ACCESS TO INNOVATIVE TREATMENTS FOR SICKLE CELL DISEASE

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Statements we make in this presentation may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. We intend these forward-looking statements, including statements regarding the therapeutic potential and safety profile of voxelotor, including the potential for voxelotor to be a disease-modifying and first-in-class treatment for SCD and the potential impact of voxelotor on TCD, stroke risk, brain injury and chronic organ damage, our ability to implement and complete our clinical development plans for voxelotor, our plan to submit a rolling NDA for voxelotor under an accelerated regulatory approval pathway and for acceptance of our NDA, the availability of, and the sufficiency of our data to support, accelerated regulatory approval, our plan to initiate a TCD confirmatory study, our ability to generate and report data from our ongoing and potential future studies of voxelotor, whether ongoing or potential future studies of voxelotor will generate data that alters the safety or efficacy profile of voxelotor, the potential for an increase in hemoglobin of 1 g/dL or greater to reduce the risk of stroke, mortality and other clinical outcomes in patients with SCD, regulatory review and actions relating to voxelotor, the potential commercial opportunity for voxelotor, the expected size of the potential sales force for voxelotor, our plans for potential commercial launch, the potential for reimbursement and for physician and patient acceptance of voxelotor, our manufacturing plans, our focus on expanding our pipeline, our plan to initiate a pivotal study for inclacumab, our ability to adequately obtain and protect our intellectual property rights, and the timing of these events, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. We can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved, and furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, the risks that our clinical and preclinical development activities may be delayed or terminated for a variety of reasons, that results of clinical trials may be subject to differing interpretations, that regulatory authorities may disagree with our clinical development plans, including the sufficiency of our clinical data and of our primary and other key endpoints in our Phase 3 HOPE Study of voxelotor to support approval, or require additional studies or data to support further clinical investigation of our product candidates, that drug-related adverse events may be observed in clinical development, and that data and results may not meet regulatory requirements or otherwise be sufficient for further development, regulatory review or approval, along with those risks set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, and in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.
SCD: AN URGENT NEED TO ADDRESS AN OVERLOOKED ORPHAN CONDITION

~100,000 patients in the United States / ~60,000 patients in Europe

Lifelong inherited blood disorder

+ Hb polymerization causes deformation and destruction of red blood cells → morbidity/mortality

No innovative therapies in 20+ years

+ Non-curate treatments don’t address underlying Hb polymerization
+ Allogeneic transplants limited by donor availability and procedural risks

Hb, hemoglobin.
DRUG DEVELOPMENT IN SCD HAS LAGGED OTHER RARE DISEASES

Number of FDA Orphan Drug Approvals

Lanthier, Insights into Rare Disease Drug Approval: Trends and Recent Developments, 2017.

*2017 figures as of 9/15/2017
DEVELOPMENT OF NEW THERAPIES CAN BE INFORMED BY WELL-UNDERSTOOD PATHOPHYSIOLOGY IN SCD

HbS polymerization, which causes red blood cell damage, is root cause of SCD

Hemolytic Anemia
- Organ Damage
  + Stroke
  + Renal failure
  + Pulmonary hypertension
  + Priapism
  + Leg ulcers
  + Mortality

Fatigue

Vaso-occlusion
- Organ Damage
  + Osteonecrosis
  + Retinopathy

Pain / Vaso-occlusive crisis (VOC)

A GROWING EMPHASIS ON ADDRESSING HbS POLYMERIZATION

Partial HbS polymerization imparts therapeutic benefit

- Normal RBC with oxygenated Hb
- Sickle RBC with polymerization of deoxygenated Hb

Block intermolecular contacts in the sickle fiber
Induce HbF synthesis
Increase oxygen affinity
Reduce concentration of 2,3-diphosphoglycerate
Reduce intracellular Hb concentration

HEMOGLOBIN AS A SURROGATE ENDPOINT PREDICTIVE OF CLINICAL BENEFIT

<table>
<thead>
<tr>
<th>Surrogate endpoint requirements (adapted from Temple, JAMA 1999)</th>
<th>Sickle Cell Disease</th>
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</thead>
<tbody>
<tr>
<td>Epidemiologic support</td>
<td>Anemia strong predictor of chronic organ damage and mortality (CNS events, renal failure, cardiopulmonary). Supported by GBT/academic collaborative meta-analysis.</td>
</tr>
<tr>
<td>Well understood disease pathogenesis</td>
<td>The first molecular disease, HbS polymerizes in proportion to deoxy HbS concentration</td>
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<tr>
<td>Drug MOA well understood</td>
<td>Molecular mechanism stabilizes oxy-HbS to delay HbS polymerization, thereby decreasing hemolytic anemia</td>
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<tr>
<td>Serious and life threatening disease</td>
<td>SCD characterized by early mortality, daily symptoms, organ damage despite best standard of care</td>
</tr>
<tr>
<td>Difficulty of studying clinical endpoint</td>
<td>Clinical benefit of hemolytic anemia on stroke, cognitive dysfunction, renal failure, cardiac diastolic dysfunction, mortality would require prohibitively large and long studies</td>
</tr>
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NEED FOR NOVEL AND SURROGATE ENDPOINTS TO ACCELERATE SCD DRUG DEVELOPMENT

**Surrogate endpoints likely to predict benefit**

- **Hb** → multi-organ dysfunction, fatigue
- Pancellular HbF → VOC, organ dysfunction, strong biologic, genetic support and interventional data
- Hemolysis measures → multi-organ dysfunction
- Spleen imaging/biomarkers → spleen function
- Cardiac biomarkers (Echo diastolic dysfunction, MRI, NT-pro BNP) → heart failure and cardiac morbidity
- Proteinuria → renal failure
- MRI Oxygen Extraction Fraction → silent infarct, stroke, cognitive dysfunction

*Industry and Academic collaboration critical to establish biological mechanisms of disease, natural history and epidemiology to support use as endpoint reasonably likely to predict clinical benefit (with subsequent confirmation of clinical benefit)*

**Well established (validated) surrogate endpoints could potentially be used for full drug approvals**

- TCD → stroke risk, supported by several well controlled interventional RCTs

*Industry and Academic collaboration critical to design rigorous interventional clinical trials and analysis of EHR data to establish surrogate endpoints as fully predictive of benefit*
GBT’S SCD PROGRAM

**Voxelotor:**
Once-Daily, Oral Therapy Targeting HbS Polymerization

- NDA acceptance under Priority Review announced September 5, 2019
- PDUFA target action date: February 26, 2020
- Potential accelerated approval based on Phase 3 HOPE Study
- Plan to initiate transcranial doppler (TCD) post-approval confirmatory study in Q4 2019
- Potential to convert voxelotor to full approval (adults and children)

**Inclacumab:**
Fully human monoclonal antibody against P-selectin

- P-selectin is a clinically-validated VOC target
- Initiation of pivotal study anticipated in 2021
- Exclusive worldwide licensing agreement with Roche\(^1,2\)
  - Novel fully human monoclonal antibody
  - Established PK, safety and tolerability in > 500 patients

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\(^1\) F. Hoffmann-LaRoche Ltd. And Hoffmann-LaRoche Inc.
\(^2\) Roche retained its license for inclacumab for diagnostic use
17 states represent roughly 85% of SCD patients in the United States.

SCD Payer Landscape

- Medicaid, 50%
- Commercial, 32%
- Medicare, 15%
- Others, 3%

1 Symphony Health Claims Data, 2012-2018.
ACCESS TO CARE IS CRITICAL TO THE HEALTH OF SCD PATIENTS

+ We expect exciting, new treatment options to be approved for use in the coming months and years.
+ But these treatments aren’t meaningful if patients are unable to access them
  - Some payers have a history of delaying access to new medicines by erecting barriers or imposing restrictions
+ Inconsistent for one hand of government to accelerate approval of new medicines based on need, safety and promise and another to delay patient access once it’s approved
+ GBT is committed to working with policymakers and others to ensure timely patient access to new medicines that could transform the treatment paradigm for SCD.
Thank You