Q1 2015 results

Shire delivers strong revenue growth and cash generation; 20% increase in Non GAAP earnings per ADS

April 30, 2015

Flemming Ornskov, MD
CEO

Jeff Poulton
CFO

Our purpose
We enable people with life-altering conditions to lead better lives.

Shire

“SAFE HARBOR” statement under the Private Securities Litigation Reform Act of 1995

Statements included in this announcement that are not historical facts are forward-looking statements. Such forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, Shire’s results could be materially adversely affected. The risks and uncertainties include, but are not limited to, that:

- Shire’s products may not be a commercial success;
- product sales from ADDERALL XR® and INTUNIV® are subject to generic competition;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for Shire's products may affect future revenues, financial condition and results of operations;
- Shire conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services. Some of the Shire’s products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of the Shire’s products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire’s products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire’s revenues, financial conditions or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire’s activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire’s ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire’s revenues, financial condition or results of operations;
- Shire faces intense competition for highly qualified personnel from other companies and organizations. Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect Shire’s ability to attract and/or retain the highly skilled personnel needed for Shire to meet its strategic objectives;
- failure to achieve Shire’s strategic objectives with respect to the acquisition of NPS Pharmaceuticals, Inc. may adversely affect Shire’s financial condition and results of operations;

and other risks and uncertainties detailed from time to time in Shire’s filings with the US Securities and Exchange Commission, including its most recent Annual Report on Form 10-K.

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Q1 2015: On track to become a leading global biotechnology company

GROWTH

- Strong top and bottom line growth and cash generation
- Close of NPS acquisition
- Launch of NATPARA in HPT
- Approval and launch of VYVANSE in BED

INNOVATION

- FDA acceptance of NDA for lifitegrast in signs and symptoms of Dry Eye Disease with Priority review
- Clear regulatory path forward for SHP465 in adult ADHD
- Acquisition of Meritage expands GI pipeline with late stage asset for eosinophilic esophagitis

EFFICIENCY

- US site consolidation well underway
- NPS integration progressing as planned

PEOPLE

- Jeff Poulton appointed as Chief Financial Officer

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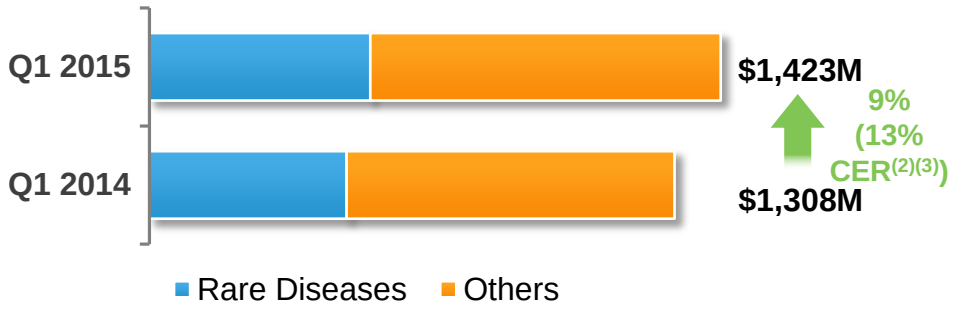
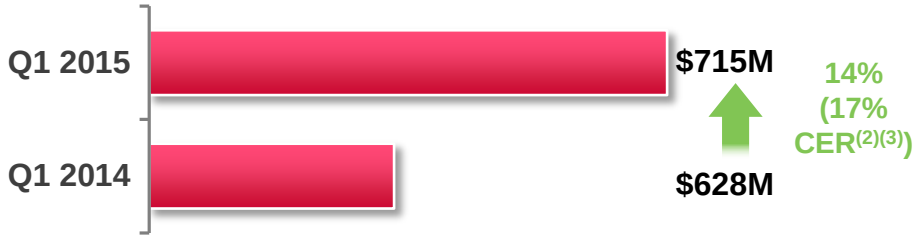
Delivering strong sales and Non GAAP EBITDA[(1)(3)] growth

Product Sales



Non GAAP EBITDA[(1)(3)]



Strong product sales and Non GAAP EBITDA[(1)(3)] growth, despite generic competition to INTUNIV and FX headwinds

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income (Q1 2015: $410m, Q1 2014: $230m).

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(3) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.

Growth across the product portfolio

GROWTH

VYVANSE sales $417M; +20%(1)

- US growth driven by volume gains – especially post launch of BED - and price
- International growth continues to benefit from gains in established markets

LIALDA sales $148M; +17%(1)

- US prescription growth of 12% (in a flat market) drove a 4% increase in market share vs. prior year
- Sales growth aided by a price increase slightly offset by higher destocking; significant destocking versus Q4 2014

CINRYZE sales $148M; +28%(2)

- Strong increase in patients and utilization
- Accelerated growth as product has benefited from Shire's Rare Disease expertise

FIRAZYR sales $92M; +26%(1)

- Increased number of patients and price
- Upward momentum continues ~3 years post US launch
- CINRYZE complementarity has accelerated gains

GATTEX sales $15M; +44%(3)

- Gattex is included in reported sales from 21 February 2015
- Integration progressing according to plan
- Second consecutive quarter of positive growth for completed patient referral forms, a precursor of therapy initiation

(1) All growth rates are at Constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2015 performance (restated using 2014 exchange rates) to actual 2014 reported performance. See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22

(2) CINRYZE refers to pro-forma growth. CER reported growth 74%.

(3) GATTEX refers to pro-forma growth.

NPS acquisition: two exciting new assets

GROWTH

	Natpara® (parathyroid hormone) for Injection	Gattex® (Teduglutide [rDNA origin]) for Injection
Launch	• NATPARA launched in the US 1st April 2015; NATPAR submitted in EU December 2014	• GATTEX US launch ongoing; REVESTIVE EU launch underway
Target physicians	• 1080 endocrinologists trained on REMS(1) program (as of 4/20)	• Improved physician targeting with an enriched target list and expanded reach
Salesforce	• 50-strong specialist sales force in place	• Salesforce optimization ongoing • From 2H 2015 LIALDA salesforce will be trained to identify candidates for GATTEX
Patients	• 101 patient referral forms received (4/20) • Primarily new patients due to ongoing BID(2) post approval commitment study • First commercial patient supplied with product on Friday 4/17	• Deployment of our leading patient services network to provide dedicated case management and patient field support for patients

- **Expect both products to benefit from Shire's rare disease patient identification and management capabilities**
- **Global footprint to deliver GATTEX/REVESTIVE and NATPARA to patients worldwide**
- **Integration progressing according to plan**

(1) REMS: Risk Evaluation and Mitigation Strategy.
(2) BID: twice daily.

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Binge Eating Disorder (BED) in adults – approved and launch underway

GROWTH

Launch	✓	Received FDA approval on January 30th
Marketing	✓	Commenced BED education activities
	✓	Launched branded & unbranded consumer and HCP promotion
Salesforce	✓	Hired, trained, & deployed all representatives on expanded targets
	✓	Held national sales meeting in early February

Early trends positive

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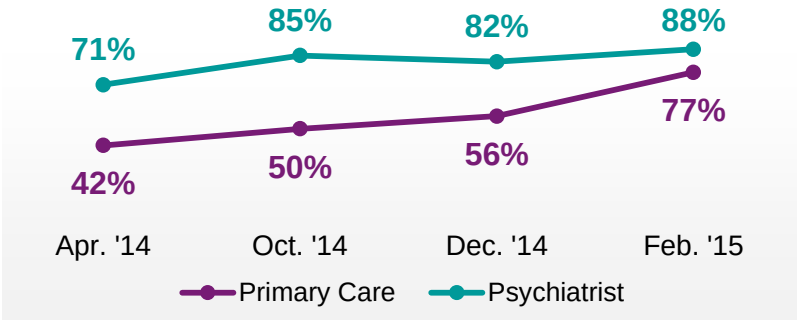
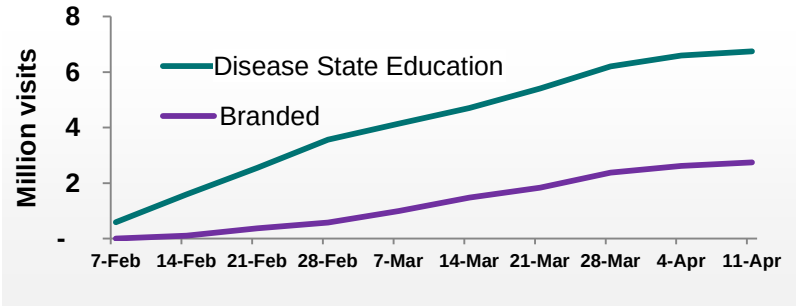
Binge Eating Disorder – early awareness efforts generating positive results

GROWTH

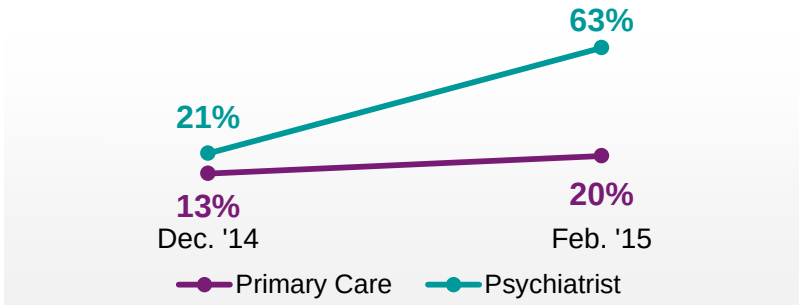
Unaided awareness of BED



Visits to BED websites



Unaided awareness of Vyvanse as a medication for BED



- Increased awareness amongst primary care physicians and psychiatrists
- Visits to both branded and unbranded BED websites have been increasing

Unaided awareness charts source: Shire market research
Websites data source: Adobe Analytics

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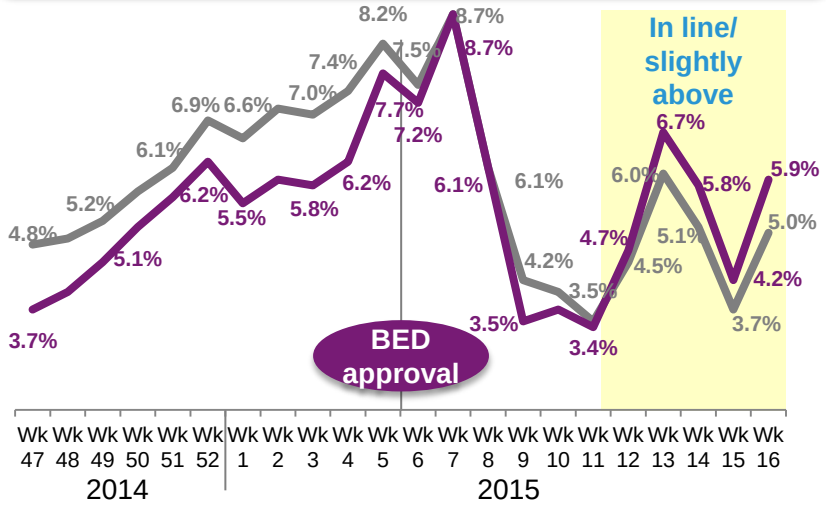
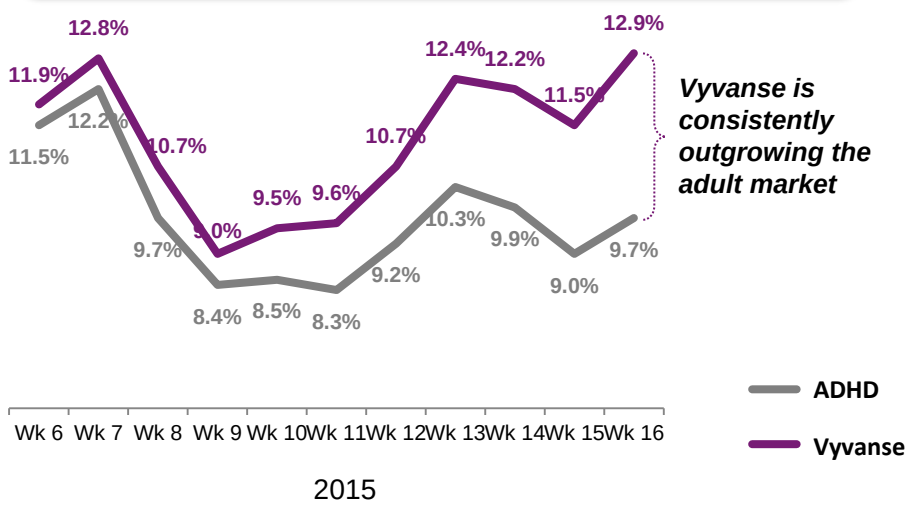
Recent Rx trends indicate positive momentum

GROWTH

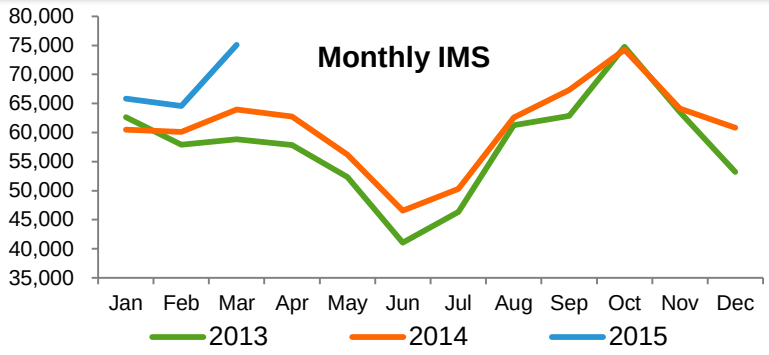
Rolling 4 week YoY TRx growth: OVERALL – Vyvanse vs. ADHD market



Rolling 4 week YoY TRx growth: ADULT – Vyvanse vs. ADHD market



New to brand Rx for Vyvanse (NBRx)



- A large portion of the strong momentum is coming from the adult market
- Vyvanse NBRx is increasing, with clear separation from prior years
- Trend break corresponds with the launch timing of the BED indication

Source: weekly IMS data

Strong and innovative pipeline

Our purpose
We enable people with life-altering conditions to lead better lives.

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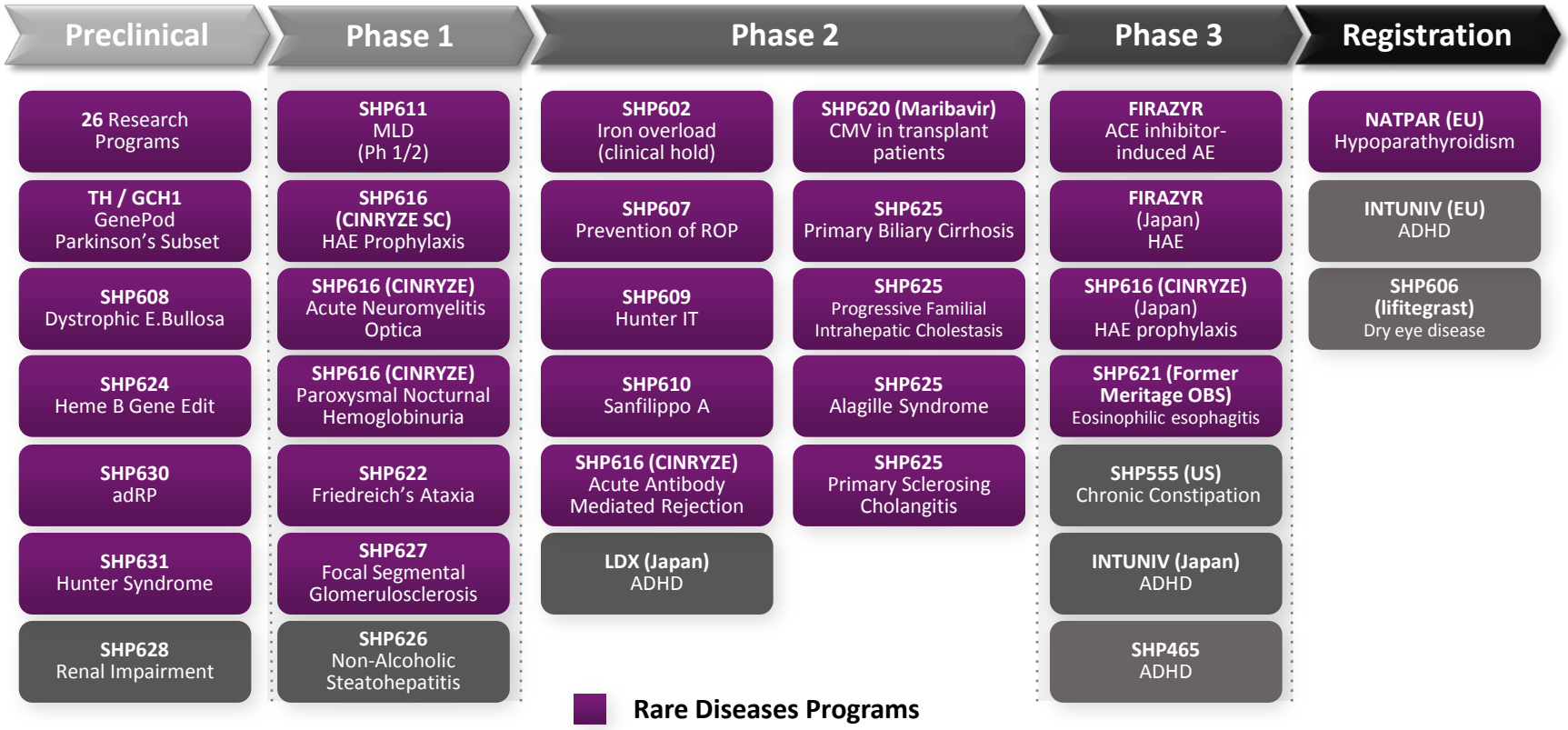
Strong pipeline continues to advance

INNOVATION



Changes since year end 2014

- Acquisition of NPS Pharma adds NATPAR in Registration in Europe.
- Acquisition of Meritage adds Oral Budesonide Suspension (OBS) now SHP621, Phase 3 ready.
- Lifitegrast NDA filed for treatment of signs and symptoms of dry eye disease in adults.
- VYVANSE BED in adults approved January 30, 2015.
- Fast track designation granted to SHP609.
- Discontinued IgAN.

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Q1 2015 Pipeline updates

INNOVATION

SHP606 (lifitegrast)
Dry eye disease

- FDA has accepted the NDA for lifitegrast (SHP606) for the treatment of the signs and symptoms of dry eye disease, and has granted a Priority Review designation
- PDUFA date of 25 October 2015
- OPUS 3 on track for read out by year end 2015

SHP465
ADHD

- Clear regulatory path forward for SHP465 in the treatment of ADHD
- Agreement with the FDA to conduct a short-term efficacy and safety study in pediatric patients with ADHD (ages 6-17)
- First patient, first visit to take place in August 2015; study completion targeted for Q4 2016
- FDA Class 2 submission expected by Q2 2017; anticipate a 6 month review time

SHP611
MLD

- Reported interim results from a Ph 1/2 study of SHP611 in late infantile metachromatic leukodystrophy (MLD)
- SHP611 was shown to be safe and well tolerated at all doses, with encouraging signs of efficacy at the highest dose in the study (100mg)

SHP625
ALGS

- Reported results from the Phase 2 IMAGO study of SHP625 in ALGS
- Given the topline results from the IMAGO study of SHP625 in pediatric patients with Alagille syndrome, we plan to analyze the totality of data to better understand the results we have seen. Data for this and other indications will be important to fully understand the safety and efficacy of SHP625 in patients with cholestatic liver disease

SHP621: late stage Orphan GI opportunity for eosinophilic esophagitis (EoE)

INNOVATION

ViroPharma and Meritage executed a development and option (to acquire the company) agreement in 2011

Company's sole product candidate, Oral Budesonide Suspension (OBS) now SHP621, is Phase 3 ready

SHP621 under development to treat a rare GI disease: eosinophilic esophagitis (EoE)

Disease prevalence in the US is ~180,000

Proof of concept (PoC) demonstrated in two Phase 2 studies with significant reduction in eosinophil counts in both studies

SHP621 has the potential to be the first approved product in the US for the treatment of EoE. FDA has granted orphan designation to SHP621 for the treatment of EoE

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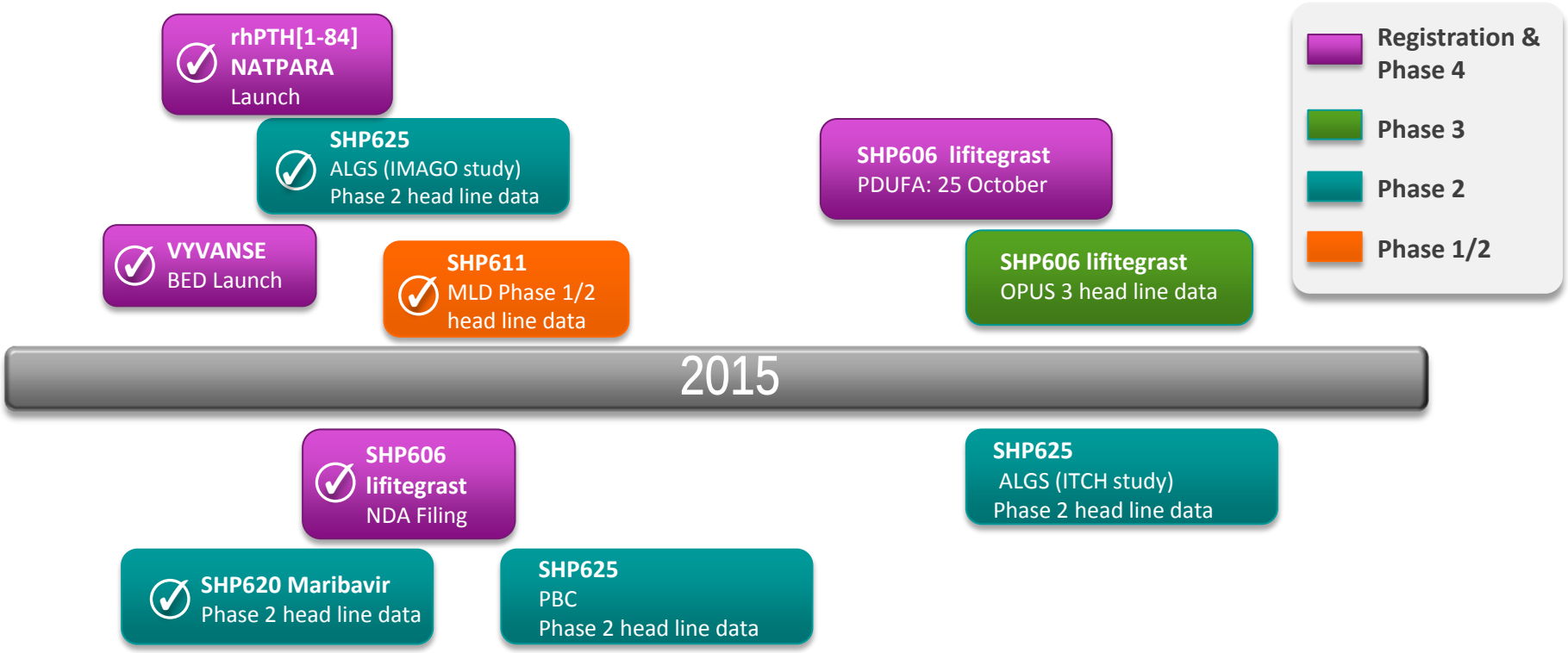
Data read outs expected in 2015

INNOVATION



Note
Future readouts of SHP625 program under review

Jeff Poulton appointed as CFO

PEOPLE

- Jeff Poulton appointed as Chief Financial Officer (CFO) and member of the Executive Committee
- Jeff will also join the Shire Board of Directors

- Jeff has served as Interim CFO since December 2014
- Jeff has been with Shire since 2003 and has extensive experience across financial, commercial and strategic leadership roles
- Recent roles include Head of Investor Relations and leading the Global Rare Diseases business unit
- Previously, Jeff served in diverse corporate finance and business development roles for Cinergy Corp. and PPG Industries
- Jeff served as a commissioned officer in the United States Navy, and has a B.A. in economics from Duke University and a MBA in Finance from the Kelly School of Business at Indiana University

Shire

Financial Review

Jeff Poulton, Chief Financial Officer

Our purpose
We enable people with life-altering conditions to lead better lives.

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Strong start to the year, with EPS[5][7] of $2.84 up 20%

	Q1 2015 $m	Q1 2014 $m	Reported Growth	CER[1][7]
Product Sales	1,423	1,308	+9%	+13%
Product Sales excluding INTUNIV	1,406	1,226	+15%	+19%
Royalties and Other Revenues	65	39	+68%	+73%
Total Revenue	1,488	1,347	+11%	+15%
Non GAAP EBITDA[2][7]	715	628	+14%	+17%
Non GAAP EBITDA % of Product Sales[3][4][7]	46%	45%	1% point	
Non GAAP diluted EPS – ADS[5][7]	2.84	2.36	+20%	+24%
Non GAAP Cash Generation[6][7]	516	331	+56%	

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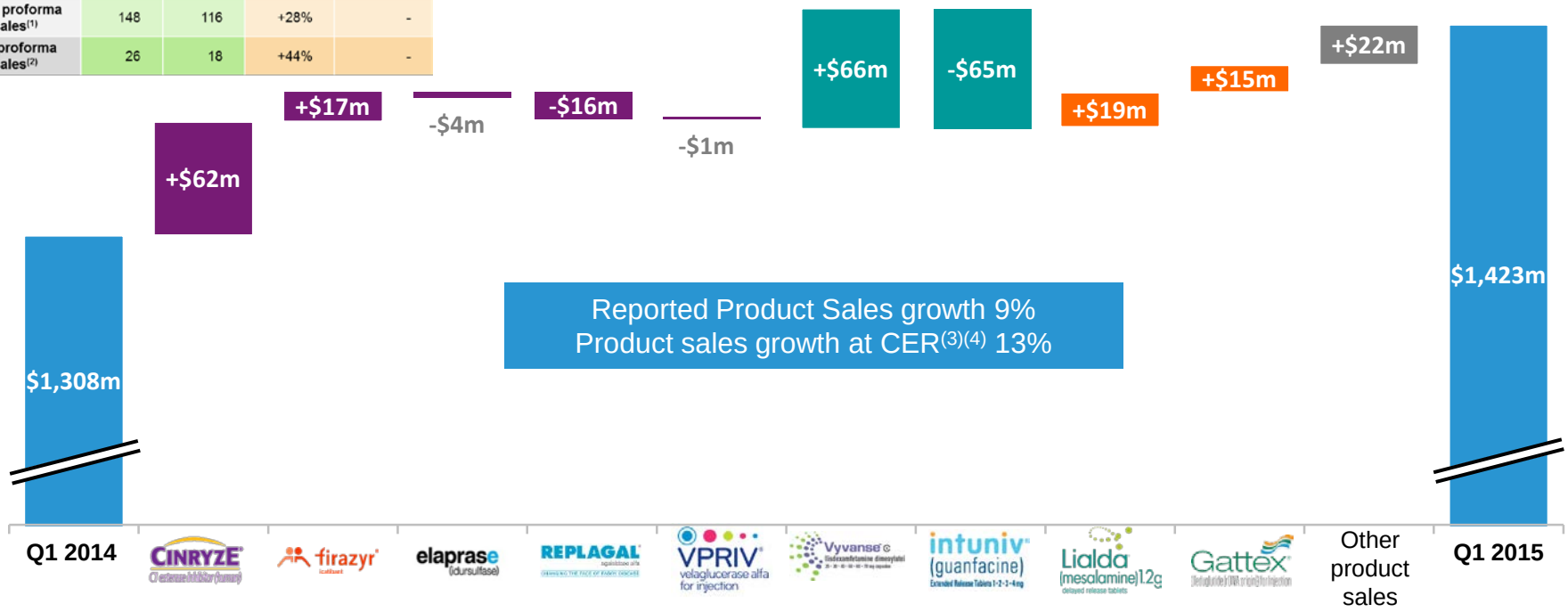
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income margin (Q1 2015: 28%, Q1 2014: 17%).
(4) Excluding Royalties and Other Revenues.
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q1 2015: $2.08, Q1 2014: $1.17).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Cash provided by operating activities (Q1 2015: $562m, Q1 2014: $246m).
(7) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.

Product sales up 13% at CER[3][4], driven by VYVANSE and the HAE products

	Q1 2015 $m	Q1 2014 $m	Reported Growth	CER Growth [3][4]
VYVANSE	417	351	+19%	+20%
LIALDA/MEZAVANT	148	129	+15%	+17%
CINRYZE	148	86	+73%	+74%
ELAPRASE	125	129	-3%	+7%
REPLAGAL	98	114	-15%	-3%
ADDERALL XR	96	85	+12%	+14%
FIRAZYR	92	75	+23%	+26%
VPRIV	86	87	-1%	+6%
PENTASA	79	72	+9%	+9%
INTUNIV	17	82	-79%	-78%
GATTEX	15	0	n/a	n/a
OTHER	102	98	+4%	+14%
Total Product Sales	1,423	1,308	+9%	+13%
CINRYZE proforma product sales[1]	148	116	+28%	-
GATTEX proforma product sales[2]	26	18	+44%	-



(1) CINRYZE acquired with ViroPharma Inc. on January 24, 2014.
(2) GATTEX acquired with NPS Pharma Inc. on February 21, 2015.
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Delivery of strong Non GAAP EBITDA margins[7][8][9] in Q1 2015

Year on Year Change:	Q1 2015	Q1 2014
Product Sales	+9%	+19%
Non GAAP R&D[1][9]	-2%	-13%
Non GAAP SG&A[2][9]	+10%	+4%
Combined Non GAAP R&D and SG&A[3][9]	+6%	-3%

Ratios:	Q1 2015	Q1 2014
% of Product Sales		
Non GAAP Gross Margin[4][9]	85.8%	86.2%
Non GAAP R&D[5][9]	13%	14%
Non GAAP SG&A[6][9]	27%	27%
Non GAAP EBITDA[7][8][9]	46%	45%

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q1 2015: -46%, Q1 2014: +63%).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2015: +18%, Q1 2014: +10%).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q1 2015: -11%, Q1 2014: +29%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross margin (Q1 2015: 84.0%, Q1 2014: 82.5%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (Q1 2015: 14%, Q1 2014: 28%).
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (Q1 2015: 36%, Q1 2014: 33%).
(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net income margin (Q1 2015: 28%, Q1 2014: 17%).
(8) Excluding Royalties and Other Revenues.
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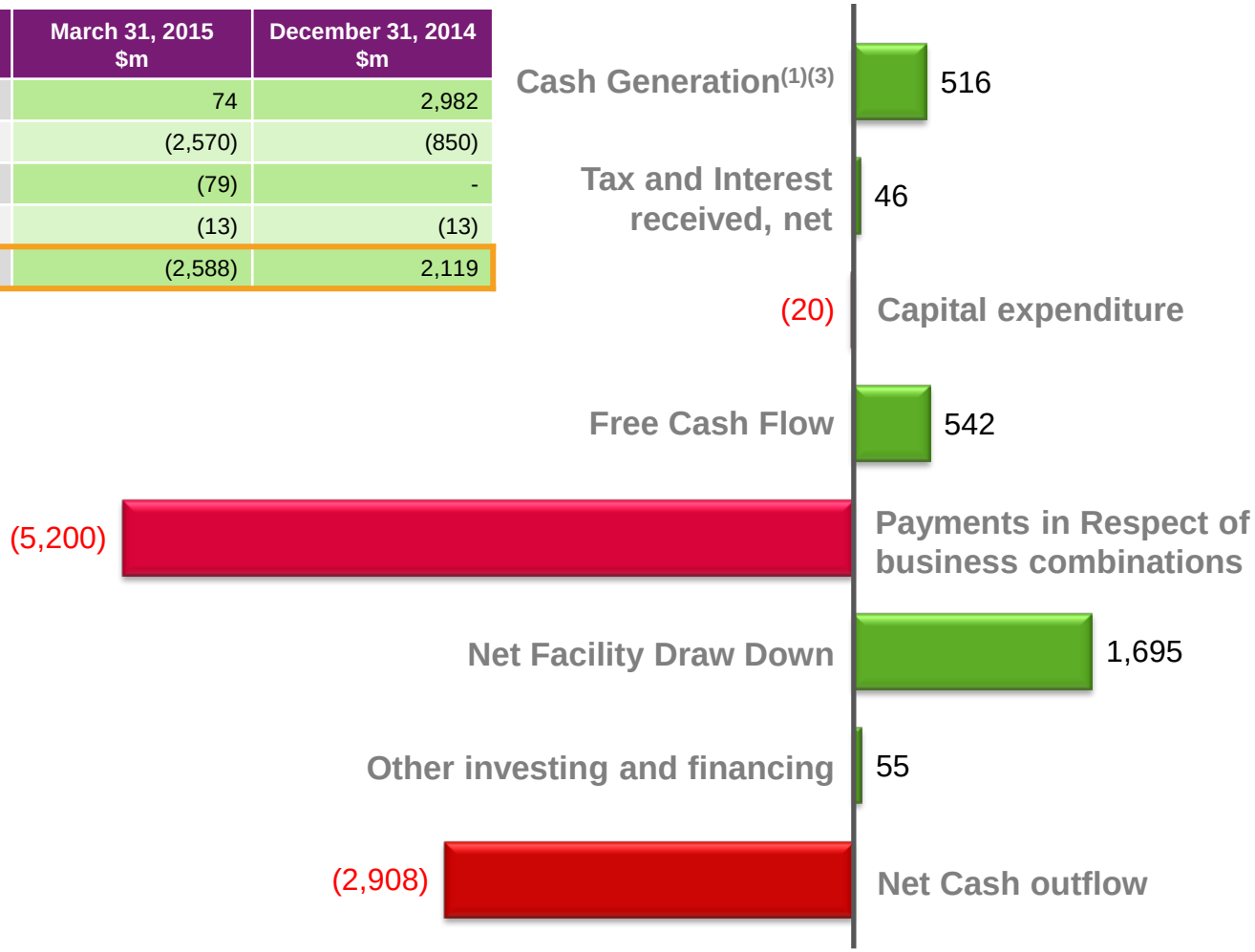
Strong Non GAAP cash generation[(1)(3)] in Q1 2015
Non GAAP net debt[(2)(3)] of $2.6B at March 31, 2015

	March 31, 2015 $m	December 31, 2014 $m
Cash and cash equivalents	74	2,982
Short-term borrowings	(2,570)	(850)
Long-term borrowings	(79)	-
Other debt	(13)	(13)
Non GAAP Net (debt)Cash[(2)(3)]	(2,588)	2,119



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(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Cash and Cash equivalents (Q1 2015: $74m, Q4 2014: $2,982m).
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Confident in delivering Non GAAP diluted earnings per ADS[(1)(2)] growth in the mid single digits

	Full Year 2015 Dynamics			
	Direction Versus FY 14	CER Growth [(2)(3)]	Impact of FX Rates on Guidance	Guidance
Total Product Sales	↑	Mid-to-high single digit growth	-3 to 4% points	Low-to-mid single digit growth
Product Sales excluding INTUNIV	↑	*Low double digit growth*		*High single digit growth*
Royalties & Other Revenues	↑			30-40% higher than in 2014
Non GAAP Gross Margins[(2)]	~			Similar to 2014
Non GAAP Combined R&D and SG&A[(2)]	↑			High single digit growth
Non GAAP Net Interest/Other[(2)]	~			Broadly in line with 2014
Non GAAP Tax Rate[(2)]	↓			Core effective tax rate of 15-17%
Non GAAP diluted Earnings per ADS[(1)(2)]	↑	High single digit growth	-4 to 5% points	Mid single digit growth

The estimated impact of a 10% appreciation in the US Dollar against the respective currency on our 2015 Guidance is as follows:

	Revenue	Earnings
EUR	(1.2%)	(2.1%)
GBP	(0.3%)	(0.3%)
CHF	(0.1%)	0.3%
CAD	(0.4%)	(0.3%)
Other	(0.6%)	(0.8%)

2015 Guidance constitutes forward looking statements. See "Safe Harbor" statement on Slide 2.

(1) Based on a latest assumption of a full year 2015 weighted average number of ordinary shares of 594 million.

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Summary

Flemming Ornskov, MD, Chief Executive Officer

Execution of strategy is delivering

Continued execution

- GROWTH
- EFFICIENCY
- INNOVATION
- PEOPLE

Delivering results in 2015

Delivering growth in revenues and earnings

Driving future growth

- Leveraging NPS assets
- Execute on BD opportunities
- Driving VYVANSE for BED in adults
- Advancing lifitegrast for Dry Eye Disease
- Multiple data read outs

On track to become a leading biotech

Shire

Questions and Answers

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We enable people with life-altering conditions to lead better lives.

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APPENDIX

Key Protections on important products

Product	Protection	Commentary
Lialda	Orange Book Listed patent expiring June 2020	• The patent has already withstood an attack on validity. • The US District Court for the Southern District of Florida upheld the validity of that patent in view of the challenges posed by Watson. In addition to withstanding the attack on validity, the US District Court for the Southern District of Florida found the patent to be infringed by Watson's proposed ANDA product. Aspects of the claim construction from that court are currently being revisited at the Court of Appeals of the Federal Circuit following Shire's successful petition to the Supreme Court. • ANDAs have been pending at the FDA for five years. None have been approved. • It has been 2.5 years since the FDA put forward revised guidelines for establishing bioequivalence to LIALDA. Shire regards these guidelines as challenging to meet. None of the pending ANDAs have been approved. • It is not certain that an IPR will be instituted. The challenged claims are presumed valid. Shire will defend the validity of the patent and will seek to have the US Patent and Trademark Office deny the request to institute an IPR.
Gattex	• GATTEX benefits from regulatory exclusivity in the US through December 2019. • There are several patents listed in the Orange Book protecting GATTEX expiring in 2015, 2022 and 2025.	• The recently filed petitions to institute inter partes reviews ("IPR") relates only to some of the claims of the patent expiring in 2025. The remainder of the claims in that patent, and the claims of the other patents are not being challenged. • It is not certain that any IPRs will be instituted. The challenged claims are presumed valid. Shire will defend the validity of the patent and will seek to have the US Patent and Trademark Office deny the request to institute an IPR.

Key Protections on important products

Product	Protection	Commentary

Vyvanse	• 18 Orange book listed patents including composition of matter patent
	• Including pediatric extension, we anticipate US patent protection until December 2023
		• On June 24, 2014 Judge Stanley Chesler of the U.S. District Court for the District of New Jersey issued an opinion and order granting Shire's summary judgment motion, holding that certain claims of the Vyvanse® patents were infringed and valid.
		• The Court ruled that 18 patent claims from four patents are both infringed and valid, including claims to the following:
		  • Vyvanse's Active Pharmaceutical Ingredient (API) compound, lisdexamfetamine dimesylate;
		  • lisdexamfetamine dimesylate compositions; and
		  • A method of treating ADHD using lisdexamfetamine dimesylate.
		• This decision prevents the ANDA-filers from launching their proposed generic Vyvanse products until:
		  • they successfully appeal the ruling to the Federal Circuit, and overturn the rulings for each of the 18 patent claims; or
		  • the expiration of the patents-in-suit in 2023.
		• This lawsuit includes all known ANDAs currently pending for Vyvanse.
		• Shire's summary judgment motion did not include every patent claim in the litigation. In the event the Court of Appeals overturns the summary judgment ruling, Shire will have the opportunity to litigate these remaining claims.
		• Shire maintains its belief that it also has strong infringement claims against the defendants for the patent claims that were not part of Shire's summary judgment motion, and strongly believes that the patent claims are valid.

SHP621 (OBS) Phase 2b summary results

INNOVATION

Study MPI-101-06: US Phase 2b study in 75 patients with EoE with persistent dysphagia assessed safety and efficacy of 2mg BID for 12 weeks compared to placebo with a 24 week open-label extension of 2mg QD

*Top Line Data released Sep 9, 2014

Endpoints	**Endpoint Met**
Co -1° Endpoints	
Induction of a histologic response in adolescent and adult subjects over a 12 week course of therapy	✔ (p=<0.0001)
And	
Induction of a symptom response using the DSQ in adolescent and adult subjects with EoE over a 12 week course of therapy	✔ (p=0.0096)
Safety and Tolerability	✔

Shire

Product sales – regional analysis

	US	Europe	LATAM	Other	Total
Q1 2015					
Product Sales $m	**1,044**	**255**	**28**	**96**	**1,423**
% of Product Sales	73%	18%	2%	7%	100%
YoY Growth	+15%	-8%	-1%	+5%	+9%
FY 2014					
Product Sales $m	**4,082**	**1,147**	**214**	**387**	**5,830**
% of Product Sales	70%	20%	4%	6%	100%
YoY Growth	+28%	+13%	+3%	+10%	+23%

Royalties and Other Revenues

	Q1 2015 $m	Q1 2014 $m	Reported Growth
INTUNIV	22	0	n/a
SENSIPAR	10	0	n/a
ADDERALL XR	9	9	-6%
FOSRENOL	8	13	-34%
3TC and ZEFFIX	8	8	0%
REMINYL & Other	6	2	+110%
Royalties	63	32	+94%
Other Revenues	2	7	-63%
Royalties & Other Revenues	65	39	+68%

Shire income statement growth analysis

	2014 Q1	2014 Q2	2014 Q3	2014 Q4	2014 FY	2015 Q1	FY 2015 Dynamics: Direction v. FY 14	FY 2015 Dynamics: Guidance
Total Product Sales	$1,308m	$1,469m	$1,552m	$1,501m	$5,830m	$1,423m	↑	Low-to-mid single digit growth
versus prior year	+19%	+22%	+33%	+17%	+23%	+9%		
Royalties & Other Revenues	$39m	$33m	$45m	$75m	$192m	$65m	↑	30-40% higher than in 2014
versus prior year	-14%	-27%	+8%	+65%	+8%	+68%		
Total Revenue	$1,347m	$1,502m	$1,597m	$1,576m	$6,022m	$1,488m		
versus prior year	+18%	+20%	+32%	+19%	+22%	+11%		
Non GAAP Gross Margin [(1)(6)]	86%	85%	86%	86%	86%	86%	~	Similar to 2014
Combined Non GAAP R&D and SG&A [(2)(6)]	$539m	$602m	$618m	$677m	$2,436m	$571m	↑	High single digit growth
versus prior year	-3%	+2%	+10%	+11%	+5%	+6%		
Non GAAP EBITDA Margin[(3)(6)]	45%	44%	46%	41%	44%	46%		
Non GAAP Tax Rate[(4)(6)]	20%	16%	18%	19%	18%	17%	↓	Core effective tax rate of 15-17%
Non GAAP diluted Earnings per ADS [(5)(6)]	$2.36	$2.67	$2.93	$2.63	$10.60	$2.84	↑	Mid single digit growth
versus prior year	+38%	+42%	+60%	+17%	+38%	+20%		

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross margin (Q1 2015: 84.0%, Q1 2014: 82.5%).
(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q1 2015: $700m, Q1 2014: $791m).
(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net income margin (Q1 2015: 28%, Q1 2014: 17%).
(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Tax rate (Q1 2015: 12%, Q1 2014: 17%).
(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q1 2015: $2.08, Q1 2014: $1.17).
(6) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.

Non GAAP cash flow measures

Non GAAP cash generation [1][3] and Non GAAP free cash flow [2][3] reconciliation	Q1 2015 $m[1]	Q1 2014 $m[1]
Non GAAP cash generation[1][3]	516	331
Tax and interest receipts/(payments), net	46	(85)
US GAAP Net cash provided by operating activities	562	246
Capital expenditure	(20)	(15)
Non GAAP free cash flow[2][3]	542	231

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (see details above). Non GAAP cash generation represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, tax and interest payments.

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (see details above). Non GAAP free cash flow represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, but including capital expenditure in the ordinary course of business.

(3) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented Shire's Q1 2015 earnings release on pages 19 to 22.

Non GAAP net (debt)/cash[1][2]

	March 31, 2015 $m	December 31, 2014 $m
Cash and cash equivalents	74	2,982
Short term borrowings	(2,570)	(850)
Long term borrowings	(79)	-
Other debt	(13)	(13)
Non GAAP net (debt)/cash[1][2]	(2,588)	2,119

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Cash and Cash equivalents (Q1 2015: $74m, Q4 2014: $2,982m).
(2) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.

Shire has a $2.1bn revolving credit facility which matures in December 2019, and $0.85bn term loan facility that matures in November 2015 and $0.85bn term loan facility to support the acquisition of NPS that matures in January 2016. The maturity date may be extended twice, at Shire's option by six months on each occasion.

Q1 2015 – Operating income US GAAP and Non GAAP

	Q1 2015 $m	Q1 2014 $m	Reported Growth
Non GAAP Operating Income[1][2] from continuing operations	**683**	**591**	**+16%**
Intangible asset amortisation	(88)	(58)	
Impairment of IPR&D intangible assets	-	(166)	
Legal and litigation costs	(1)	(2)	
Integration and acquisition costs	(87)	(45)	
Gains on sale of non-core assets	5	36	
Reorganization costs	(15)	(49)	
Other	(22)	-	
US GAAP Operating Income from continuing operations	**475**	**307**	**+55%**

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is US GAAP Operating income (see details above).
(2) See slide 35 for a list of items excluded from the US GAAP equivalent used to calculate all Non GAAP measures detailed above. A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.

Non GAAP measures

This presentation contains financial measures not prepared in accordance with US GAAP. These measures are referred to as "Non GAAP" measures and include: *Non GAAP operating income; Non GAAP net income; Non GAAP diluted earnings per ADS; effective tax rate on Non GAAP income before income taxes and earnings/(losses) of equity method investees ("effective tax rate on Non GAAP income"); Non GAAP cost of product sales; Non GAAP* R&D*; Non GAAP* SG&A*; Non GAAP other income/(expense); Non GAAP interest income; Non GAAP cash generation; Non GAAP free cash flow, Non GAAP net cash/(debt), Non GAAP EBITDA and Non GAAP EBITDA Margin as percentage of product sales*. These Non GAAP measures exclude the effect of certain cash and non-cash items, that Shire's management believes are not related to the core performance of Shire's business.

These Non GAAP financial measures are used by Shire's management to make operating decisions because they facilitate internal comparisons of Shire's performance to historical results and to competitors' results. Shire's Remuneration Committee uses certain key Non GAAP measures when assessing the performance and compensation of employees, including Shire's executive director.

The Non GAAP measures are presented in this presentation as Shire's management believe that they will provide investors with a means of evaluating, and an understanding of how Shire's management evaluates, Shire's performance and results on a comparable basis that is not otherwise apparent on a US GAAP basis, since many non-recurring, infrequent or non-cash items that Shire's management believe are not indicative of the core performance of the business may not be excluded when preparing financial measures under US GAAP.

These Non GAAP measures should not be considered in isolation from, as substitutes for, or superior to financial measures prepared in accordance with US GAAP.

Where applicable the following items, including their tax effect, have been excluded when calculating Non GAAP earnings for both 2015 and 2014, and from our Outlook:

Amortization and asset impairments:
- Intangible asset amortization and impairment charges; and
- Other than temporary impairment of investments.

Acquisitions and integration activities:
- Up-front payments and milestones in respect of in-licensed and acquired products;
- Costs associated with acquisitions, including transaction costs, fair value adjustments on contingent consideration and acquired inventory;
- Costs associated with the integration of companies; and
- Noncontrolling interests in consolidated variable interest entities.

Divestments, reorganizations and discontinued operations:
- Gains and losses on the sale of non-core assets;
- Costs associated with restructuring and reorganization activities;
- Termination costs; and
- Income/(losses) from discontinued operations.

Legal and litigation costs:
- Net legal costs related to the settlement of litigation, government investigations and other disputes (excluding internal legal team costs).

Other:
- Net income tax credit (being income tax, interest and estimated penalties) related to the settlement of certain tax positions with the Canadian revenue authorities.
- Costs associated with AbbVie's terminated offer for Shire, including costs of employee retention awards.
- Break fee received in relation to AbbVie's terminated offer for Shire.

Depreciation, which is included in Cost of product sales, R&D and SG&A costs in our US GAAP results, has been separately disclosed for the presentation of 2015 and 2014 Non GAAP earnings.

Cash generation represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, tax and interest payments.

Free cash flow represents net cash provided by operating activities, excluding up-front and milestone payments for in-licensed and acquired products, but including capital expenditure in the ordinary course of business.

Growth at CER, which is a Non GAAP measure, is computed by restating 2015 results using average 2014 foreign exchange rates for the relevant period.

Average exchange rates for Q1 2015 were $1.54:£1.00 and $1.15:€1.00 (Q1 2014: $1.66:£1.00 and $1.37:€1.00).

A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire's Q1 2015 earnings release on pages 19 to 22.