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Third-Quarter 2018 Earnings Call

October 24, 2018

Agenda

Introduction

Michael Partridge, Senior Vice President, Investor Relations

Business Highlights

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

Third-Quarter 2018 Financial Results

Ian Smith, Executive Vice President and Chief Operating Officer

Q&A

Stuart Arbuckle, Executive Vice President and Chief Commercial Officer

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

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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 titled "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 CF net product revenues and 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 from Vertex's pre-tax net income (loss) (i) stock-based compensation expense, (ii) revenues and expenses related to business development transactions including collaboration agreements, asset acquisitions and consolidated variable interest entities, which included an asset impairment charge and the effects of the deconsolidation of a variable interest entity in 2017 and (iii) other adjustments, including gains or losses related to the fair value of the company's strategic investment in CRISPR. The company's non-GAAP financial results also exclude from its provision for or benefit from income taxes (i) the estimated tax impact related to its non-GAAP adjustments to pre-tax net income (loss) described above as well as (ii) non-operating tax adjustments, which are not associated with Vertex's normal, recurring operations. 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 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 October 24, 2018 press release.

Key Milestones and Goals

	2017	2018
ACHIEVE OUR VISION IN CYSTIC FIBROSIS	☑ Approval of KALYDECO in residual function mutations ☑ Phase 3 tezacaftor/ivacaftor data in multiple mutations ☑ Phase 1 and 2 proof-of-concept data for multiple triple combination regimens in CF patients	☑ 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	☑ Initiated additional Phase 2 studies of VX-150 in acute and neuropathic pain ☑ Bolstered CF and non-CF pipeline with internal and external assets	☐ 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	☑ Achieved total 2017 CF product revenues of $2.17B; 29% growth vs. 2016 ☑ Disciplined management of expenses (combined non-GAAP R&D and SG&A); <12% percent growth vs. 2016 ☑ Significant increase in operating margins	☑ 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 ☑ Continue to increase operating margins and cash flows

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Recent Progress in CF

Treating Younger Patients with our CF Medicines

- sNDA submission for tezacaftor/ivacaftor combination in children ages 6 to 11 expected by end of 2018
- FDA approval of KALYDECO in ages 12 to <24 months and ORKAMBI in ages 2 to 5
- Regulatory submissions in U.S. and EU for ivacaftor in infants ages 6 to <12 months planned for late 2018
- Dosing underway in Phase 3 study of lumacaftor/ivacaftor combination in children ages 12 to <24 months

SYMDEKO/SYMKEVI

- Continued strong demand in the U.S. from wide range of eligible patients
- Received CHMP positive opinion for SYMKEVI for people ages 12 and older; EU approval expected in Q4 2018

Establishing Long-Term Reimbursement Outside of the U.S.

- Recent agreements in Australia, Demark and Austria provide immediate access to ORKAMBI and a potential pathway for access and rapid reimbursement for certain future CF medicines
- VRTX continues to work toward establishing reimbursement agreements in other countries outside of the U.S.

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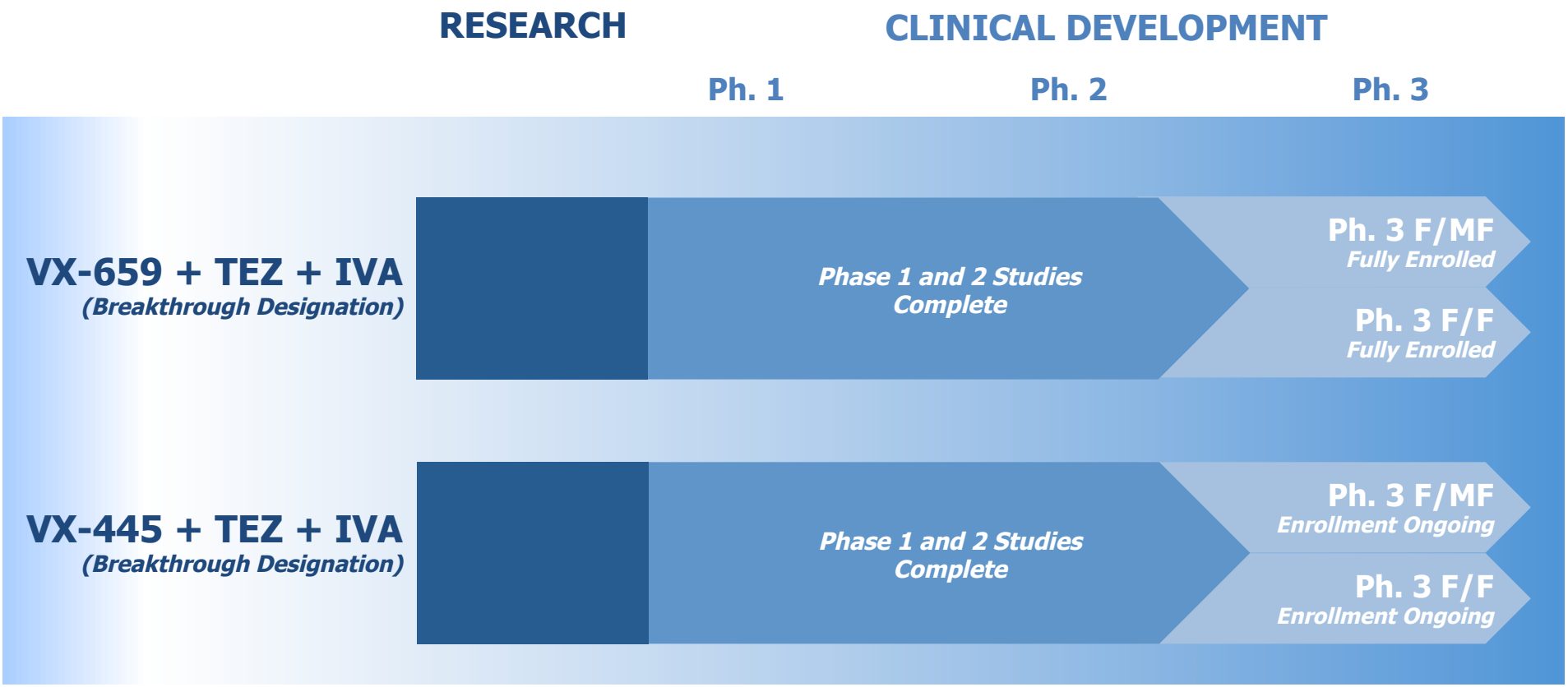
Rapid Progress Across Phase 3 Programs Evaluating Two Triple Combination Regimens



- VX-659 Phase 3 data expected in late 2018
- VX-445 Phase 3 data expected in Q1 2019
- NDA submission anticipated no later than mid-2019
- Studies in children ages 6 through 11 underway

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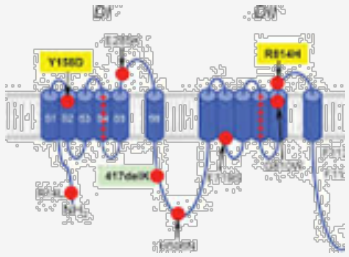
Beyond CF: Multiple First-in-Class Molecules



Pain

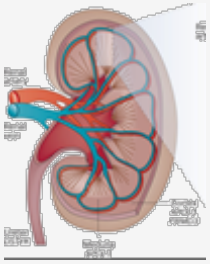
VX-150: First NaV1.8 inhibitor to demonstrate proof-of-concept in pain; Ongoing research to discover/develop additional NaV1.8 inhibitors and other potential pain molecules

Sickle Cell Disease / Beta Thalassemia

CTX001: Initiated Phase 1/2 study in Beta Thalassemia; Initiation of Phase 1/2 study in Sickle Cell Disease planned for Q4 2018

Alpha-1 Antitrypsin Deficiency

AAT: Multiple molecules in late preclinical development; Plan to advance first molecule into clinical development by end of 2018



Focal Segmental Glomerulosclerosis

FSGS: Novel approach to underlying biology of severe kidney disease

Vertex Strategy and Business Model

CORPORATE STRATEGY

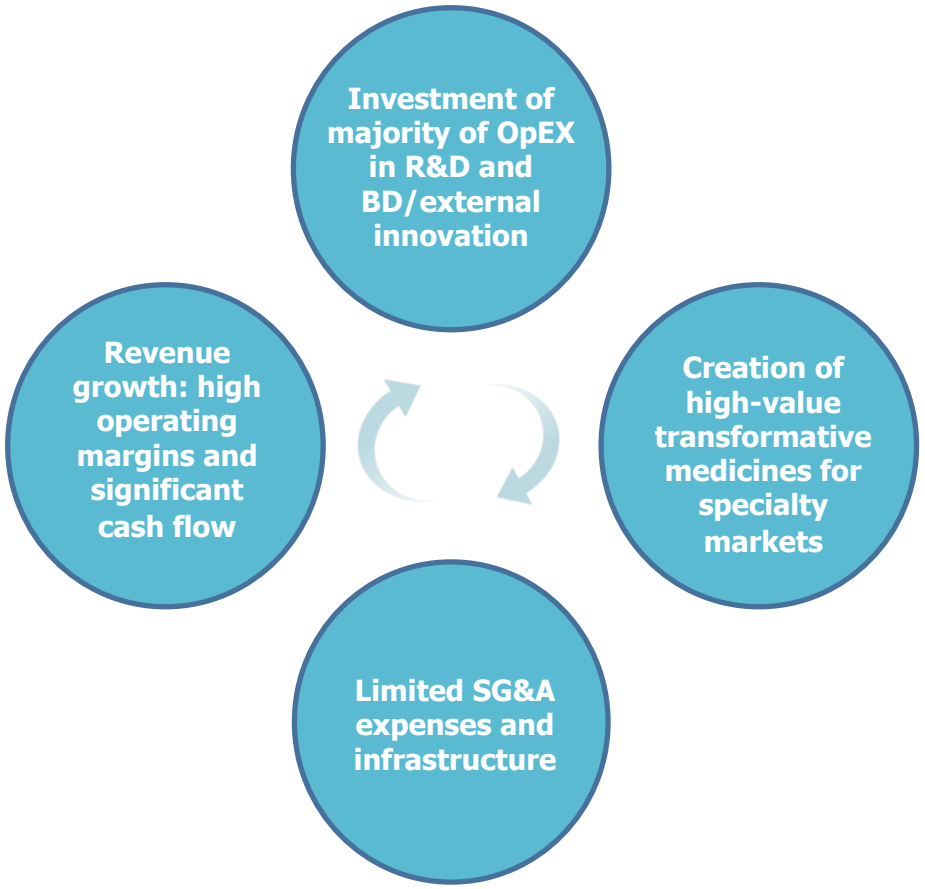
Vertex invests in **scientific innovation** to create **transformative medicines** for people with **serious diseases** with a focus on **specialty markets**

RESEARCH STRATEGY

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

- ✓ **Life-threatening, unmet need**
- ✓ **Insights into human biology; novel therapeutic approach**
- ✓ **Predictive assays and biomarkers**
- ✓ **Efficient clinical trial path**
- ✓ **Specialty sales and G&A model**

DIFFERENTIATED BUSINESS MODEL



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Q3 2018 Financial Highlights

($ in millions except per share data and percentages)	Q3 17	FY 2017	Q1 18	Q2 18	Q3 18	YTD 2018
Total CF product revenues	$550	$2.17B	$638	$750	**$783**	$2.17B
KALYDECO	213	845	250	253	**246**	748
ORKAMBI	336	1.32B	354	311	**282**	947
SYMDEKO			34	186	**255**	475
Combined non-GAAP R&D and SG&A	334	1.33B	360	388	**379**	1.13B
Non-GAAP operating income	145	564	208	260	**295**	763
Non-GAAP operating margin	26%	26%	33%	35%	**38%**	35%
Non-GAAP net income	136	495	196	244	**282**	722
Non-GAAP net income per share - diluted	$0.53	$1.95	$0.76	$0.94	**$1.09**	$2.79
Cash, cash equivalents & marketable securities (quarter-end)		$2.1B			**$3.1B**	

- *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 Q3 2018 press release dated October 24, 2018*
- *Reconciliation of non-GAAP operating income and non-GAAP operating margin to corresponding GAAP measures is included in the Appendix of this presentation*

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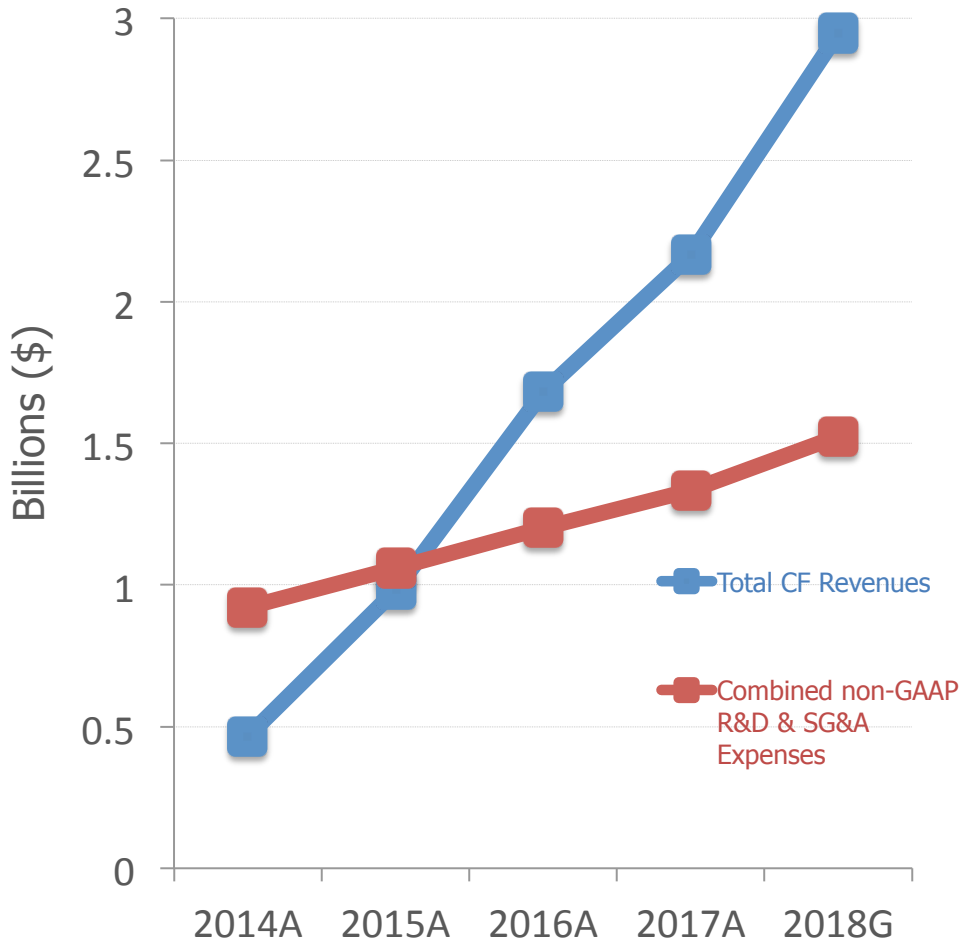
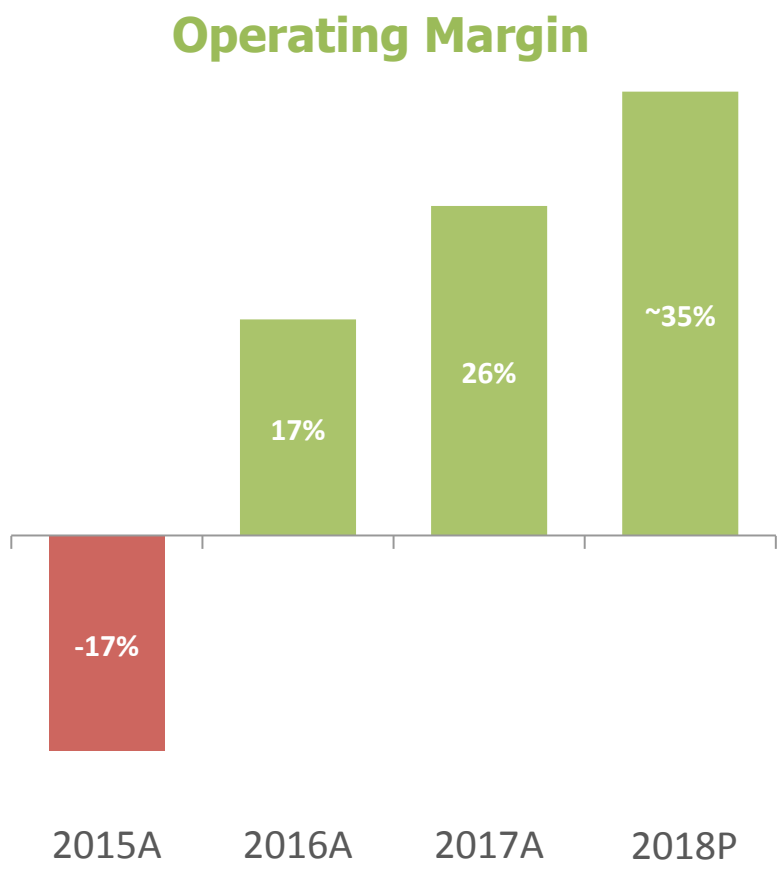
2018 Financial Guidance

	FY 2017 Actuals	2018 Guidance	2018 Guidance Commentary
Total CF Product Revenues	$2.17B	**$2.9 - $3.0B**	Guidance unchanged and based on: • Continued uptake and strong demand for SYMDEKO in U.S. among ages 12+
Combined non-GAAP R&D and SG&A	$1.33B	**$1.50 - $1.55B**	Guidance unchanged and based on: • Execution of Phase 3 studies for two separate triple combination regimens • Supply chain investment for triple combination regimens • Incremental investment to support SYMDEKO launch
Combined GAAP R&D and SG&A	$1.82B	**$1.80 - $1.95B**	

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 2018 press release dated October 24, 2018

Significant Growth in Revenue Driving Operating Margin Expansion





- *2018 Total CF Revenues (guidance: $2.9– $3.0B) and combined non-GAAP R&D and SG&A expenses (guidance: $1.50 - $1.55B) graphed to reflect the midpoint of guidance ranges.*
- *Operating margins reflect total CF revenues, combined non-GAAP R&D and SG&A expenses and cost of sales.*
- *2018 projected operating margin based on the midpoint of guidance ranges and assumes a ~13.5% cost of sales; not intended as financial guidance.*

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Principles of Future Guidance

Revenue growth in 2019 will be based on:

- Impact of the SYMDEKO and SYMKEVI launches
- Recently completed reimbursement agreements and label expansions of CF medicines
- Additional growth dependent upon gaining new reimbursement agreements in key countries, including the UK and France

Growth beyond 2019 will be driven by:

- Potential approval, reimbursement and uptake of a triple combination medicine for the large number of patients with a minimal function mutation who currently do not have a treatment for the cause of their CF

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Appendix

Reconciliation of GAAP to non-GAAP Financial Information

	Q3 2017	FY 2017	Q1 2018	Q2 2018	Q3 2018
GAAP total revenues	$578	$2,489	$641	$752	**$785**
Non-GAAP total revenues	$552	$2,174	$639	$751	**$784**
GAAP (loss) income from operations	(326)	123	129	173	**206**
Stock compensation expense	74	291	78	82	**86**
Collaborative and transaction revenues and expenses	397	133	1	4	**2**
Other adjustments	1	17	0	2	**1**
Non-GAAP income from operations	$145	$564	$208	$260	**$295**
Operating Margin %:					
GAAP	(56)%	5%	20%	23%	**26%**
Non-GAAP	26%	26%	33%	35%	**38%**
Net (loss) income					
GAAP	(103)	263	210	207	**129**
Non-GAAP	136	495	196	244	**282**
Net (loss) income per share - diluted					
GAAP	$(0.41)	$1.04	$0.81	$0.80	**$0.50**
Non-GAAP	$0.53	$1.95	$0.76	$0.94	**$1.09**

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