sales**
- **Generate top-tier performance for our shareholders**

CAGR: Compound annual growth rate. | DD: Double-digit. | EBITDA: Earnings before interest, taxes, depreciation, and amortization. Adjusted EBITDA is a non-GAAP measure; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.
(1) Midpoint of full-year 2022 net sales and adjusted EBITDA guidance as of May 4, 2022.

Executing on Our Strategy Has Positioned Horizon as a Leading, High-Growth, Global Biotech

Expanding our pipeline for sustainable growth

Maximizing the value of our key growth drivers

Building a global presence

Progress and Expected Milestones in 2022

- ✓ U.S. FDA granted priority review of the Company's sBLA for co-treatment of KRYSTEXXA plus methotrexate
- ✓ Announced positive topline data in dazodalibep rheumatoid arthritis trial; first proof-of-concept data for this mechanism of action
- ✓ UPLIZNA approved in Europe for NMOSD
- ✓ Initiated build-out of infrastructure in Brazil to support potential approvals of TEPEZZA and UPLIZNA
- Launch KRYSTEXXA plus methotrexate following July 7th PDUFA action date(1); begin to actively promote its many benefits, including >30% improvement in response rate(2)
- Initiate seven clinical trials; two initiated in the first quarter
- Launch UPLIZNA in Europe, starting with Germany
- Expect second dazodalibep data readout in kidney transplant rejection
- Expand pipeline through internal innovation and business development

Expected Milestones in 2023 and Beyond

- Anticipate 6 data readouts in 2023, including TEPEZZA chronic TED trial and UPLIZNA in MG and IgG4-RD(3)
- Launch UPLIZNA in other targeted international markets, including Brazil(1)
- Complete TEPEZZA OPTIC-J trial for potential approval in Japan; prepare for potential launch in Brazil and other targeted international markets(1)
- Continue to expand pipeline to drive long-term growth
- Obtain regulatory approval for Waterford biologics drug product manufacturing facility
- Advance toward peak annual net sales expectations:
  - TEPEZZA: >$3.5B(4)
  - KRYSTEXXA: >$1B(4)
  - UPLIZNA: >$1B(4)

(1) Assuming marketing approval in applicable jurisdictions. (2) MIRROR: Randomized, placebo-controlled trial with 152 patients. 71% (71 of 100 patients) who were randomized to receive KRYSTEXXA plus methotrexate achieved the primary endpoint – the proportion of sUA responders (sUA <6mg/dL) during Month 6 compared to 39% (20 of 52 patients) who were randomized to receive KRYSTEXXA plus placebo. (3) Because the UPLIZNA IgG4-RD trial is an event-driven trial, the readout timing may extend beyond 2023. (4) Horizon estimate of TEPEZZA and KRYSTEXXA peak U.S. annual net sales of >$3B and >$1B, respectively, and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales. Horizon estimate of UPLIZNA peak global annual net sales of >$1B assumes three global indications in NMOSD, MG and IgG4-RD. UPLIZNA is currently approved for NMOSD in the U.S., EU member states, Japan and China. | NMOSD: neuromyelitis optica spectrum disorder.
sBLA: Supplemental biologics license application. | MG: Myasthenia gravis. | IgG4-RD: Immunoglobulin G4-related disease. | FSGS: focal segmental glomerulosclerosis. | PDUFA: Prescription drug user fee act. | TED: Thyroid eye disease.

Pipeline Update

Enhancing Horizon's Profile as an Innovation-Driven Biotech

Advancing Horizon's Position as a Leading Biotech With a Rapidly Growing Pipeline

Expanding Our Pipeline Through Aggressive Internal Investment and External Business Development

- Expanding therapeutic areas of focus
- Maximizing pipeline molecules
- Expanding our early-stage pipeline through partnerships and collaborations
- Building research capabilities to generate discovery-stage candidates

2020

- **13 pipeline programs**
- **Acquired HZN-825**, an $LPAR_1$ antagonist; added new therapeutic area in respiratory
- **Initiated development program** to assess potential for TEPEZZA subcutaneous administration
- **Announced 4 new programs** for TEPEZZA, KRYSTEXXA and HZN-825
- **R&D spend** at 7% of net sales

2022

- **>20 pipeline programs**
- **Initiate 7 new clinical trials**, including five across daxdilimab and dazodalibep
- **U.S. FDA granted priority review** of sBLA for co-treatment of KRYSTEXXA plus methotrexate; PDUFA action date of July 7th
- **2 data readouts** for dazodalibep
- **Progress our preclinical collaborations** with Arrowhead and Alpine
- **R&D spend** expected to be double-digits as a % of net sales

Long Term

- **10 potential approvals** in the second half of the decade
- **6 data readouts** expected in 2023(1)
- **Significantly increase R&D spend**; double-digits as a % of net sales
- **Expand pipeline** through internal innovation and business development
- **Generate high-quality** INDs through internal R&D
- Continue to build out our R&D organization with **top talent**

$LPAR_1$: Lysophosphatidic acid receptor 1. | IND: Investigational new drug. | IgG4-RD: Immunoglobulin G4-related disease. | PDUFA: Prescription drug user fee act. | sBLA: Supplemental biologics license application.
(1) Because the UPLIZNA IgG4-RD trial is an event-driven trial, the readout timing may extend beyond 2023.

Expanding Our Pipeline to Drive Long-Term Growth

Medicine/Candidate	Program/Potential Indication
UPLIZNA	Myasthenia Gravis (MG)
	IgG4-Related Disease (IgG4-RD)
Daxdilimab (HZN-7734)	Systemic Lupus Erythematosus (SLE)
	Alopecia Areata (AA)(1)
	Discoid Lupus Erythematosus (DLE)(1)
	Lupus Nephritis (LN)(1)
	Dermatomyositis (DM)(1)
Dazodalibep (HZN-4920)	Sjögren's Syndrome
	Rheumatoid Arthritis(2)
	Kidney Transplant Rejection
	Focal Segmental Glomerulosclerosis (FSGS)(1)
HZN-825	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
	Idiopathic Pulmonary Fibrosis (IPF)
TEPEZZA	TED in Japan (OPTIC-J)
	Subcutaneous Administration
	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
HZN-1116	Autoimmune Diseases
Alpine	Autoimmune Diseases
ARO-XDH	Next-Gen Uncontrolled Gout
HemoShear	Novel Gout Targets

- **>20 programs** in total
- **7 programs** expected to initiate in 2022; 2 already initiated in 1Q
- **8 data readouts** anticipated in 2022-2023(3)
- **10 potential approvals** in the second half of the decade
- **4 additional Phase 4 programs:**
  - TEPEZZA chronic TED
  - KRYSTEXXA shorter infusion duration
  - KRYSTEXXA monthly dosing
  - KRYSTEXXA retreatment

IgG4: Immunoglobulin G4. TED: Thyroid eye disease.
(1) Planned programs; not yet initiated.
(2) Trial complete. Announced positive topline results on May 3, 2022. The trial met the primary endpoint across all doses and was well tolerated.
(3) Because the UPLIZNA IgG4-RD trial is an event-driven trial, the readout timing may extend beyond 2023.

Upcoming Trial Initiations and Data Readouts

7 Trials Expected to Initiate in 2022

HZN-825:

- ✓ Idiopathic Pulmonary Fibrosis (IPF)

Daxdilimab (HZN-7734):

- Alopecia Areata (AA)
- Discoid Lupus Erythematosus (DLE)
- Lupus Nephritis (LN)
- Dermatomyositis (DM)

Dazodalibep (HZN-4920):

- Focal Segmental Glomerulosclerosis (FSGS)

TEPEZZA:

- ✓ TED in Japan (OPTIC-J)

8 Data Readouts Anticipated in 2022-2023

TEPEZZA:

- Chronic TED
- TED in Japan (OPTIC-J)

Dazodalibep (HZN-4920):

- ✓ Rheumatoid Arthritis
- Kidney Transplant Rejection
- Sjögren's Syndrome

UPLIZNA:

- Myasthenia Gravis (MG)
- IgG4-Related Disease (IgG4-RD)(1)

Daxdilimab (HZN-7734):

- Systemic Lupus Erythematosus (SLE)

(1) Because the UPLIZNA IgG4-RD trial is an event-driven trial, the readout timing may extend beyond 2023.
TED: Thyroid eye disease.

Strong Start to Our Target to Initiate Seven Clinical Trials in 2022

Initiated Two New Clinical Trials in the First Quarter

HZN-825 for Idiopathic Pulmonary Fibrosis (IPF)

- **IPF** is a rare progressive lung disease characterized by dyspnea, chronic cough and potentially death; IPF is the most common interstitial lung disease
- **Phase 2b trial design:** 360 patients; 1:1:1 randomization ratio to receive HZN-825 (one of two dosing groups) or placebo
- **Primary Endpoint:** Change in forced vital capacity (FVC) % predicted after 52 weeks of treatment; measures lung capacity and is used to assess the progression of lung disease and the effectiveness of the treatment
- **Prevalence:** ~100K patients in the U.S.[(1)]; median survival of less than five years

TEPEZZA for Thyroid Eye Disease (TED) in Japan (OPTIC-J)

- **TED** is a serious, progressive and potentially vision-threatening rare autoimmune disease
- **Phase 3 trial design:** 50 patients; 1:1 randomization to receive TEPEZZA or placebo once every 3 weeks for a total of 8 infusions
- **Primary Endpoint:** Proptosis response rate at Week 24, measured by the percentage of participants with at least a 2 mm reduction in proptosis from baseline in the study eye, without deterioration in the fellow eye (≥ 2 mm increase)
- **Incidence:** ~3K-5K, estimated addressable annual incidence of acute moderate-to-severe TED patients in Japan[(2)]

(1) Barratt SL, Creamer A, Hayton C, Chaudhuri N. Idiopathic pulmonary fibrosis (IPF): an overview. J Clin Med. 2018;7(8):201. (2) Horizon estimate.

Alopecia Areata (AA) is a Compelling Indication for Daxdilimab Given the Presence of pDCs and Elevated Type 1 Interferon in AA Lesions

Alopecia Areata

- Autoimmune disorder characterized by nonscarring hair loss that can range from uneven hair loss, to total loss of hair on the scalp and even across the entire body
- pDCs have been detected in AA lesions and Type 1 interferon signatures are elevated in AA lesions[1]
- Preclinical models implicate pDCs in AA[2]

U.S. Patient Population and Opportunity

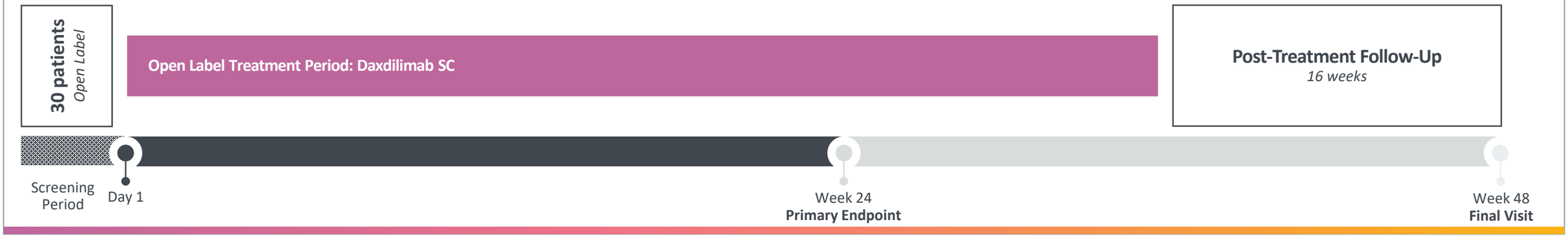
- >600K patients of which **~40K would be appropriate for novel therapies including biologics[3]**
- AA patients experience a significant impairment in quality of life, reduced vitality, depression and increased risk of comorbidities (e.g., thyroid disease, diabetes mellitus)[4,5]
- High unmet need given there are no approved therapies; current treatment involves off-label medicines which are subject to significant side effects and variable efficacy

pDC: Plasmacytoid dendritic cell.

(1) Rahal et al. JEADV (2014) 30(1): 119-123. (2) Ito et. al. Allergology International (2020) 69(1): 121-131. (3) Horizon estimate. (4) Rencz et al. Brit J of Dermatol (2016) 175: 561-571, Huang et al. Am Med Assoc (2013) 789-794, Liu et al. J Am Acad Dermatol (2016) 149(6): 1207-1213. (5) Aghaei et al. ISRN Dermatol (2014) 75(4):806-812.

Daxdilimab Phase 2 Trial in Alopecia Areata (AA) Expected to Initiate in the Second Quarter

Phase 2 Open-Label, Proof-of-Concept Trial Design in AA



Key Inclusion Criteria

- Moderate-to-severe AA (≥50% and ≤95% total scalp hair loss as defined by the SALT score at baseline); current episode of hair loss >3 months and <7 years at baseline
- Investigators' assessment that hair regrowth is possible; no evidence of active regrowth present at baseline; no known history of significant regrowth over last 6 months

- ***Primary Endpoint:*** Percent change from baseline in SALT score at Week 24
- ***Secondary Endpoints:*** Percent change from baseline in SALT score at Weeks 12-20 and 28-36; Proportion of participants who achieve ≥50% reduction in SALT from baseline at Weeks 12-36; Proportion of participants with absolute SALT score ≤10, 20, 30, 50 at Weeks 12-36; Same endpoints above for post-treatment duration from Weeks 40-48

SC: Subcutaneous. | SALT: Severity of Alopecia Tool.

Discoid Lupus Erythematosus (DLE) is a Compelling Indication for Daxdilimab Given the Presence of pDCs in DLE Skin Lesions and Elevated Type 1 Interferon Activity

Discoid Lupus Erythematosus

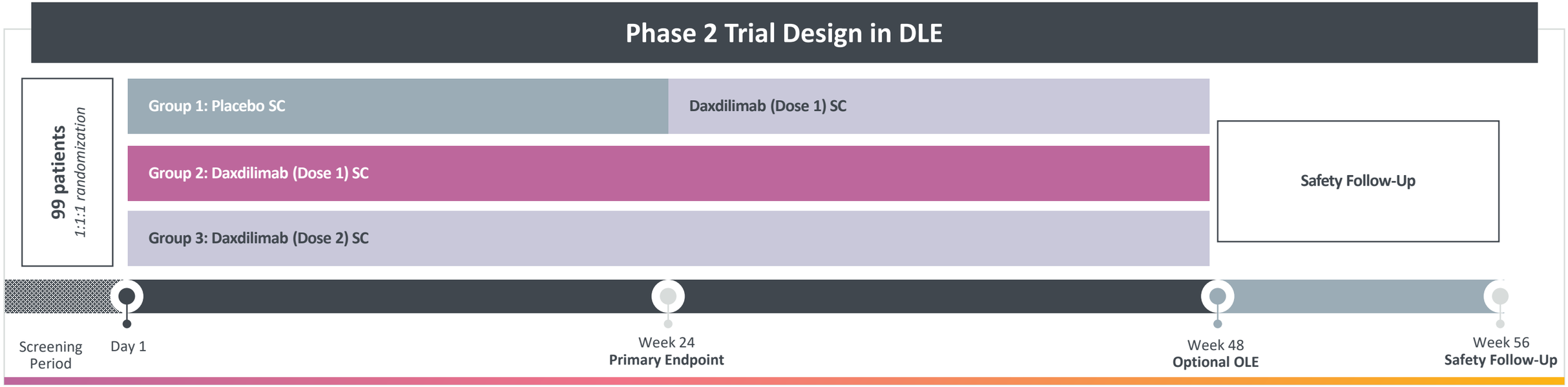
- Chronic, inflammatory skin condition that presents as intense inflamed lesions that heal with scarring, mostly observed on the head and neck
- Primary DLE is considered the most challenging scarifying skin manifestation to treat
- pDCs reported to be abundant in DLE skin lesions[1,2]
- Significantly elevated Type 1 interferon activity in DLE compared to healthy tissue[3]

U.S. Patient Population and Opportunity

- **~30K patients** would be appropriate for novel therapies, including biologics[4]
- Distinct, robust population; high disease burden
- Current standard of care is not uniformly effective and is associated with potential side effects

pDC: Plasmacytoid dendritic cell.
(1) Vermi et. al. Immunobiology (2009) 214: 877–886. (2) Rakhshan et al. An Bras Dermatol. 2020; 95(3): 307-13. (3) Braunstein et al. Br J. Dermatol (2012) 166(5): 971-5. (4) Horizon estimate.

Daxdilimab Phase 2 Trial in Discoid Lupus Erythematosus (DLE) Expected to Initiate Mid-Year



Key Inclusion Criteria

- Adults aged ≥ 18 to ≤ 75 years
- Moderate-to-severely active primary DLE refractory to standard of care
- Diagnosis of DLE for ≥ 6 months prior to screening

- ***Primary Endpoint:*** Mean change in CLASI-A score from baseline (Day 1) at Week 24
- ***Secondary Endpoints:*** Proportion of participants who achieve 0 or 1 on the CLA-IGA scale at Week 24 (5-point Likert scale [0-4]); Proportion of participants who achieve a ≥ 50% reduction in CLASI-A score from baseline at Week 24; Mean change in the SADDLE from baseline at Week 24

SC: Subcutaneous. | OLE: Open-label extension. | CLASI-A: Cutaneous lupus erythematosus disease area and severity index-activity. | CLA-IGA: Cutaneous lupus activity investigator's global assessment. | SADDLE: Score of activity and damage in discoid lupus erythematosus.

TEPEZZA

The First and Only Medicine Approved for Thyroid Eye Disease

TEPEZZA: One of the Most Successful Rare Disease Medicine Launches; Investing to Drive Continued Strong Double-Digit Net Sales Growth in the Years Ahead

TEPEZZA is the First and Only Medicine Approved for Thyroid Eye Disease

- **15K-20K:** Estimated U.S. annual incidence of acute moderate-to-severe TED patients (lasts 1-3 years)[1]
- **>70K:** Estimated U.S. prevalence of chronic TED patients[1]
- **3K-5K:** Estimated addressable annual incidence of acute moderate-to-severe TED patients in Japan[1]
- Evaluating launches in several additional countries

2020

- **$820M** of U.S. net sales
- **Initiated** TED market education efforts 6-12 months prior to January 2020 FDA approval
- **Educated** patients and physicians on TEPEZZA and TED; initiated DTC campaigns
- **Established** market structure and site-of-care network to simplify the patient journey

2022

- Expect U.S. net sales percentage **growth in mid-30s**
- Initiated **OPTIC-J trial in Japan**
- **Increase penetration** among our core prescribers and continue to expand the overall prescriber base
- **Expand field force** to drive referral strategy and invest further in DTC
- **Attend key medical meetings** to highlight the benefits of TEPEZZA
- **Expect to complete enrollment** in the chronic TED trial

Long Term

- **>$3.5B** peak global annual net sales potential[2]
- **Chronic TED trial** readout expected in 1H 2023
- **OPTIC-J** trial data readout expected in 2H 2023
- Launch TEPEZZA in **Japan, Brazil and other international markets**[3]
- Improve patient experience with **subcutaneous administration program**

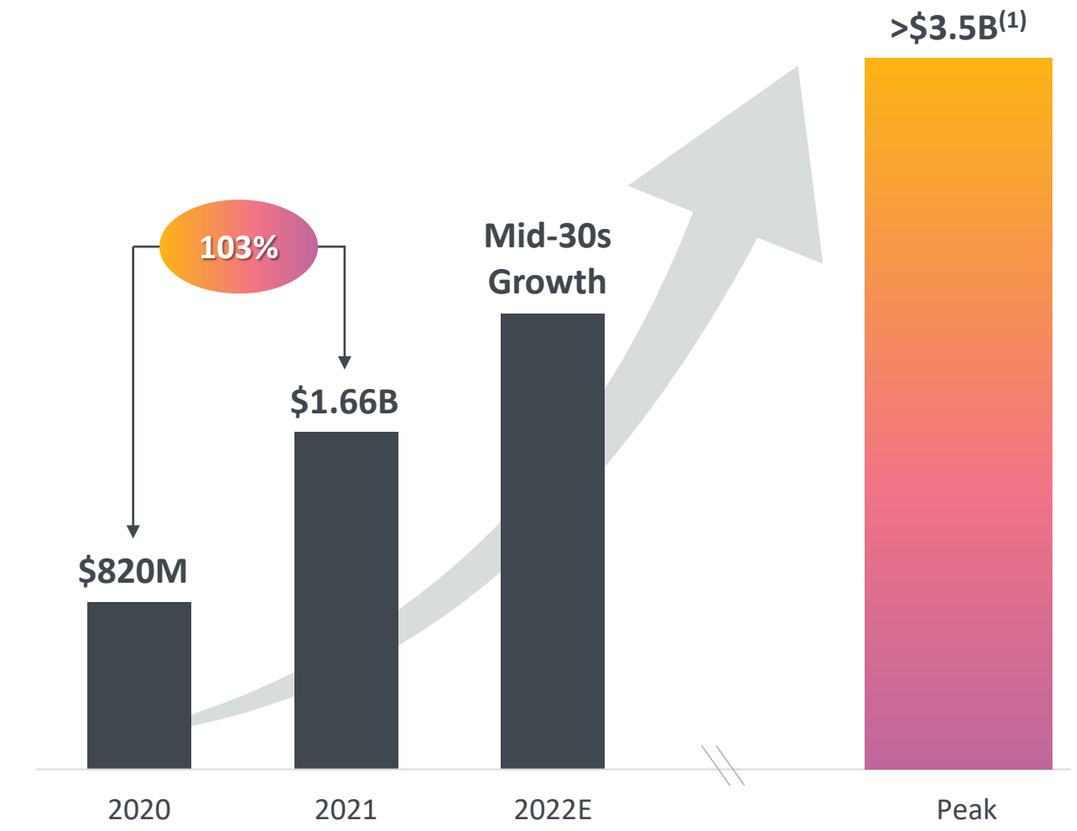
TED: Thyroid eye disease. | DTC: Direct-to-consumer. (1) Horizon estimate. (2) Horizon estimate of TEPEZZA peak U.S. annual net sales of >$3B and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales. (3) Subject to successful clinical trials and regulatory approvals.

TEPEZZA: Significant Opportunity Exists to Exceed $3.5B in Global Peak Annual Net Sales

Growth Drivers: Objective to Drive Continued Strong Uptake and Expand TEPEZZA to More Patients

1. Increase the reach to new prescribers while further penetrating our existing prescriber base
2. Increase penetration in the chronic population through data generation
3. Maximize the potential of TEPEZZA through global expansion

Exceptional Launch and Significant Peak Annual Net Sales Opportunity



(1) Horizon estimate of TEPEZZA peak U.S. annual net sales of >$3B and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales.

KRYSTEXXA

The First and Only Medicine Approved For Uncontrolled Gout

KRYSTEXXA: Our Strategy Has Significantly Accelerated Growth; Expect to Drive Strong Double-Digit Net Sales Growth in the Years Ahead

KRYSTEXXA is the Only Medicine Approved For Uncontrolled Gout

- **9.5M:** Estimated U.S. gout patients growing at low-single digits per year(1)
- **>100K:** Uncontrolled gout patients appropriate for KRYSTEXXA in the U.S., growing in line with gout population(2)
- **<5% penetration**(3); significant opportunity exists

2017

- **$156M** of U.S. net sales
- **Initiated** immunomodulation strategy
- Immunomodulation use in the **low-to-mid single digits**(4)
- **Doubled** commercial team; rheumatology focused
- **Identified nephrology** as an additional therapeutic area

2022

- Expect U.S. net sales **growth of more than 20%**
- Immunomodulation use at **approximately 50%** of new patient starts
- **U.S. FDA granted priority review** of sBLA for co-treatment of KRYSTEXXA plus methotrexate
- **Disseminate** MIRROR data at medical meetings
- **Launch KRYSTEXXA plus methotrexate** following July 7th PDUFA action date(5)

Long Term

- **>$1B** peak U.S. net sales potential(6); **>70% immunomodulation use**(7)
- Establish KRYSTEXXA plus immunomodulation as the **standard of care**
- **Increase penetration** in our core specialties of rheumatology and nephrology
- Improve patient experience with **monthly dosing** and **shorter infusion duration**

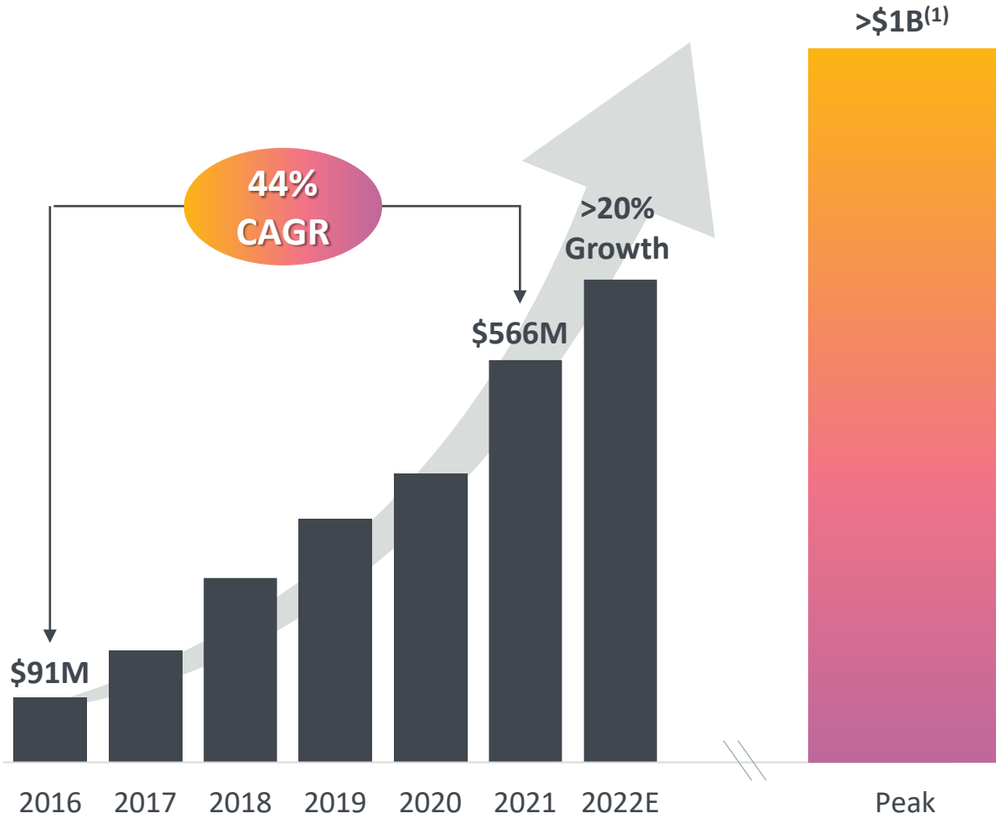
Uncontrolled gout: Chronic gout refractory (unresponsive) to conventional therapies. (1) Prevalence of gout and hyperuricemia in the U.S. general population: The National Health and Nutrition Examination Survey (NHANES) 2007-2016. Arthritis Rheum. 2019 Jun;71(6):991-999. (2) Approximate number of patients in our annual addressable target market in rheumatology and nephrology; Horizon estimate. (3) Horizon estimate of patients treated in 2020. (4) Horizon estimate. (5) Assuming sBLA approval. (6) Horizon estimate of KRYSTEXXA peak annual U.S. net sales of >$1B. (7) Horizon target. PDUFA: Prescription drug user fee act. | sBLA: Supplemental biologics license application.

KRYSTEXXA: Significant Opportunity Exists to Exceed $1B in U.S. Peak Annual Net Sales

Growth Drivers: Objective to Increase Total Patients and Vials Per Patient

1. Redefine KRYSTEXXA plus immunomodulation as the standard of care
2. Expand utilization in core specialty areas and elevate urgency to treat
3. Invest to improve the patient experience

Continued Strong Growth and Significant Peak Annual Net Sales Opportunity



(1) Horizon estimate of KRYSTEXXA peak annual U.S. net sales of >$1B. | CAGR: Compound annual growth rate.

UPLIZNA

First and Only FDA-Approved B-Cell-Depleting Therapeutic for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD)

Relaunch of UPLIZNA to Drive Increased Adoption; Expect Strong Double-Digit Net Sales Growth in the Years Ahead

UPLIZNA is the First and Only FDA-Approved B-Cell-Depleting Therapeutic for NMOSD

- **~10K:** Diagnosed NMOSD patients in the U.S.; **~8K** AQP4+[1]
- **400:** New diagnoses each year[1]
- Pursuing additional indications where B-cell dysregulation plays an important role

2020

- **FDA approved** for the treatment of NMOSD
- **Launched** by Viela Bio
- **$12M** of net sales[2]

2022

- **$31M** of net sales YTD[3]
- **Expand prescriber base** to generate continuous PEF and patient start growth
- **Continue to invest** in medical and scientific engagement to establish scientific leadership position in NMOSD
- **UPLIZNA approved in Europe and China** for NMOSD; expect to initiate commercialization efforts, starting with Germany

Long Term

- **>$1B** peak global annual net sales potential[4]
- **Raise awareness** of the benefits of UPLIZNA versus other therapies
- Drive **patient and physician conviction** of UPLIZNA
- **Launch** in Brazil and other targeted international markets[5]
- MG and IgG4-RD **data readouts in 2023**[6]
- Establish UPLIZNA as **leading treatment** in NMOSD, MG and IgG4-RD[7]

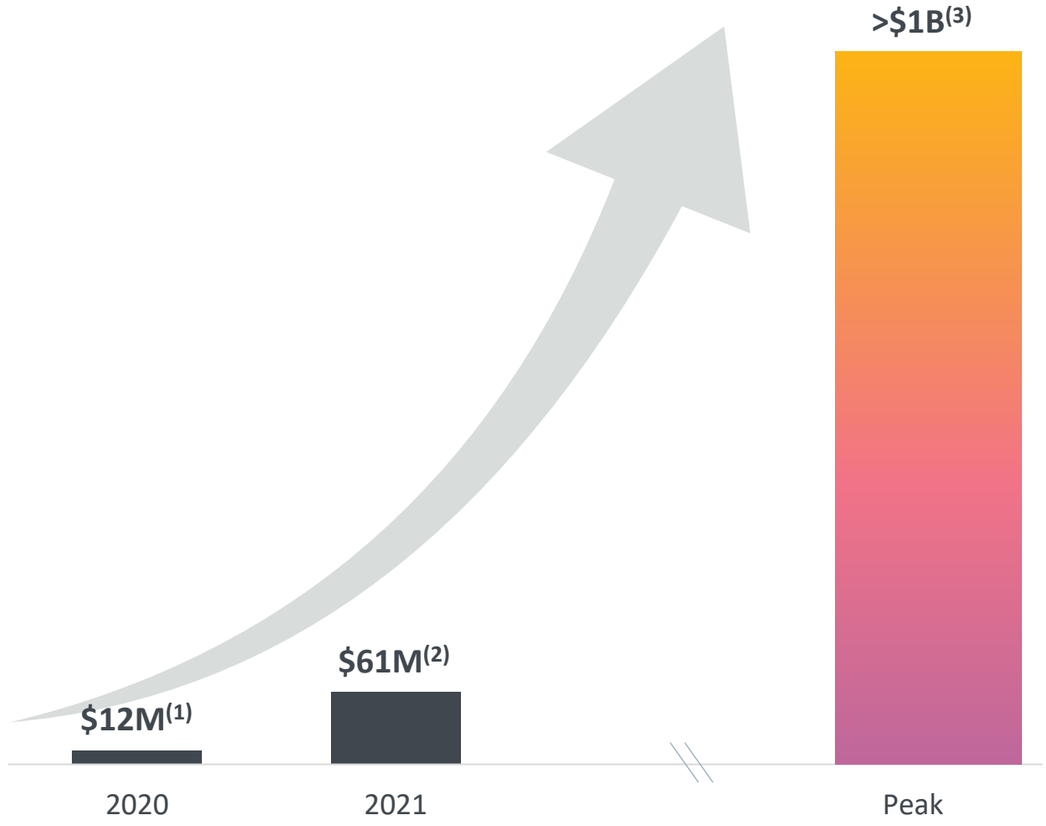
NMOSD: neuromyelitis optica spectrum disorder. | AQP4: Aquaporin-4. | YTD: Year to date. | MG: Myasthenia gravis. | IgG4-RD: Immunoglobulin G4-related disease. | PEF: Patient enrollment form. (1) Horizon estimate. (2) Viela sales. (3) First-quarter 2022 UPLIZNA net sales included $5.2 million in revenue and milestone payments from the Company's international partners. (4) Horizon estimate of UPLIZNA peak global annual net sales of >$1B. Assumes three global indications in NMOSD, MG and IgG4-RD. UPLIZNA is currently approved for NMOSD in the U.S., EU member states, Japan and China. (5) Subject to regulatory approvals. (6) Because the UPLIZNA IgG4-RD trial is an event-driven trial, the readout timing may extend beyond 2023. (7) Subject to successful clinical trials and regulatory approval for MG and IgG4-RD indications.

UPLIZNA: Significant Opportunity Exists to Exceed $1B in Global Peak Annual Net Sales

Growth Drivers: Objective in NMOSD to Transition Existing Patients and Drive Uptake in New Patients

1. Drive awareness and understanding of UPLIZNA's full range of benefits and differentiated clinical profile
2. Drive patient initiation and adherence, and cultivate a positive patient experience
3. Maximize the potential of UPLIZNA through additional indications and global expansion

UPLIZNA Global Net Sales Opportunity



(1) Viela sales. (2) UPLIZNA was acquired on March 15, 2021. Does not include the $10.6M that Viela reported prior to the acquisition. (3) Horizon estimate of UPLIZNA peak global annual net sales of >$1B. Assumes three global indications in neuromyelitis optica spectrum disorder (NMOSD), myasthenia gravis (MG) and immunoglobulin G4-related disease (IgG4-RD). UPLIZNA is currently approved for NMOSD in the U.S., EU member states, Japan and China.

Reconciliations of GAAP to Non-GAAP Measures

Note Regarding Use of Non-GAAP Financial Measures

EBITDA, or earnings before interest, taxes, depreciation and amortization, and adjusted EBITDA are used and provided by Horizon as non-GAAP financial measures. Horizon provides certain other financial measures such as non-GAAP net income, non-GAAP diluted earnings per share, non-GAAP operating expenses and non-GAAP operating income, each of which include adjustments to GAAP figures. These non-GAAP measures are intended to provide additional information on Horizon's performance, operations, expenses, profitability and cash flows. Adjustments to Horizons GAAP figures as well as EBITDA exclude acquisition and/or divestiture-related costs, manufacturing plant start-up costs, restructuring and realignment costs and litigation settlements, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, non-cash interest expense, long-lived assets impairment charges, loss on debt extinguishments, gain (loss) on sale of assets, gain on equity security investments and other non-cash adjustments. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. Horizon maintains an established non-GAAP cost policy that guides the determination of what costs will be excluded in non-GAAP measures. Horizon believes that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of Horizon's financial and operating performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of the Company's historical and expected 2022 financial results and trends and to facilitate comparisons between periods and with respect to projected information. In addition, these non-GAAP financial measures are among the indicators Horizon's management uses for planning and forecasting purposes and measuring the Company's performance. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures used by the Company may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies. Horizon has not provided a reconciliation of its full-year 2022 adjusted EBITDA outlook to an expected net income (loss) outlook because certain items such as acquisition/divestiture-related expenses and share-based compensation that are a component of net income (loss) cannot be reasonably projected due to the significant impact of changes in Horizon's stock price, the variability associated with the size or timing of acquisitions/divestitures and other factors. These components of net income (loss) could significantly impact Horizon's actual net income (loss).

GAAP to Non-GAAP Reconciliation

EBITDA and Adjusted EBITDA – Three Months Ended March 31

$ in thousands	Three Months Ended March 31,		Twelve Months Ended December 31,		
	2022	2021	2021	2020	2019
GAAP net income (loss)	**$ 204,261**	**$ (123,351)**	**$ 534,491**	**$ 389,796**	**$ 573,020**
Depreciation	5,852	4,451	17,475	24,303	6,733
Amortization and step-up:					
Intangible amortization expense	89,260	66,369	336,277	255,148	230,424
Inventory step-up expense	27,201	911	27,572	-	89
Interest expense, net (including amortization of debt discount and deferred financing costs)	21,256	13,460	81,063	59,616	87,089
(Benefit) expense for income taxes	(31,522)	(47,751)	(71,664)	11,849	(593,244)
EBITDA	**$ 316,308**	**$ (85,911)**	**$ 925,214**	**$ 740,712**	**$ 304,111**
Other non-GAAP adjustments:					
Acquisition/divestiture-related costs	1,589	49,108	95,929	49,196	3,556
Loss (Gain) on equity security investments	4,646	-	(1,257)	-	-
Restructuring and realignment costs	537	6,093	26,309	(141)	237
Manufacturing plant start-up costs	807	-	3,622	-	-
Impairment of long-lived asset	-	12,371	12,371	1,713	-
(Gain) Loss on sale of assets	-	-	(2,000)	(4,883)	10,963
Share-based compensation	47,300	61,166	219,086	146,627	91,215
Litigation settlement	-	-	5,000	-	1,000
Fees related to refinancing activities	-	-	-	54	2,292
Loss on debt extinguishment	-	-	-	31,856	58,835
Drug substance harmonization costs	-	-	-	542	457
Charges relating to discontinuation of Friedreich's ataxia program	-	-	-	-	1,076
Total of other non-GAAP adjustments	**54,879**	**128,738**	**359,060**	**224,964**	169,631
Adjusted EBITDA	**$ 371,187**	**$ 42,827**	**$ 1,284,274**	**$ 965,676**	**$ 473,742**

GAAP to Non-GAAP Reconciliation

Operating Income – Three Months Ended March 31

$ in thousands	Three Months Ended March 31, 2022	2021
GAAP operating income (loss)	**$ 194,317**	**$ (160,018)**
Non-GAAP adjustments:		
Acquisition/divestiture-related costs	1,589	49,391
Restructuring and realignment costs	537	6,093
Manufacturing plant start-up costs	807	-
Amortization and step-up:		
Intangible amortization expense	89,260	66,369
Inventory step-up expense	27,201	911
Impairment of long-lived asset	-	12,371
Share-based compensation	47,300	61,166
Depreciation	5,852	4,451
Total of non-GAAP adjustments	**172,546**	**200,752**
Non-GAAP operating income	**$ 366,863**	**$ 40,734**
Foreign exchange gain (loss)	420	(848)
Other income, net	3,904	2,941
Adjusted EBITDA	**$ 371,187**	**$ 42,827**

GAAP to Non-GAAP Reconciliation

Non-GAAP Net Income – Three Months Ended March 31

$ in thousands	Three Months Ended March 31, 2022	2021
GAAP net income (loss)	**$ 204,261**	**$ (123,351)**
Non-GAAP adjustments:		
Acquisition/divestiture-related costs	1,589	49,108
Loss on equity security investments	4,646	-
Restructuring and realignment costs	537	6,093
Manufacturing plant start-up costs	807	-
Amortization and step-up:		
Intangible amortization expense	89,260	66,369
Inventory step-up expense	27,201	911
Amortization of debt discount and deferred financing costs	1,577	773
Impairment of long-lived asset	-	12,371
Share-based compensation	47,300	61,166
Depreciation	5,852	4,451
Total of pre-tax non-GAAP adjustments	**178,769**	**201,242**
Income tax effect of pre-tax non-GAAP adjustments	(67,212)	(73,129)
Total of non-GAAP adjustments	**111,557**	**128,113**
Non-GAAP net income	**$ 315,818**	**$ 4,762**

GAAP to Non-GAAP Reconciliation

Non-GAAP Earnings Per Share – Basic and Diluted – Three Months Ended March 31

$ in thousands except share and per share data	Three Months Ended March 31, 2022	2021
Non-GAAP Earnings Per Share:		
Weighted average ordinary shares - Basic	**229,094,311**	**223,920,768**
Non-GAAP Earnings Per Share - Basic:		
GAAP earnings (loss) per share - Basic	**$ 0.89**	**$ (0.55)**
Non-GAAP adjustments	0.49	0.57
Non-GAAP earnings per share - Basic	**$ 1.38**	**$ 0.02**
Weighted average ordinary shares - Diluted		
Weighted average ordinary shares - Basic	229,094,311	223,920,768
Ordinary share equivalents	6,859,007	10,190,012
Weighted average ordinary shares - Diluted	**235,953,318**	**234,110,780**
Non-GAAP Earnings Per Share - Diluted		
GAAP earnings (loss) per share - Diluted	**$ 0.87**	**$ (0.55)**
Non-GAAP adjustments	0.47	0.57
Non-GAAP earnings per share - Diluted	**$ 1.34**	**$ 0.02**