Third-Quarter 2019 Financial Results

October 30, 2019
Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

CEO Perspective

Jeff Leiden, M.D., Ph.D., Chairman, President and Chief Executive Officer

Commercial Update & TRIKAFTA Launch

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

Clinical Update

Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer

Financial Results

Charlie Wagner, Executive Vice President and Chief Financial Officer
Safe Harbor Statement &
Non-GAAP Financial Measures

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, the information provided regarding future financial performance, including in the section captioned "Full Year 2019 Financial Guidance" and statements regarding (i) the timing and expected outcome of regulatory applications and reimbursement for CF medicines globally and (ii) the development plan and timelines for our product development candidates, including CTX001, VX-814, VX-864, VX-147 and VX-961. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company’s beliefs only as of the date of this presentation and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that the company’s expectations regarding its 2019 CF net product revenues, expenses and effective tax rates may be incorrect (including because one or more of the company’s assumptions underlying its expectations may not be realized), that data from the company’s development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex’s annual report and subsequent quarterly reports filed with the Securities and Exchange Commission and available through the company’s website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this presentation as new information becomes available.

In this presentation, Vertex’s financial results and financial guidance are provided in accordance with accounting principles generally accepted in the United States (GAAP) and using certain non-GAAP financial measures. In particular, non-GAAP financial results and guidance exclude from Vertex’s pre-tax income (i) stock-based compensation expense, (ii) revenues and expenses related to business development transactions including collaboration agreements, asset acquisitions and consolidated variable interest entities, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) acquisition-related costs and (v) other adjustments. The company’s non-GAAP financial results also exclude from its provision for or benefit from income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above. These results are provided as a complement to results provided in accordance with GAAP because management believes these non-GAAP financial measures help indicate underlying trends in the company’s business, are important in comparing current results with prior period results and provide additional information regarding the company’s financial position. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally and to manage the company’s business and to evaluate its performance. The company adjusts, where appropriate, for both revenues and expenses in order to reflect the company’s operations. The company provides guidance regarding product revenues in accordance with GAAP and provides guidance regarding combined research and development and sales, general, and administrative expenses on both a GAAP and non-GAAP basis. The company also provides guidance regarding its anticipated income taxes as a percentage of pre-tax income on a non-GAAP basis. The guidance regarding GAAP research and development expenses and sales, general and administrative expenses does not include estimates associated with any potential future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the attached financial information.
2019 Key Goals and Milestones

ACHIEVE OUR VISION IN CYSTIC FIBROSIS

- Phase 2 data for triple combinations in CF patients
- Initiation of pivotal development of up to two triple combination regimens
- Approval for tezacaftor/ivacaftor combination in the U.S. (Europe anticipated in 2H 2018)
- Advance additional next-generation correctors into development

EXPAND PIPELINE BEYOND CF

- Advance one or more compounds from research into clinical development
- Initiate clinical development of CRISPR-Cas9 treatment in Beta Thalassemia & Sickle Cell Disease

BUILD FINANCIAL STRENGTH

- Significantly increase 2018 total CF product revenues
- Obtain reimbursement for ORKAMBI in additional countries outside the U.S.
- Continued management of non-GAAP combined R&D and SG&A expenses

EXPAND PIPELINE BEYOND CF

- Complete Phase 1 studies in at least two new diseases
- Bolster pipeline with internal and external assets
- Advance one or more compounds from research into clinical development

BUILD FINANCIAL STRENGTH

- Continued CF product revenue growth
- Continued uptake and reimbursement for ORKAMBI and SYMDEKO in additional countries outside the U.S.
- Continued management of non-GAAP combined R&D and SG&A expenses
- Continued expansion of non-GAAP operating margins and cash flow
Vertex Strategy and Business Model
*A Blueprint for Serial Innovation*

**CORPORATE STRATEGY**
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

**RESEARCH STRATEGY**
Combine **transformative advances** in the **understanding of human disease** and in the **science of therapeutics** to dramatically advance human health

- Focus on **validated targets** that address causal human biology
- Create **predictive lab assays** and **clinical biomarkers**
- Identify **rapid path to registration** and approval
- Discover and develop medicines that offer **transformative benefit**, **regardless of modality**

**DIFFERENTIATED BUSINESS MODEL**
- Investment of majority of OpEX in R&D and BD/external innovation
- Revenue growth: high operating margins and significant cash flow
- Creation of high-value transformative medicines for specialty markets
- Limited SG&A expenses and infrastructure
Multiple Medicines to Treat Underlying Cause of CF
Increasing Access and Reimbursement for CF Patients Globally

KALYDECO
Recent Accomplishments:
• CHMP positive opinion received in EU for ages 6 - <12mos.
• Reimbursement received in England for ages 18+ with R117H mutation and for ages 12mos.+ with gating mutations

ORKAMBI
Recent Accomplishments:
• Reimbursement received in England, Spain, Australia and Scotland for eligible patients

SYMDEKO/SYMKEVI
Recent Accomplishments:
• Reimbursement received in England, Spain, Australia and Scotland for eligible patients

TRIKAFTA
Recent Accomplishments:
• Approved in U.S. for ages 12+
• MAA submitted to EMA for ages 12+

- Full-year 2019 total CF product revenue guidance of $3.70 - $3.75 billion -
U.S. TRIKAFTA Launch Underway

- FDA approval received on October 21, 2019 for people ages 12+ who have at least one *F508del* mutation

- ~18,000 patients in the U.S. eligible, representing largest patient population at the time of launch
  - ~6,000 newly eligible F/MF patients

- Broad coverage and reimbursement is anticipated from both commercial and government payers in the U.S.
  - First patients have already been prescribed medicine

- EU MAA submitted

- Phase 3 study in children ages 6-11 currently enrolling
# Beyond CF

**Multiple Opportunities for Transformative Medicines**

<table>
<thead>
<tr>
<th>Alpha-1 Antitrypsin Deficiency</th>
<th>Sickle Cell Disease &amp; Beta Thalassemia</th>
<th>APOL1-Mediated Kidney Diseases</th>
</tr>
</thead>
</table>
| _Small molecule to correct protein misfolding and enable secretion of AAT from the liver_  
- Phase 2 study of VX-814 expected to begin in Q4 2019; clinical data from this study expected in 2020 | _Ex vivo gene editing with goal of providing one-time curative therapy_  
- First clinical data from Phase 1/2 study of CTX001 expected in Q4 2019 | _Small molecule inhibitor of APOL1 function, a causal genetic factor in FSGS/other proteinuric kidney diseases_  
- Phase 1 study of VX-147 in healthy volunteers expected to be complete in Q4 2019  
- Advancing multiple other molecules in late-stage research |

<table>
<thead>
<tr>
<th>Pain</th>
<th>DMD and DM1</th>
<th>Type 1 Diabetes</th>
</tr>
</thead>
</table>
| _Small molecule inhibitors of NaV1.8 as a novel treatment for pain_  
- Proof-of-concept established in multiple pain types  
- Advancing multiple selective NaV1.8 inhibitors through late-stage research and early clinical development | _Novel gene editing platform to potentially restore and repair dystrophin in DMD_  
- Exonics Therapeutics acquisition and expanded collaboration with Crispr Therapeutics completed in Q3 2019 | _Potentially curative cell-based treatment and delivery system_  
- Semma Therapeutics acquisition completed in October 2019 |
## Q3 2019 Financial Highlights

<table>
<thead>
<tr>
<th>2019</th>
<th>FY 2018</th>
<th>Q1 19</th>
<th>Q2 19</th>
<th>Q3 19</th>
<th>YTD 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total CF product revenues</strong></td>
<td>$783</td>
<td>$3.04B</td>
<td>$857</td>
<td>$940</td>
<td>$950</td>
</tr>
<tr>
<td>KALYDECO</td>
<td>246</td>
<td>1.01B</td>
<td>244</td>
<td>262</td>
<td>249</td>
</tr>
<tr>
<td>ORKAMBI</td>
<td>282</td>
<td>1.26B</td>
<td>293</td>
<td>316</td>
<td>297</td>
</tr>
<tr>
<td>SYMDEKO/SYMKEVI</td>
<td>255</td>
<td>769</td>
<td>320</td>
<td>362</td>
<td>404</td>
</tr>
<tr>
<td><strong>Combined non-GAAP R&amp;D and SG&amp;A</strong></td>
<td>379</td>
<td>1.53B</td>
<td>388</td>
<td>394</td>
<td>416</td>
</tr>
<tr>
<td>Non-GAAP operating income</td>
<td>295</td>
<td>1.11B</td>
<td>377</td>
<td>413</td>
<td>403</td>
</tr>
<tr>
<td>Non-GAAP operating margin</td>
<td>38%</td>
<td>37%</td>
<td>44%</td>
<td>44%</td>
<td>42%</td>
</tr>
<tr>
<td>Non-GAAP net income</td>
<td>282</td>
<td>1.06B</td>
<td>296</td>
<td>327</td>
<td>322</td>
</tr>
<tr>
<td>Non-GAAP net income per share - diluted</td>
<td>$1.09</td>
<td>$4.08</td>
<td>$1.14</td>
<td>$1.26</td>
<td>$1.23</td>
</tr>
<tr>
<td>Cash, cash equivalents &amp; marketable securities (period-end)</td>
<td>$3.2B</td>
<td></td>
<td></td>
<td></td>
<td>$4.0B</td>
</tr>
</tbody>
</table>

**Notes**
- An explanation of non-GAAP financial measures and reconciliation of combined non-GAAP R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company’s Q3 2019 press release dated October 30, 2019.
- Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in the appendix of this presentation; totals may not add due to rounding.
Increasing Cash Flow Enables Investment for Future Growth

Increasing Cash Flow Enables Continued Investment in Internal R&D and Execution of Business Development Strategy

Business Development and Capital Allocation Strategy

- Complement ongoing R&D in CF
- Access novel platform technologies and targets
- In-license or acquire pipeline assets

Notes:
- Period-end cash includes cash, cash equivalents and marketable securities
- $950M payment for the acquisition of Semma Therapeutics will be reflected in the period-end December 31, 2019 cash balance
## 2019 Financial Guidance

<table>
<thead>
<tr>
<th></th>
<th>FY 2018 Actuals</th>
<th>FY 2019 Guidance</th>
<th>FY 2019 Guidance Commentary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CF Product Revenues</td>
<td>$3.04B</td>
<td>$3.70 - $3.75B</td>
<td>Guidance reflects early approval of TRIKAFTA</td>
</tr>
<tr>
<td>Combined Non-GAAP R&amp;D and SG&amp;A</td>
<td>$1.53B</td>
<td>$1.65 - $1.70B</td>
<td>Non-GAAP guidance unchanged</td>
</tr>
<tr>
<td>Combined GAAP R&amp;D and SG&amp;A</td>
<td>$1.97B</td>
<td>$2.35 - $2.45B</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP Effective Tax Rate</td>
<td></td>
<td>21% - 22%</td>
<td>The vast majority of the company's tax provision will be a non-cash expense until NOLs are fully utilized</td>
</tr>
</tbody>
</table>

*Note: An explanation of non-GAAP financial measures and reconciliation of non-GAAP combined R&D and SG&A expense is included in the company’s Q3 2019 press release dated October 30, 2019*
# Appendix

## Reconciliation of GAAP to non-GAAP Financial Information

<table>
<thead>
<tr>
<th></th>
<th>Q3 2018</th>
<th>FY 2018</th>
<th>Q1 2019</th>
<th>Q2 2019</th>
<th>Q3 2019</th>
<th>YTD 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GAAP total revenues</strong></td>
<td>$785</td>
<td>$3,048</td>
<td>$858</td>
<td>$941</td>
<td>$950</td>
<td>$2.75B</td>
</tr>
<tr>
<td><strong>Non-GAAP total revenues</strong></td>
<td>784</td>
<td>$3,043</td>
<td>$858</td>
<td>$941</td>
<td>950</td>
<td>2.75B</td>
</tr>
<tr>
<td><strong>GAAP operating income</strong></td>
<td>206</td>
<td>635</td>
<td>277</td>
<td>270</td>
<td>99</td>
<td>646</td>
</tr>
<tr>
<td>Stock compensation expense</td>
<td>86</td>
<td>325</td>
<td>94</td>
<td>90</td>
<td>85</td>
<td>269</td>
</tr>
<tr>
<td>Other adjustments</td>
<td>4</td>
<td>152</td>
<td>6</td>
<td>53</td>
<td>218</td>
<td>278</td>
</tr>
<tr>
<td><strong>Non-GAAP operating income</strong></td>
<td>295</td>
<td>1.11B</td>
<td>377</td>
<td>413</td>
<td>403</td>
<td>1.19B</td>
</tr>
<tr>
<td><strong>Operating Margin %:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP</td>
<td>26%</td>
<td>21%</td>
<td>32%</td>
<td>29%</td>
<td>10%</td>
<td>23%</td>
</tr>
<tr>
<td>Non-GAAP</td>
<td>38%</td>
<td>37%</td>
<td>44%</td>
<td>44%</td>
<td>42%</td>
<td>43%</td>
</tr>
<tr>
<td><strong>Net income</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP</td>
<td>129</td>
<td>2.10B</td>
<td>269</td>
<td>267</td>
<td>58</td>
<td>594</td>
</tr>
<tr>
<td>Non-GAAP</td>
<td>282</td>
<td>1.06B</td>
<td>296</td>
<td>327</td>
<td>322</td>
<td>945</td>
</tr>
<tr>
<td><strong>Net income per share - diluted</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP</td>
<td>$0.50</td>
<td>$8.09</td>
<td>$1.03</td>
<td>$1.03</td>
<td>$0.22</td>
<td>$2.28</td>
</tr>
<tr>
<td>Non-GAAP</td>
<td>$1.09</td>
<td>$4.08</td>
<td>$1.14</td>
<td>$1.26</td>
<td>$1.23</td>
<td>$3.63</td>
</tr>
</tbody>
</table>

*Note: All numbers in the above reconciliation table are in millions except per share data and percentages; totals may not add due to rounding*