Acquisition of Curzion Pharmaceuticals

April 2, 2020
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## Horizon Acquiring Curzion, Gaining Rights to LPAR$_1$ Antagonist in Development for Rare, Fibrotic Disease

### Transaction Overview
- Horizon acquired privately held Curzion and its LPAR$_1$ 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 LPAR$_1$ 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

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LPAR$_1$: Lysophosphatidic acid 1 receptor.
Diffuse Cutaneous Systemic Sclerosis (dcSSc) Impacts Approximately 30K Patients in the U.S.

Disease Overview and U.S. Prevalence

Scleroderma ~300K

Localized Scleroderma
- Affects a local area of skin either in patches, in a line down an arm or leg, or a line down the forehead

Systemic Sclerosis (SSc) ~100K
- Usually affects the internal organs or internal systems of the body including skin

Limited Cutaneous SSc
- Less widespread skin thickening, only the hands and forearms, lower legs, feet and face
- Less frequent/severe organ involvement
- Other clinical features can include Raynaud's phenomenon, esophageal disorders (GERD) and telangiectasias

Diffuse Cutaneous SSc ~30K
- Rapid skin thickening affecting wider areas including hands, forearms, upper arms, thighs, trunk and face
- Higher risk of internal organ involvement including interstitial lung disease, kidney and bowel disease
- Similar additional clinical features to Limited Cutaneous SSc

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

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

Note: Figure adapted from Ninou et al. Frontiers in Medicine doi: 10.3389/fmed.2018.00180
(1) Horizon internal data.
Mechanistic Rationale and Early Clinical Evidence are Promising

**Research and Pre-Clinical Evidence**

- Research implicates LPAR\textsubscript{1} as a target in the pathogenesis of dcSSc
- Extensive pre-clinical evaluation supports the anti-fibrotic potential of LPAR\textsubscript{1} 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

- **Clinical Outcomes:**
  - Numerically greater median change in Modified Rodnan Skin Thickness Score (mRSS) baseline to Week 8
  - Box plots comparing Placebo and HZN-825 treatments:
    - Placebo:
    - HZN-825:
    - Figure indicates statistically similar improvement in mRSS, with no significant difference (P=NS).

### 16-week Open Label Extension Period

- **Clinical Outcomes:**
  - Median Decrease in mRSS and Responder Rate:
    - 24-weeks of continuous treatment:
      - HZN-825: -7.5
      - Placebo: -7.0
      - Responder Rate: 78.6% vs. 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

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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.