Business Update & Full-Year and Q4’17 Financial Results

January 31, 2018
Agenda

Introduction

Michael Partridge, Vice President, Investor Relations

Key Progress and Next Steps

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

Data Highlights

Jeff Chodakewitz, M.D., Executive Vice President and Chief Medical Officer

Fourth-Quarter and Full-Year 2017 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

Q&A

Stuart Arbuckle, Executive Vice President, Chief Commercial 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 in the slide captioned “2018 Financial Guidance” and statements regarding (i) the timing and expected outcome of regulatory applications, including NDAs and MAAs and (ii) the development plan and timelines for our product development candidates, including tezacaftor in combination with ivacaftor and our next-generation triple combination regimens. While Vertex believes the forward-looking statements contained in this presentation 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the company's expectations regarding its 2018 expenses 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 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 (i) stock-based compensation expense, (ii) revenues and expenses related to business development transactions including collaboration agreements and asset acquisitions, (iii) revenues and expenses related to consolidated variable interest entities, including asset impairment charges and related income tax benefits and the effects of the deconsolidation of a variable interest entity and (iv) other adjustments. 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 combined research and development and sales, general, and administrative expenses on both a GAAP and a non-GAAP basis. The guidance regarding GAAP research and development expenses and sales, general and administrative expenses does not include estimates regarding expenses associated with any potential future business development activities. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the Company’s January 31, 2018 press release.
Developing Medicines for All People with CF

2018 Growth Drivers

- **EU Reimbursement**
- **Planned Label Expansions to Ages 2-5 & 6-11**
- **Anticipated Approval in the U.S. and E.U.**

34,000 Patients Currently Eligible

- 6,000 Patients Eligible
- 28,000 Patients Eligible
- Two F508del Mutations
- ~12,500 Patients Initiated Tx.

44,000 → 68,000

Investigational Triple Combination Regimens

- F508del/Minimal CFTR Function

Gene Editing mRNA

Potential to treat all people with CF

68,000 → 75,000

Any CF patient with at least one F508del mutation

EU Reimbursement

Planned Label Expansions to Ages 2-5 & 6-11

Anticipated Approval in the U.S. and E.U.

2018 Growth Drivers

- **EU Reimbursement**
- **Planned Label Expansions to Ages 2-5 & 6-11**
- **Anticipated Approval in the U.S. and E.U.**

34,000 Patients Currently Eligible

- 6,000 Patients Eligible
- 28,000 Patients Eligible
- Two F508del Mutations
- ~12,500 Patients Initiated Tx.

44,000 → 68,000

Investigational Triple Combination Regimens

- F508del/Minimal CFTR Function

Gene Editing mRNA

Potential to treat all people with CF

68,000 → 75,000

Any CF patient with at least one F508del mutation
We have selected VX-659 and VX-445 to advance into Phase 3 development as part of two separate triple combination regimens, one of which may be a once-daily regimen.

- In Phase 2, both VX-659 and VX-445 triple combination regimens were well-tolerated and have a favorable safety profile.

We are finalizing designs of Phase 3 studies now and remain on track to begin the first Phase 3 program in the first half of 2018.

We remain focused on bringing forward the best triple combination regimen to patients as quickly as possible.
# Key Milestones and Goals

<table>
<thead>
<tr>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACHIEVE OUR VISION IN CYSTIC FIBROSIS</strong></td>
<td></td>
</tr>
<tr>
<td>✓ Approval of KALYDECO in residual function mutations</td>
<td>✓ Phase 2 data for triple combinations in CF patients</td>
</tr>
<tr>
<td>✓ Phase 3 tezacaftor/ivacaftor data in multiple mutations</td>
<td>✓ Initiation of pivotal development of up to two triple combination regimens</td>
</tr>
<tr>
<td>✓ Phase 1 and 2 proof-of-concept data for multiple triple combination regimens in CF patients</td>
<td>✓ Approval for tezacaftor/ivacaftor combination in the U.S. (Europe anticipated in 2H 2018)</td>
</tr>
<tr>
<td><strong>EXPAND PIPELINE BEYOND CF</strong></td>
<td>✓ Advance additional next-generation correctors into development</td>
</tr>
<tr>
<td>✓ Initiated additional Phase 2 studies of VX-150 in acute and neuropathic pain</td>
<td></td>
</tr>
<tr>
<td>✓ Bolstered CF and non-CF pipeline with internal and external assets</td>
<td></td>
</tr>
<tr>
<td><strong>BUILD FINANCIAL STRENGTH</strong></td>
<td></td>
</tr>
<tr>
<td>✓ Achieved total 2017 CF product revenues of $2.17B; 29% growth vs. 2016</td>
<td>✓ Significantly increase 2018 total CF product revenues</td>
</tr>
<tr>
<td>✓ Disciplined management of expenses (combined non-GAAP R&amp;D and SG&amp;A); &lt;12% percent growth vs. 2016</td>
<td>✓ Obtain reimbursement for ORKAMBI in additional countries outside the U.S.</td>
</tr>
<tr>
<td>✓ Significant increase in operating margins</td>
<td>✓ Continued management of non-GAAP combined R&amp;D and SG&amp;A expenses</td>
</tr>
<tr>
<td></td>
<td>✓ Continue to increase operating margins and cash flows</td>
</tr>
</tbody>
</table>
VX-659 & VX-445
Phase 2 Evaluations in Cystic Fibrosis Patients

Jeff Chodakewitz, M.D.,
Executive Vice President and Chief Medical Officer
**VX-659**

*Dosing in CF Patients with F508del/Minimal Function Mutations*

- **Primary Objectives:** Safety, tolerability and efficacy as assessed by mean absolute change in ppFEV₁ from baseline
- **Secondary Endpoints:** Sweat chloride and respiratory domain of CFQ-R
- **Key eligibility criteria for these cohorts:**
  - F508del/minimal function mutations
  - ≥18 years old
  - ppFEV₁, 40-90% inclusive
VX-659: F508del/Minimal Function

• VX-659 in combination with tezacaftor and ivacaftor was generally well tolerated and the overall safety profile was favorable

• Majority of adverse events were mild or moderate

• No discontinuations due to adverse events
  - One interruption in triple combination dosing due to rash, which resolved following interruption of treatment; Patient restarted and completed triple combination dosing without any further rash
**VX-659**

**Absolute Change in Lung Function Over Time**

**VX-659: F508del/Minimal Function**

- **Placebo**
- **VX-659 80 mg QD + TEZ/IVA**
- **VX-659 240 mg QD + TEZ/IVA**
- **VX-659 400 mg QD + TEZ/IVA**

*Values expressed as “Through Day 29” are the average of Day 15 and Day 29 measures*
**VX-659**

*Sweat Chloride Significantly Reduced*

**VX-659: F508del/Minimal Function**

Study Visit

- **Placebo**
- **VX-659 80 mg QD + TEZ/IVA**
- **VX-659 240 mg QD + TEZ/IVA**
- **VX-659 400 mg QD + TEZ/IVA**

*Values expressed as “Through Day 29” are the average of Day 15 and Day 29 measures*
## VX-659

**Significant Improvements in Respiratory Symptoms**

**VX-659: F508del/Minimal Function**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Mean Absolute Change in Respiratory Domain of CFQ-R at Day 29 (mean, points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple Placebo</td>
<td>+4.7</td>
</tr>
<tr>
<td>VX-659 80mg + TEZ/IVA</td>
<td>+24.6</td>
</tr>
<tr>
<td>VX-659 240mg + TEZ/IVA</td>
<td>+19.8</td>
</tr>
<tr>
<td>VX-659 400mg + TEZ/IVA</td>
<td>+21.8</td>
</tr>
</tbody>
</table>

*CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R*
VX-445
Dosing in CF Patients with F508del/Minimal Function Mutations

- **Primary Objectives:** Safety, tolerability and efficacy as assessed by mean absolute change in ppFEV₁ from baseline
- **Secondary Endpoints:** Sweat chloride and respiratory domain of CFQ-R
- **Key eligibility criteria for these cohorts:**
  - F508del/minimal function mutations
  - ≥18 years old
  - ppFEV₁, 40-90% inclusive

<table>
<thead>
<tr>
<th>Dose</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>VX-445 50 mg QD + TEZ/IVA</td>
<td>10</td>
</tr>
<tr>
<td>VX-445 100 mg QD + TEZ/IVA</td>
<td>22</td>
</tr>
<tr>
<td>VX-445 200 mg QD + TEZ/IVA</td>
<td>21</td>
</tr>
<tr>
<td>Triple Placebo</td>
<td>12</td>
</tr>
</tbody>
</table>
VX-445: F508del/Minimal Function

- VX-445 in combination with tezacaftor and ivacaftor was generally well tolerated and the overall safety profile was favorable.
- Majority of adverse events were mild or moderate.
- Two discontinuations due to adverse events in triple combination treatment groups (none in the placebo group):
  - Increased bilirubin (without concomitant transaminase elevations) - observed on final day of dosing; patient’s bilirubin levels returned to baseline during safety follow-up period after discontinuation of treatment.
  - Rash – resolved following discontinuation of treatment.
**VX-445**

*Absolute Change in Lung Function Over Time*

**VX-445: F508del/Minimal Function**

<table>
<thead>
<tr>
<th>Study Visit</th>
<th>Placebo</th>
<th>VX-445 50 mg QD + TEZ/IVA</th>
<th>VX-445 100 mg QD + TEZ/IVA</th>
<th>VX-445 200 mg QD + TEZ/IVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 15</td>
<td></td>
<td>+7.8</td>
<td>+11.1</td>
<td>+13.8</td>
</tr>
<tr>
<td>Day 29</td>
<td></td>
<td>+13.8</td>
<td>+11.1</td>
<td>+7.8</td>
</tr>
</tbody>
</table>

* Values expressed as “Through Day 29” are the average of Day 15 and Day 29 measures*
**VX-445**

*Sweat Chloride Significantly Reduced*

**VX-445: F508del/Minimal Function**

- **Mean Absolute Change in Sweat Chloride, (Mean +/- SE) (mmol/L)**

- **Day 1**
  - Placebo: -2.2
  - VX-445 50 mg QD + TEZ/IVA: -33.2
  - VX-445 100 mg QD + TEZ/IVA: -38.2
  - VX-445 200 mg QD + TEZ/IVA: -39.1

- **Day 15**
  - Placebo: -2.2
  - VX-445 50 mg QD + TEZ/IVA: -33.2
  - VX-445 100 mg QD + TEZ/IVA: -38.2
  - VX-445 200 mg QD + TEZ/IVA: -39.1

- **Day 29**
  - Placebo: -2.2
  - VX-445 50 mg QD + TEZ/IVA: -33.2
  - VX-445 100 mg QD + TEZ/IVA: -38.2
  - VX-445 200 mg QD + TEZ/IVA: -39.1

*Values expressed as “Through Day 29” are the average of Day 15 and Day 29 measures*
## VX-445

**Significant Improvements in Respiratory Symptoms**

### VX-445: F508del/Minimal Function

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Mean Absolute Change in Respiratory Domain of CFQ-R at Day 29 (mean, points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple Placebo</td>
<td>+4.2</td>
</tr>
<tr>
<td>VX-445 50 mg + TEZ/IVA</td>
<td>+20.8</td>
</tr>
<tr>
<td>VX-445 100 mg + TEZ/IVA</td>
<td>+15.4</td>
</tr>
<tr>
<td>VX-445 200 mg + TEZ/IVA</td>
<td>+25.7</td>
</tr>
</tbody>
</table>

*CFQ-R results reported are based on a mixed effect model not adjusted for baseline CFQ-R*
Phase 3 Program Next Steps

Focused on finalizing design of Phase 3 programs and remain on track to initiate first Phase 3 program for VX-659 in 1H 2018 upon completion of discussions with FDA.

Expect to conduct two separate studies for each VX-659 and VX-445 triple combination regimen - F508del/minimal function and F508del/F508del.

Full-Year and Fourth-Quarter 2017 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer
# Full-Year and Q4 2017 Financial Highlights

<table>
<thead>
<tr>
<th></th>
<th>FY 2016</th>
<th>Q1 17</th>
<th>Q2 17</th>
<th>Q3 17</th>
<th>Q4 17</th>
<th>FY 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORKAMBI</td>
<td>980</td>
<td>295</td>
<td>324</td>
<td>336</td>
<td>365</td>
<td>1.32B</td>
</tr>
<tr>
<td>KALYDECO</td>
<td>703</td>
<td>186</td>
<td>190</td>
<td>213</td>
<td>256</td>
<td>845</td>
</tr>
<tr>
<td>Total CF product revenues</td>
<td>$1.68B</td>
<td>481</td>
<td>514</td>
<td>550</td>
<td>621</td>
<td>$2.17B</td>
</tr>
<tr>
<td>Combined non-GAAP R&amp;D and SG&amp;A</td>
<td>$1.20B</td>
<td>313</td>
<td>333</td>
<td>334</td>
<td>355</td>
<td>$1.33B</td>
</tr>
<tr>
<td>Non-GAAP operating income</td>
<td>288</td>
<td>122</td>
<td>112</td>
<td>145</td>
<td>184</td>
<td>564</td>
</tr>
<tr>
<td>Non-GAAP operating margin</td>
<td>17%</td>
<td>25%</td>
<td>22%</td>
<td>26%</td>
<td>30%</td>
<td>26%</td>
</tr>
<tr>
<td>Non-GAAP net income</td>
<td>211</td>
<td>101</td>
<td>99</td>
<td>136</td>
<td>158</td>
<td>495</td>
</tr>
<tr>
<td>Non-GAAP net income per share - diluted</td>
<td>$0.85</td>
<td>$0.41</td>
<td>$0.39</td>
<td>$0.53</td>
<td>$0.61</td>
<td>$1.95</td>
</tr>
<tr>
<td>Cash, cash equivalents &amp; marketable securities (quarter-end)</td>
<td>$1.43B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$2.09B</td>
</tr>
</tbody>
</table>

(1) An explanation of non-GAAP financial measures and reconciliation of non-GAAP combined R&D and SG&A expense, non-GAAP net income and non-GAAP net income per share is included in the company’s January 31, 2018 press release

(2) Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in Appendix A of this presentation
## 2018 Financial Guidance

<table>
<thead>
<tr>
<th></th>
<th>FY 2017 Actuals</th>
<th>2018 Guidance</th>
<th>2018 Guidance Commentary</th>
</tr>
</thead>
</table>
| Combined non-GAAP R&D and SG&A | $1.33B | $1.50 - $1.55B | Year-over-year increase from:  
  - Execution of Phase 3 studies for two separate triple combination regimens  
  - Supply chain investment for triple combination regimens  
  - Incremental investment for tezacaftor/ivacaftor planned launch |
| Combined GAAP R&D and SG&A | $1.82B | $1.80 - $1.95B | |

*The company expects to provide 2018 total CF product revenue guidance upon the anticipated U.S. approval of the tezacaftor/ivacaftor combination*
Significant Growth in Revenue Driving Operating Margin Expansion

Operating margins reflect total CF revenues, combined non-GAAP R&D and SG&A expenses and cost of revenues
Thank You

...to the hundreds of patients who took part in our clinical trials, and the physicians, nurses, families and others who care for them.

...to our employees for their dedication to helping advance the treatment of CF.

...and to the CF community for their support and commitment to changing the course of CF.
## Appendix A

### Reconciliation of GAAP to non-GAAP Financial Information

<table>
<thead>
<tr>
<th>$( in millions except per share data and percentages)</th>
<th>FY 2016</th>
<th>Q1 2017</th>
<th>Q2 2017</th>
<th>Q3 2017</th>
<th>Q4 2017</th>
<th>FY 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAAP total revenues</td>
<td>$1,702</td>
<td>$715</td>
<td>$544</td>
<td>$578</td>
<td>$652</td>
<td>$2,489</td>
</tr>
<tr>
<td>Non-GAAP total revenues</td>
<td>$1,701</td>
<td>$482</td>
<td>$517</td>
<td>$552</td>
<td>$623</td>
<td>$2,174</td>
</tr>
<tr>
<td>GAAP income (loss) from operations</td>
<td>$10</td>
<td>$271</td>
<td>$53</td>
<td>$(326)</td>
<td>$126</td>
<td>$123</td>
</tr>
<tr>
<td>Stock compensation expense</td>
<td>238</td>
<td>69</td>
<td>73</td>
<td>74</td>
<td>75</td>
<td>291</td>
</tr>
<tr>
<td>Concert upfront and transaction expenses</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>161</td>
<td>-</td>
<td>165</td>
</tr>
<tr>
<td>Revenues and expenses related to VIEs</td>
<td>10</td>
<td>2</td>
<td>(18)</td>
<td>(16)</td>
<td>1</td>
<td>(32)</td>
</tr>
<tr>
<td>Other collaborative and transaction revenue and expenses</td>
<td>33</td>
<td>(230)</td>
<td>(3)</td>
<td>252</td>
<td>(19)</td>
<td>0</td>
</tr>
<tr>
<td>Other adjustments</td>
<td>(2)</td>
<td>11</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Non-GAAP income from operations</td>
<td>$288</td>
<td>$122</td>
<td>$112</td>
<td>$145</td>
<td>$184</td>
<td>$564</td>
</tr>
</tbody>
</table>

**Operating Margin %:**

- **GAAP**
  - 1%
  - 38%
  - 10%
  - -56%
  - 19%
  - 5%

- **Non-GAAP**
  - 17%
  - 25%
  - 22%
  - 26%
  - 30%
  - 26%

**Net income (loss)**

- **GAAP**
  - (112)
  - 248
  - 18
  - (103)
  - 101
  - 263

- **Non-GAAP**
  - 211
  - 101
  - 99
  - 136
  - 158
  - 495

**Net income (loss) per share - diluted**

- **GAAP**
  - $(0.46)
  - $0.99
  - $0.07
  - $(0.41)
  - $0.39
  - $1.04

- **Non-GAAP**
  - $0.85
  - $0.41
  - $0.39
  - $0.53
  - $0.61
  - $1.95

*All numbers in the above reconciliation table are in millions except per share data, totals may not add due to rounding*