



Acquisition of Curzion Pharmaceuticals

April 2, 2020

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to the acquisition of Curzion Pharmaceuticals, Inc. and the benefits thereof, Horizon's strategy, plans, objectives, expectations and intentions, including with respect to HZN-825, the timing of regulatory meetings and a planned Phase 2b pivotal clinical study of HZN-825, the potential benefits of HZN-825 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 associated with clinical development, such as the risk that guidance from regulatory authorities differs from Horizon's expectations or that clinical trials are not initiated or completed on time and the fact that prior clinical results may not predict the outcome of future trials; 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, as well as those described in Horizon's filings with the United States Securities and Exchange Commission, including those factors discussed under the caption "Risk Factors" in those filings. Forward-looking statements speak only as of the date of this presentation and Horizon does not undertake any obligation to update or revise these statements, except as may be required by law.

Horizon Acquiring Curzion, Gaining Rights to LPAR₁ Antagonist in Development for Rare, Fibrotic Disease

Transaction Overview

- Horizon acquired privately held Curzion and its LPAR₁ antagonist product candidate, CZN001 (renamed HZN-825), for \$45M in cash
- Consideration includes additional payments contingent on the achievement of development and commercialization milestones
- Manageable investment with significant potential
- One of several transactions Horizon intends to complete to build out development stage portfolio

Strategic Rationale

- HZN-825 is an oral selective LPAR₁ antagonist with early signals of benefit in diffuse cutaneous systemic sclerosis (dcSSc)
- dcSSc is a rare, chronic autoimmune disease with a high unmet need
 - One of the highest mortality rates of any rheumatic disease⁽¹⁾
 - No FDA-approved treatments
- Primarily managed by rheumatologists; the acquisition falls within one of Horizon's core areas of expertise
- Expands and diversifies Horizon's rare disease pipeline

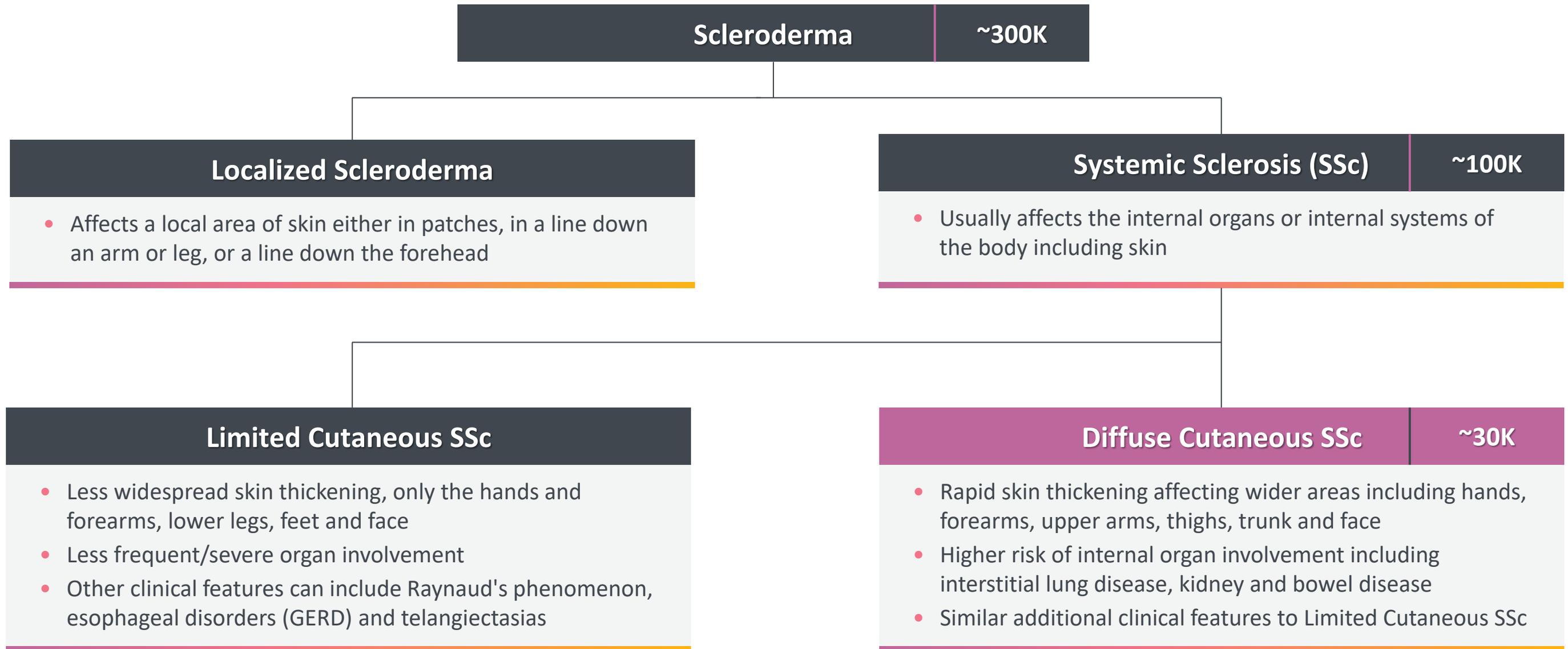
Development Plan

- Plan to conduct pharmacokinetics study in 2020 to support new product formulation
- Will engage U.S. FDA on clinical development plan, including appropriate registrational endpoints and timelines
- Plan to begin Phase 2b pivotal study in 1H 2021; anticipate 12-month endpoint considering the progressive nature of dcSSc

(1) Nikpour M, Baron M. Curr Opin Rheumatol. 2014 Mar;26(2):131-7.
LPAR₁: Lysophosphatidic acid 1 receptor.

Diffuse Cutaneous Systemic Sclerosis (dcSSc) Impacts Approximately 30K Patients in the U.S.

Disease Overview and U.S. Prevalence



Note: All prevalence numbers are U.S. only.
Source: Scleroderma Foundation.

Current dcSSc Treatment Options are Limited; Significant Unmet Need Exists

Diffuse Cutaneous Systemic Sclerosis

- Rare, chronic autoimmune disease marked by fibrosis, including hardening of skin and internal organ involvement
- Patients typically suffer extensive fibrosis that can progress to internal organ damage
- Primarily managed by rheumatologists

Unmet Needs

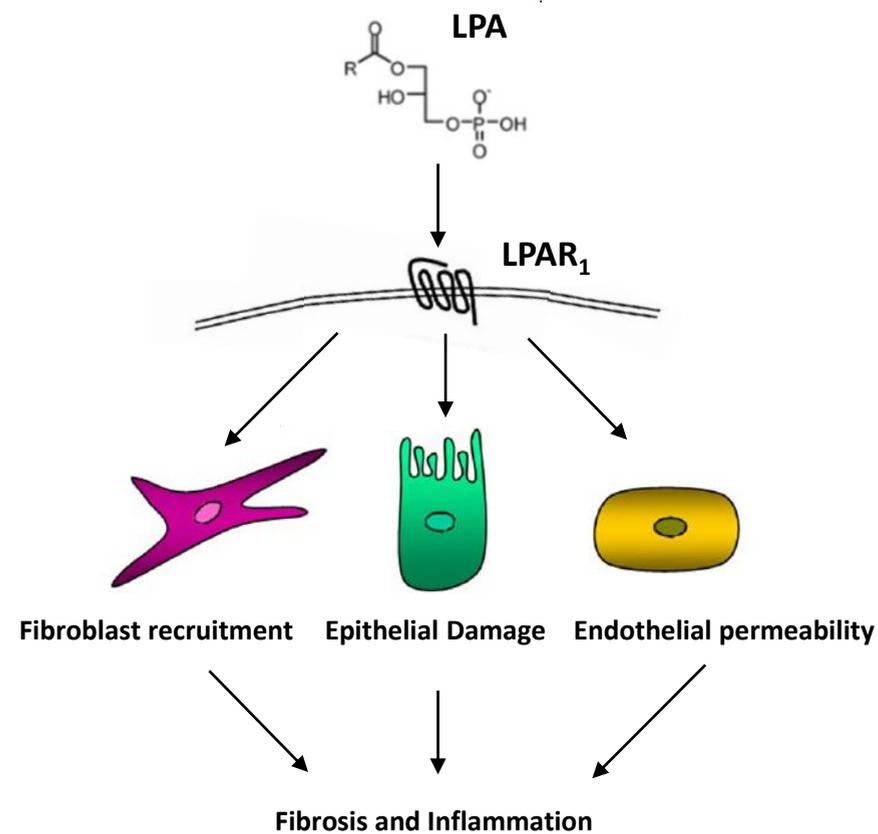
- One of highest mortality rates of any rheumatic disease⁽¹⁾
 - 10-year survival rate after diagnosis is 65%⁽²⁾
- Current treatment approaches focused on providing organ-specific symptomatic relief and attempting to slow disease progression
 - No FDA-approved therapies

(1) Nikpour M, Baron M. Curr Opin Rheumatol. 2014 Mar;26(2):131-7.

(2) Al-Dhafer FF, Pope JE, Ouimet JM. Semin Arthritis Rheum. 2010 Feb;39(4):269-77.

HZN-825 is a Potent Antagonist of LPAR₁ with Rationale for Continued Development in dcSSc

Model of LPAR₁ Role in Lung Injury and Fibrosis



Overview of LPAR₁

- Lysophosphatidic Acid Receptor 1 (LPAR₁) signaling has been implicated in fibrosis and inflammation

Preclinical Evidence

- Animal models of fibrosis demonstrate that LPAR₁ is involved in fibrosis of skin, lung, kidney and heart⁽¹⁾⁽²⁾⁽³⁾
- LPAR₁ deletion in mice was protective against dermal and lung fibrosis⁽³⁾⁽⁴⁾
- LPAR₁ antagonism protects against development of fibrosis and reverses established fibrosis⁽⁴⁾
- LPAR₁ antagonism reduced immune cell infiltration into lungs in an experimental model of lung irritation⁽¹⁾

Translational Evidence from Scleroderma Patients

- Serum LPA levels are elevated in patients with systemic sclerosis⁽⁵⁾
- Fibroblasts from patients show elevated LPAR₁ levels and increased sensitivity to LPAR₁ antagonism versus normal fibroblasts⁽¹⁾

Note: Figure adapted from Ninou et al Frontiers in Medicine doi: 10.3389/fmed.2018.00180

(1) Horizon internal data.

(2) Pradere et al J Am Soc Nephrol 18:3110-3118.

(3) Tager et al Nature Medicine doi:10.1038/nm1685.

(4) Castelino et al Arthritis Rheum 63(5):1405-1415.

(5) Tokumura et al Int J Med Sci 6(4):168-176.

Mechanistic Rationale and Early Clinical Evidence are Promising

Research and Pre-Clinical Evidence

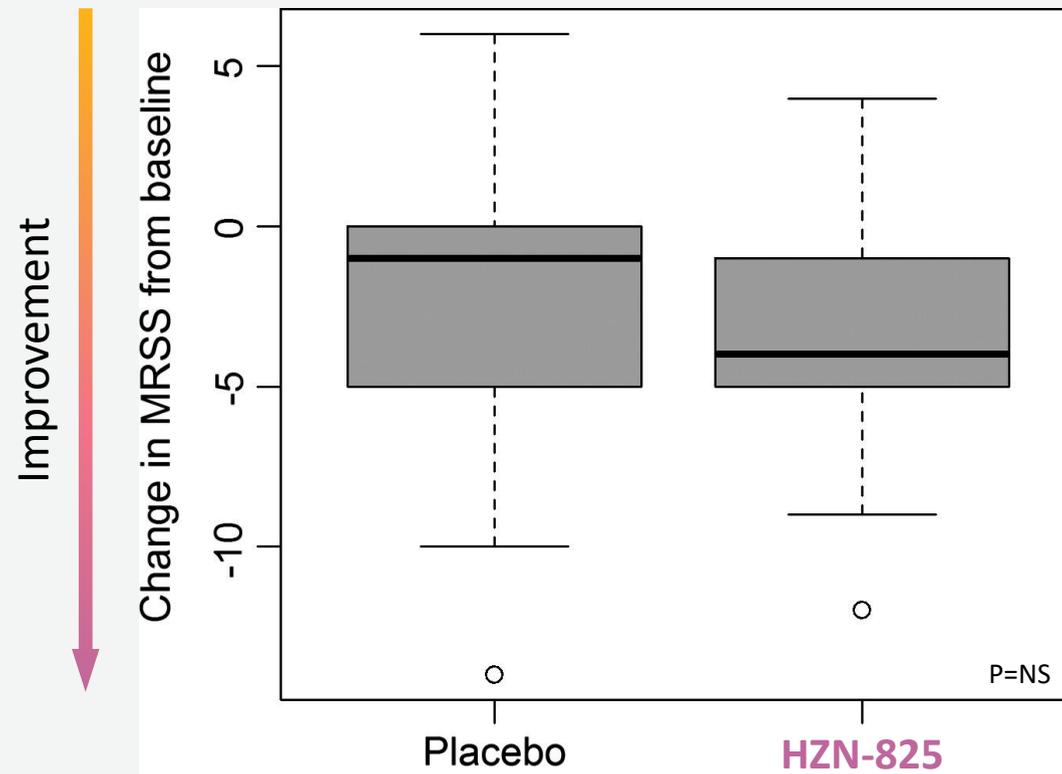
- ✓ Research implicates LPAR₁ as a target in the pathogenesis of dcSSc
- ✓ Extensive pre-clinical evaluation supports the anti-fibrotic potential of LPAR₁ antagonism

Clinical Evidence to Date

- ✓ In five Phase 1 studies, HZN-825 was safe and well tolerated
- ✓ Positive signal observed in short, 8-week placebo-controlled period of Phase 2a studies
- ✓ Longer open-label period data suggest longer duration of treatment may demonstrate meaningful benefit

Promising Efficacy and Safety Data in Phase 2 Double-Blind Phase and Open Label Extension

8-week Double-Blind Period



Numerically greater median change in Modified Rodnan Skin Thickness Score (mRSS) baseline to Week 8

Boxes represent the 25th to 75th percentiles, dark lines in boxes represent the median, the lines outside the box represents 10th and 90th percentiles

16-week Open Label Extension Period

Clinical Outcomes:

	Median Decrease in mRSS	Responder Rate ⁽¹⁾
24-weeks of continuous treatment	-7.5	78.6%
Subjects switched from placebo to HZN-825	-7.0	69.2%

- A minimum clinically important difference in mRSS is an improvement/reduction of 5 units
- After Week 8, all patients were placed on HZN-825 treatment
- Biomarker analysis of skin biopsies showed reductions in LPA-related genes

Safety

- Similar proportions of adverse events in active and placebo arms
- No safety concerns seen on laboratory parameters

Source: Allanore et al, Arth & Reum Oct 2018. SAR100842 was renamed HZN-825.

NS: Not significant.

mRSS: Modified Rodnan Skin Score is a measure of skin thickness intended to measure disease severity and mortality. The minimal clinically important difference (MCID) is an improvement of 5 units.

(1) Responder rate defined as ≥ 5 point improvement/reduction in mRSS.



HORIZON