

# Q3 2015 results

## Progressing our transformation to a leading global biotech

October 23, 2015



Flemming Ornskov, MD  
*CEO*

Jeff Poulton  
*CFO*

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



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

Statements included herein that are not historical facts, including without limitation statements concerning our 10x20 ambitions and targets, 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 Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of 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 condition 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;
- Shire's strategy to acquire Baxalta may not be successful: Baxalta may refuse to cooperate with Shire; if the proposed combination is consummated, the businesses may not be integrated successfully, including that expected synergies and other benefits of the combination may not be realized and unforeseen costs may arise; and disruption caused by the proposed transaction may adversely affect Shire; and

other risks and uncertainties detailed from time to time in Shire's filings with the Securities and Exchange Commission, including those risks outlined in “Item 1A: Risk Factors” in Shire's Annual Report on Form 10-K for the year ended December 31, 2014.

# Agenda

**Our progression towards becoming a leading global biotech**



**Flemming Ornskov, MD**

**Financial review**



**Jeff Poulton**

**Summary**



**Flemming Ornskov, MD**

**Q & A**

**All**

# Our continuous transformation

2013

2014

2015

2016

2017

2018

2019

2020+

Investing to create  
further long-term value

## 2013-2015 Becoming OneShire

- Step-change in performance
- Effective and efficient organization
- Set basis for long-term growth

## 2014-2020+ Building a leading global biotech company

- Creating scale and momentum
- Culture of bold innovation – internal and external
- Patient-centric Rare Diseases mindset to all business

On track to meet 10x20 targets

# Q3 2015: Progress towards becoming a leading global biotechnology company



## GROWTH

- ✔ **Double digit CER<sup>(1)</sup> product sales growth excluding INTUNIV**
- ✔ **Non GAAP diluted earnings per ADS growth guidance reiterated at mid-to-high single digit percent range for the full year**
- ✔ **Continued investment and progress in expected future growth drivers, including VYVANSE BED, GATTEX/REVESTIVE, NATPARA and lifitegrast**
- ✔ **Strong performance driven by VYVANSE, CINRYZE, and FIRAZYR**
- ✔ **GATTEX and NATPARA continue to benefit from Shire's Rare Disease expertise**



## INNOVATION

- ✔ **European approval for INTUNIV**
- ✔ **Phase 3 OPUS3 study for lifitegrast in symptoms of dry eye disease completed: topline results expected Q4 2015 and, if positive, to form the basis of Shire's response to the CRL**
- ✔ **Phase 3 pediatrics study for SHP465 enrolling ahead of schedule**
- ✔ **Multiple Phase 3 trials expected to start in late Q4 2015/early-to-mid 2016, including SHP620 for cytomegalovirus ("CMV") infection in transplant patients, SHP621 for Eosinophilic Esophagitis ("EoE"), and CINRYZE in AMR**
- ✔ **Acquired Foresight Biotherapeutics, bringing global rights to FST-100 (now referred to as SHP640), a late stage asset for the treatment of infectious conjunctivitis**

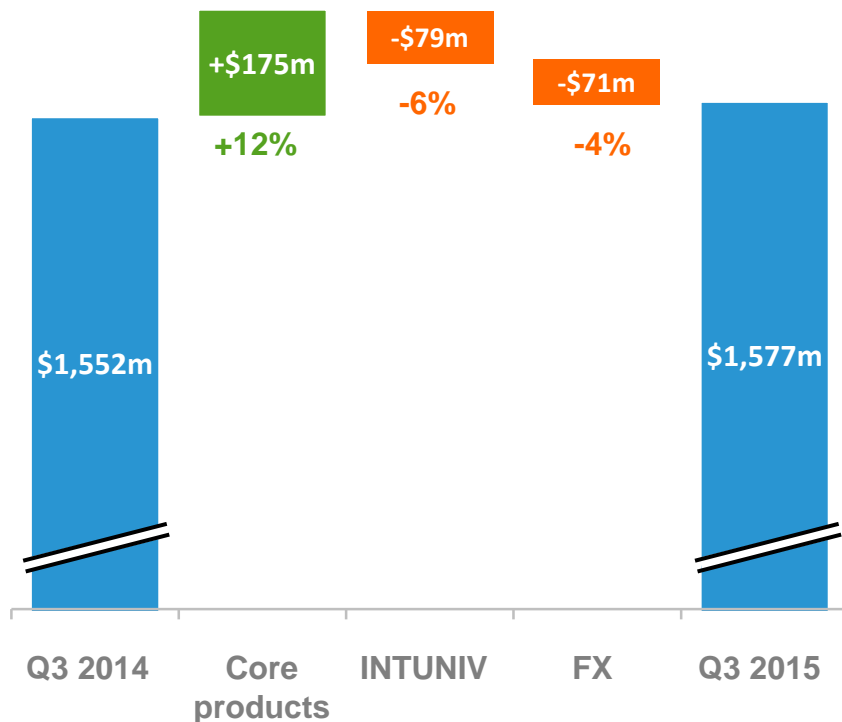
(1) Growth at Constant exchange rates ("CER"), a Non GAAP financial measure. CER performance is determined by comparing 2015 performance (restated using 2014 exchange rates) to actual 2014 reported performance. See slide 33 for a list of items excluded from the US GAAP equivalent used to calculate all 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 Q3 2015 earnings release on pages 22 to 28.

# Delivering double digit core product sales<sup>(1)</sup> growth while investing for the future



GROWTH

## Product Sales



- Core product sales excluding INTUNIV growing 12% on a constant exchange rate basis<sup>(2)(4)</sup>
- Continued investment and progress in expected future growth drivers, including VYVANSE BED, GATTEX/REVESTIVE, NATPARA and lifitegrast
- Q3 Non GAAP diluted earnings per ADS<sup>(3)(4)</sup> up 11% on a reported basis; 15% on a CER basis<sup>(2)(4)</sup>

**Non GAAP diluted earnings per ADS growth guidance reiterated**

(1) Results include NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015). Core product sales exclude INTUNIV and are stated at CER.

(2) Growth in constant exchange rate ("CER"). This is a Non GAAP financial measure. CER performance is determined by comparing 2015 performance (restated using average 2014 foreign exchange rates for the relevant period) to actual 2014 reported performance.

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2015: \$2.29, Q3 2014: \$2.43).

(4) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Q3 growth highlights



GROWTH



## VYVANSE sales \$427M; +22%<sup>(1)</sup>

- VYVANSE performing strongly in the adult market, both in ADHD and in the new BED indication
- US growth driven by volume gains (TRx up 9% YoY), price, and favourable stocking patterns
- International growth continues to benefit from gains in established markets
- VYVANSE patents held to be valid and infringed on appeal; patents expire in 2023



## CINRYZE sales \$187M; +30%<sup>(1)</sup>

- Sales growth driven primarily by an increase in patients on therapy, combined with a modest price increase
- Sales also benefitted from a re-stock in Q3 2015 after a destock in Q2 2015
- Strengthened our manufacturing position through renegotiation of agreement with Sanquin; Shire now in a position to seek a second source of supply



## FIRAZYR sales \$123M; +28%<sup>(1)</sup>

- Continued double digit growth primarily driven by new patient additions
- Sales also benefitted from price increases taken since Q3 2014



## GATTEX sales \$43M; +54%<sup>(2)</sup>

- Strong performance in US since acquisition of NPS; over 550 patients on therapy in US
- International roll out on track; favourable reimbursement obtained in France and Germany and encouraging early reception from patients and physicians



## NATPARA sales \$7M

- Strong US launch
- ~ 2000 HCPs REMS trained; ~ 400 patients on therapy

(1) 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 for the relevant period) to actual 2014 reported performance. See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

(2) GATTEX refers to pro-forma growth including product sales recorded by NPS prior to acquisition by Shire on a CER basis.

# Strong and innovative pipeline

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





# Late stage pipeline poised to deliver



INNOVATION

Preclinical	Phase 1	Phase 2		Phase 3	Registration
27 Research Programs	SHP611 MLD (Ph 1/2)	SHP607 Prevention of ROP	SHP625 Primary Biliary Cirrhosis	FIRAZYR (Japan) HAE	NATPAR (EU) Hypoparathyroidism
TH / GCH1 GenePod Parkinson's Subset	SHP616* (CINRYZE SC) HAE Prophylaxis	SHP609 Hunter IT (Ph 2/3)	SHP625 Progressive Familial Intrahepatic Cholestasis	SHP616 (CINRYZE) (Japan) HAE prophylaxis	SHP606 (lifitegrast) Dry eye disease
SHP608 Dystrophic E.Bullosa	SHP616 (CINRYZE) Acute Neuromyelitis Optica	SHP610 Sanfilippo A	SHP625 Alagille Syndrome	INTUNIV (Japan) ADHD	INTUNIV (EU) ADHD Approved Sep 21, 2015
SHP623 (rC1-INH) HAE prophylaxis	SHP622 Friedreich's Ataxia	SHP616 (CINRYZE)* Acute Antibody Mediated Rejection	SHP625 Primary Sclerosing Cholangitis	SHP465 ADHD	
SHP630 adRP	SHP627 Focal Segmental Glomerulosclerosis	SHP620 (maribavir)* CMV in transplant patients	SHP640 (FST-100)* Infectious Conjunctivitis	SHP555 (US) Chronic Constipation	
SHP636 MRT for CF	SHP631 Hunter Syndrome	SHP621 (Former Meritage OBS)* Eosinophilic esophagitis	LDX (Japan) ADHD		
SHP637 MRT for UCD	SHP626 Non-Alcoholic Steatohepatitis				
SHP639 Glaucoma					

## Changes since Q2 2015

■ Rare Diseases Programs  
\* Programs are Phase 3 ready

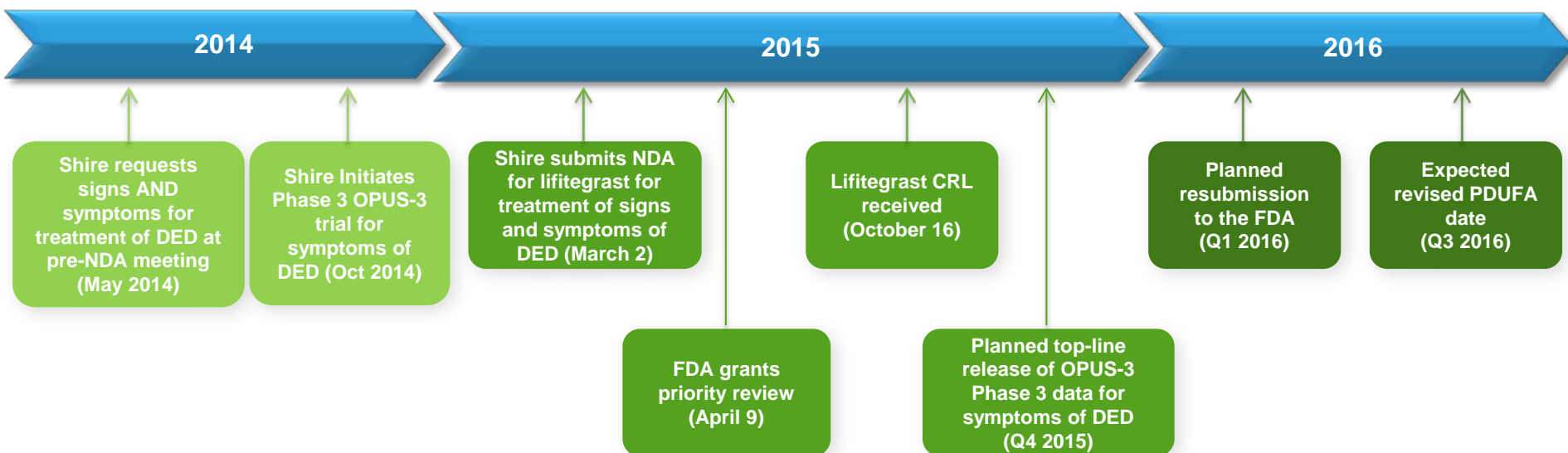
- INTUNIV (EU) approved September 21, 2015
- Addition of SHP623, SHP636, SHP637 and SHP639 in Preclinical, and SHP640 (FST-100) in Phase 2 (Phase 3 ready from the acquisition of Foresight Biotherapeutics Inc.)
- SHP624 reverted to Sangamo
- Firazyr ACE inhibitor induced AE and SHP628 discontinued
- Totality of SHP625 data being assessed; programs under review

# Lifitegrast: next steps for potential first agent to treat signs and symptoms of Dry Eye Disease (DED)



INNOVATION

- FDA issued a CRL requesting an additional clinical study on October 16, 2015
- Shire has recently completed a Phase 3 study of lifitegrast, OPUS-3. Top line results are expected before year-end, and, and if positive, Shire plans to submit these data as part of a resubmission to the FDA during the first quarter of 2016
- In its review of product quality the FDA also requested more information on lifitegrast, which Shire will address in its CRL response



# SHP640 (FST-100): potential to become first agent to treat viral and bacterial conjunctivitis



INNOVATION

## Significant unmet patient need

- No approved therapy for the treatment of both viral and bacterial conjunctivitis
- There are 5.9 million cases of infectious conjunctivitis annually in the United States and approximately 5.4 million cases in the EU annually.
- If approved by regulatory agencies, SHP640 has the potential to become the first agent to treat both viral and bacterial conjunctivitis.
  - Important as it is frequently difficult to ascertain the etiology of the condition based on clinical presentation.

## Shire to conduct Phase 3 studies

- Two phase 2 studies completed in adenoviral conjunctivitis
- Path forward for Phase 3 development in adenoviral conjunctivitis discussed with FDA
- Foresight has conducted preclinical studies that support investigation in bacterial conjunctivitis
- Shire to design and conduct Phase 3 development, to include investigation for the treatment of bacterial conjunctivitis

## Building an innovative portfolio in Ophthalmology

- Strategic fit with lifitegrast
- Solidifies Shire's commitment to building an innovative portfolio in ophthalmology
- An exciting addition to Shire's ophthalmics pipeline of investigational products in dry eye, retinopathy of prematurity, autosomal dominant retinitis pigmentosa and glaucoma



## INTUNIV EU approval

- EC granted marketing authorisation for INTUNIV for the treatment of ADHD in children and adolescents (aged 6-17 years) for whom stimulants are not suitable, not tolerated or have been shown to be ineffective
- Launches planned for 2016

## Multiple Phase 3 studies expected to start in late Q4 2015/early to mid 2016

## SHP616

- FDA granted Fast Track designation to CINRYZE (SHP616) in the treatment of AMR in patients receiving kidney transplants
  - Phase 3 studies to start October 2015
- CINRYZE subcutaneous (SC) IND submitted, potential for Phase 2/3 study to start in Q4 2015

## SHP620

- SHP620 for cytomegalovirus (“CMV”) infection in transplant patients to start a Phase 3 study in 1H 2016

## SHP621

- SHP621 (oral budesonide suspension) for use in the treatment of eosinophilic esophagitis to move into Phase 3 studies by early 2016
  - Studies to commence by early 2016 to include a 12 week induction study with a 36 week treatment extension study

# Financial review

Jeff Poulton, Chief Financial Officer

# Double digit product sales growth (excluding INTUNIV at CER<sup>(1)(2)(8)</sup>) and delivery of robust Non GAAP EBITDA margin <sup>(4)(5)(8)</sup>

	Q3 2015 \$m <sup>(1)</sup>	Q3 2014 \$m	Reported Growth	CER Growth <sup>(2)(8)</sup>
<b>Product Sales</b>	1,577	1,552	+2%	+6%
<b>Product Sales excluding INTUNIV</b>	1,559	1,455	+7%	+12%
<b>Royalties and Other Revenues</b>	78	45	+73%	+80%
<b>Total Revenue</b>	1,655	1,597	+4%	+8%
<b>Non GAAP EBITDA<sup>(3)(8)</sup></b>	758	760	0%	+3%
<b>Non GAAP EBITDA margin<sup>(4)(5)(8)</sup></b>	43%	46%	-3% points	-3% points
<b>Non GAAP diluted EPS – ADS<sup>(6)(8)</sup></b>	3.24	2.93	+11%	+15%
<b>Non GAAP Cash Generation<sup>(7)(8)</sup></b>	588	612	-4%	

(1) Results include NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015).

(2) This is a Non GAAP financial measure. Constant exchange rates ("CER") performance is determined by comparing 2015 performance (restated using average 2014 foreign exchange rates for the relevant period) to actual 2014 reported performance.

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income (Q3 2015: \$453m, Q3 2014: \$480m).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income margin (Q3 2015: 27%, Q3 2014: 30%).

(5) Non GAAP earnings before interest, tax, depreciation and amortization ("EBITDA") as a percentage of product sales, excluding royalties and other revenues.

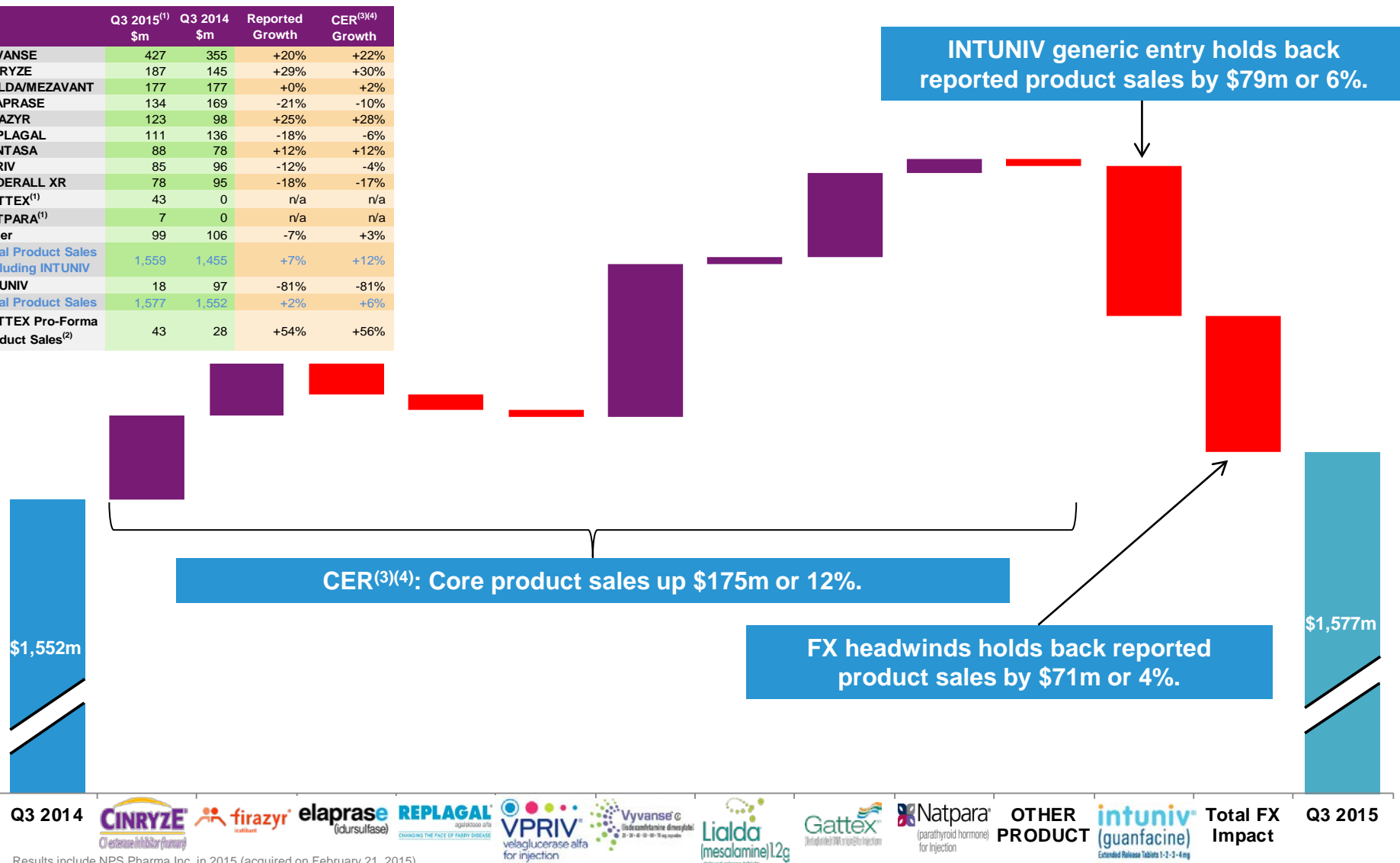
(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2015: \$2.29, Q3 2014: \$2.43).

(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Cash provided by operating activities (Q3 2015: \$561m, Q3 2014: \$593m).

(8) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Strong product sales growth in Q3 2015, up 12% (excluding INTUNIV and at CER<sup>(1)(3)(4)</sup>)

	Q3 2015 <sup>(1)</sup> \$m	Q3 2014 \$m	Reported Growth	CER <sup>(3)(4)</sup> Growth
VYVANSE	427	355	+20%	+22%
CINRYZE	187	145	+29%	+30%
LIALDA/MEZAVANT	177	177	+0%	+2%
ELAPRASE	134	169	-21%	-10%
FIRAZYR	123	98	+25%	+28%
REPLAGAL	111	136	-18%	-6%
PENTASA	88	78	+12%	+12%
VPRIV	85	96	-12%	-4%
ADDERALL XR	78	95	-18%	-17%
GATTEX <sup>(1)</sup>	43	0	n/a	n/a
NATPARA <sup>(1)</sup>	7	0	n/a	n/a
Other	99	106	-7%	+3%
<b>Total Product Sales excluding INTUNIV</b>	<b>1,559</b>	<b>1,455</b>	<b>+7%</b>	<b>+12%</b>
INTUNIV	18	97	-81%	-81%
<b>Total Product Sales</b>	<b>1,577</b>	<b>1,552</b>	<b>+2%</b>	<b>+6%</b>
GATTEX Pro-Forma Product Sales <sup>(2)</sup>	43	28	+54%	+56%



(1) Results include NPS Pharma Inc. in 2015 (acquired on February 21, 2015).

(2) Gattex growth on a pro-forma basis, including product sales recorded by NPS prior to acquisition by Shire.

(3) This is a Non GAAP financial measure. Constant exchange rates ("CER") performance is determined by comparing 2015 performance (restated using average 2014 foreign exchange rates for the relevant period) to actual 2014 reported performance.

(4) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Robust YTD 2015 Non GAAP EBITDA margin<sup>(8)(9)(10)</sup> whilst investing for future growth

Year on Year Change:	YTD 2015 <sup>(1)</sup>
Product Sales	+3%
Product Sales excluding INTUNIV	+9%
Non GAAP R&D <sup>(2)(10)</sup>	+8%
Non GAAP SG&A <sup>(3)(10)</sup>	+10%
Combined Non GAAP R&D and SG&A <sup>(4)(10)</sup>	+9%

Ratios:	YTD 2015 <sup>(1)</sup>	YTD 2014 <sup>(1)</sup>
% of Product Sales		
Non GAAP Gross Margin <sup>(5)(10)</sup>	85.4% ←	85.6%
Non GAAP R&D <sup>(6)(10)</sup>	15% ←	14%
Non GAAP SG&A <sup>(7)(10)</sup>	28% ←	27%
Non GAAP EBITDA <sup>(8)(9)(10)</sup>	43% ←	45%

(1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (YTD 2015: +47%, YTD 2014: +17%).

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2015: +18%, YTD 2014: +21%).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (YTD 2015: +28%, YTD 2014: +20%).

(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross Margin (YTD 2015: 83.9%, YTD 2014: 82.4%).

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is R&D (YTD 2015: 27%, YTD 2014: 19%).

(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is SG&A (YTD 2015: 38%, YTD 2014: 33%).

(8) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net income Margin (YTD 2015: 22%, YTD 2014: 28%).

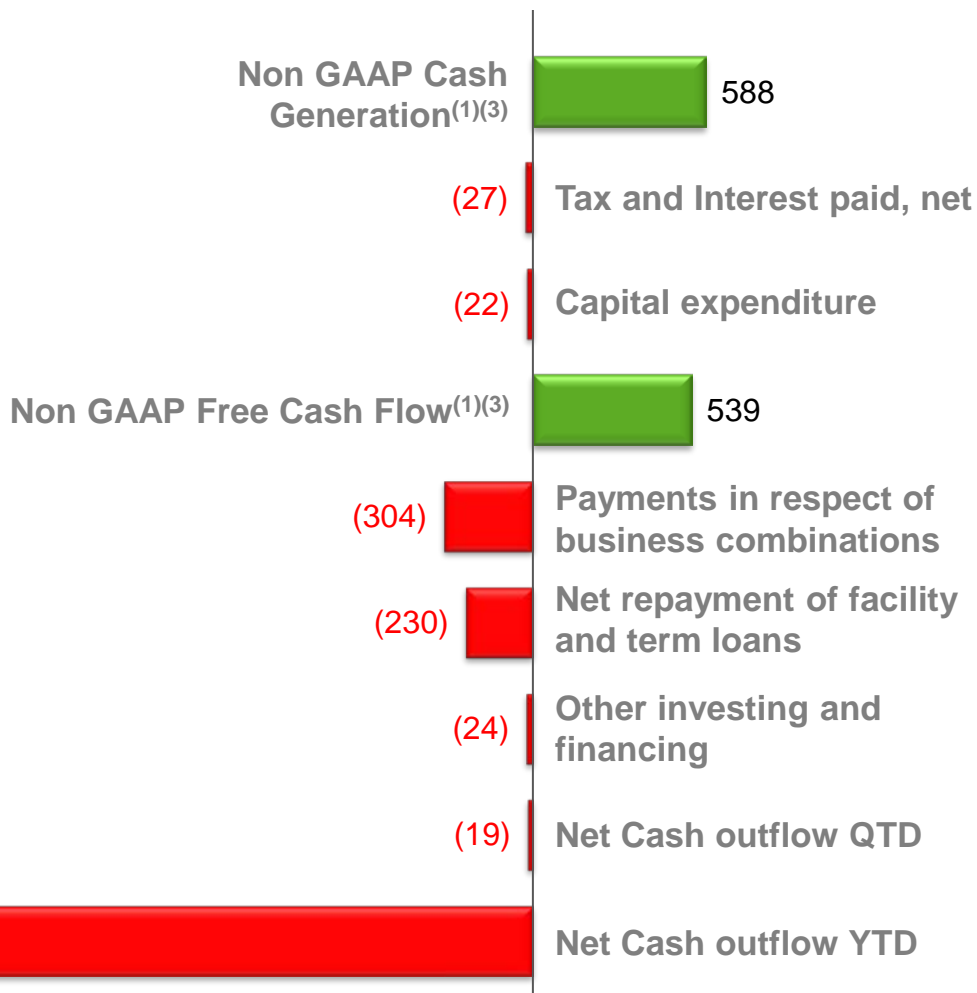
(9) Excluding Royalties and Other Revenues.

(10) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.



# Strong Non GAAP cash generation<sup>(1)(3)</sup> of \$0.6B in Q3 2015. Non GAAP net debt<sup>(2)(3)</sup> of \$2.05B at September 30, 2015

	September 30, 2015 \$m	December 31, 2014 \$m
Cash and cash equivalents	45	2,982
Long-term borrowings	(71)	-
Short-term borrowings	(2,006)	(850)
Other debt	(13)	(13)
<b>Non GAAP Net (debt)/cash<sup>(2)(3)</sup></b>	<b>(2,045)</b>	<b>2,119</b>









(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net cash provided by operating activities (Q3 2015: \$561m, Q3 2014: \$593m).

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Cash and cash equivalents (September 30, 2015: \$45m, December 31, 2014: \$2,982m).

(3) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# 2015 Guidance reiterated

## Full Year 2015 Dynamics

	Direction Versus FY 14 <sup>(1)</sup>	CER Growth <sup>(3)(4)</sup>	Impact of FX Rates on Guidance	Guidance
<b>Total Product Sales</b>		High single digit growth	-3 to 4% points	4-5% higher than 2014
<b>Product Sales excluding INTUNIV</b>		Low teens growth		Low double digit
<b>Royalties &amp; Other Revenues</b>				45-55% higher than in 2014
<b>Non GAAP Gross Margins<sup>(3)</sup></b>	~			Similar to 2014
<b>Non GAAP Combined R&amp;D and SG&amp;A<sup>(3)</sup></b>				High single digit growth
<b>Non GAAP Net Interest/Other<sup>(3)</sup></b>	~			Broadly in line with 2014
<b>Non GAAP Tax Rate<sup>(3)</sup></b>				Core effective tax rate of 15-17%
<b>Non GAAP diluted Earnings per ADS<sup>(2)(3)</sup></b>		Low double digit growth	-4 to 5% points	Mid-to-high single digit growth

Our 2015 Outlook is based on an average of YTD 2015 actual exchange rates and the September 30, 2015 exchange rates holding for Q4 2015 (implied full year rates of Euro:\$1.12, £:\$1.53, CHF:\$1.04, CAD:\$0.79). The estimated impact of a 10% appreciation in the US Dollar against the respective currency, over the full year, on our 2015 Guidance is as follows:

	Revenue	Earnings
<b>EUR</b>	(1.3%)	(2.2%)
<b>GBP</b>	(0.3%)	(0.2%)
<b>CHF</b>	(0.1%)	0.4%
<b>CAD</b>	(0.3%)	(0.4%)
<b>Other</b>	(0.6%)	(0.8%)

- (1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).
- (2) Based on a latest assumption of a full year 2015 weighted average number of ordinary shares of 594 million.
- (3) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.
- (4) This is a Non GAAP financial measure. Constant exchange rates ("CER") performance is determined by comparing 2015 guidance (restated using average 2014 foreign exchange rates for the relevant period) to actual 2014 reported performance.

# Summary

Flemming Ornskov, MD, Chief Executive Officer

# Proposed combination with Baxalta would create the global leader in rare diseases with compelling financials and strong outlook

## The global leader in rare diseases

- ~\$20B in product sales by 2020 (“20x20”)
- Multiple \$1B+ high-value rare diseases franchises with substantial barriers to entry
- Complementary expertise in rare diseases R&D, commercial, and manufacturing, supported by global scale and infrastructure

## Compelling financial profile and value creation

- Projected double-digit top-line growth
- Substantial operating synergies
- Accretive to Non GAAP earnings<sup>(1)</sup> – breakeven in year one with accretion thereafter, supported by a share buyback program
- Attractive sustainable returns including IRR projected in excess of 10%

## Strong future outlook

- >30 new product launches planned with ~\$5B sales potential by 2020<sup>(2)</sup>
- Strong balance sheet and robust pro forma cash flow support future organic growth and M&A

(1) Including impact of anticipated share buyback program.

(2) Based on Shire management projections and Baxalta investor presentations.

# Execution of strategy is delivering

## Continued execution

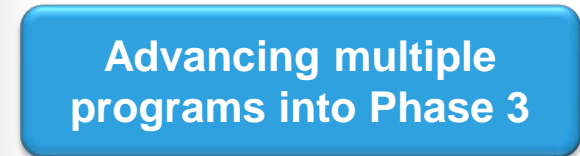


Delivering results  
in 2015 ...



...and beyond

## Investing for future growth



*On track to become a leading biotech*

# Questions and Answers



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



# APPENDIX

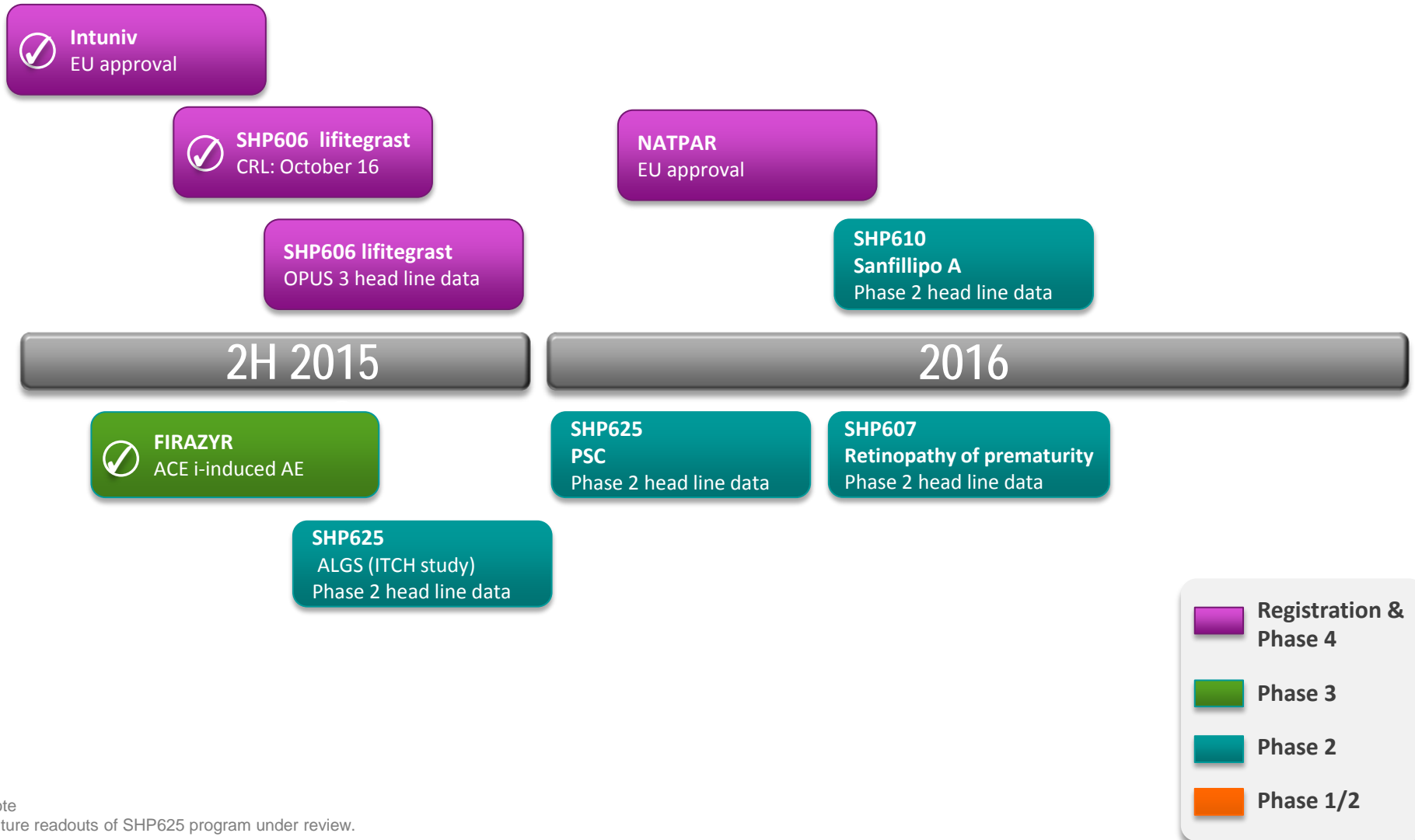
Our purpose  
We enable people with life-altering conditions to lead better lives.



# Data read outs expected in 2015 & 2016



INNOVATION



Note  
Future readouts of SHP625 program under review.



# YTD 2015 Performance summary

	YTD 2015 \$m <sup>(1)</sup>	YTD 2014 \$m <sup>(1)</sup>	Reported Growth	CER Growth <sup>(2)(8)</sup>
<b>Product Sales</b>	4,476	4,330	+3%	+8%
<b>Product Sales excluding INTUNIV</b>	4,431	4,051	+9%	+14%
<b>Royalties and Other Revenues</b>	225	116	+93%	+99%
<b>Total Revenue</b>	4,701	4,446	+6%	+10%
<b>Non GAAP EBITDA<sup>(3)(8)</sup></b>	2,127	2,063	+3%	+7%
<b>Non GAAP EBITDA margin<sup>(4)(5)(8)</sup></b>	43%	45%	-2% points	-3% points
<b>Non GAAP diluted EPS – ADS<sup>(6)(8)</sup></b>	8.71	7.95	+10%	+14%
<b>Non GAAP Cash Generation<sup>(7)(8)</sup></b>	1,609	1,602	0%	

(1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).

(2) This is a Non GAAP financial measure. Constant exchange rates ("CER") performance is determined by comparing 2015 performance (restated using average 2014 foreign exchange rates for the relevant period) to actual 2014 reported performance.

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income (YTD 2015: \$1,023m, YTD 2014: \$1,233m).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Income margin (YTD 2015: 22%, YTD 2014: 28%).

(5) Non GAAP earnings before interest, tax, depreciation and amortization ("EBITDA") as a percentage of product sales, excluding royalties and other revenues.

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (YTD 2015: \$5.17, YTD 2014: \$6.25).

(7) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net Cash provided by operating activities (YTD 2015: \$1,575m, YTD 2014: \$1,674m).

(8) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Product Sales – Regional analysis

	US	Europe	LATAM	Other	Total
<b>Q3 2015</b>					
Product Sales \$m <sup>(1)</sup>	1,169	258	55	95	1,577
% of Product Sales	74%	16%	4%	6%	100%
YoY Growth	+8%	-11%	-32%	-2%	+2%
<b>YTD 2015</b>					
Product Sales \$m <sup>(1)</sup>	3,267	769	147	293	4,476
% of Product Sales	73%	17%	3%	7%	100%
YoY Growth	+8%	-10%	-13%	+3%	+3%
<b>FY 2014</b>					
Product Sales \$m <sup>(1)</sup>	4,082	1,147	214	387	5,830
% of Product Sales	70%	20%	4%	6%	100%
YoY Growth	+28%	+13%	+3%	+10%	+23%

(1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).

# Royalties and Other Revenues

	Q3 2015 <sup>(1)</sup> \$m	Q3 2014 \$m	Reported Growth
<b>SENSIPAR</b>	35	-	n/a
<b>FOSRENOL</b>	13	15	-10%
<b>3TC and ZEFFIX</b>	12	9	+35%
<b>ADDERALL XR</b>	7	10	-25%
<b>Other</b>	9	6	+33%
<b>Royalties</b>	76	40	+91%
<b>Other Revenues</b>	2	5	-63%
<b>Royalties &amp; Other Revenues</b>	78	45	+73%

(1) Results include NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015).

# Shire income statement growth analysis

	2014					FY 2015 Dynamics				
	2014 Q1 (1)	2014 Q2 (1)	2014 Q3 (1)	2014 Q4 (1)	2014 FY (1)	2015 Q1 (1)	2015 Q2 (1)	2015 Q3 (1)	Direction v. FY 14	Guidance
<b>Total Product Sales</b>	\$1,308m	\$1,470m	\$1,552m	\$1,500m	\$5,830m	\$1,423m	\$1,476m	\$1,577m	↑	4-5% higher than in 2014
<i>versus prior year</i>	+19%	+22%	+33%	+17%	+23%	+9%	+0%	+2%		
<b>Royalties &amp; Other Revenues</b>	\$39m	\$32m	\$45m	\$76m	\$192m	\$65m	\$81m	\$78m	↑	45-55% higher than in 2014
<i>versus prior year</i>	-14%	-27%	+8%	+65%	+8%	+68%	+150%	+73%		
<b>Total Revenue</b>	\$1,347m	\$1,502m	\$1,597m	\$1,576m	\$6,022m	\$1,488m	\$1,558m	\$1,655m		
<i>versus prior year</i>	+18%	+20%	+32%	+19%	+22%	+11%	+4%	+4%		
<b>Non GAAP Gross Margin (2)(7)</b>	86%	85%	86%	86%	86%	86%	86%	84%	~	Similar to 2014
<b>Combined Non GAAP R&amp;D and SG&amp;A (3)(7)</b>	\$539m	\$602m	\$618m	\$677m	\$2,436m	\$571m	\$697m	\$652m	↑	High single digit growth
<i>versus prior year</i>	-3%	+2%	+10%	+11%	+5%	+6%	+16%	+5%		
<b>Non GAAP EBITDA Margin (4)(7)</b>	45%	44%	46%	41%	44%	46%	39%	43%		
<b>Non GAAP Tax Rate (5)(7)</b>	20%	16%	18%	19%	18%	17%	13%	10%	↓	Core effective tax rate of 15-17%
<b>Non GAAP diluted Earnings per ADS (6)(7)</b>	\$2.36	\$2.67	\$2.93	\$2.63	\$10.60	\$2.84	\$2.63	\$3.24	↑	Mid-to-high single digit growth
<i>versus prior year</i>	+38%	+42%	+60%	+17%	+38%	+20%	-2%	+11%		

(1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Gross Margin (Q3 2015: 83.3%, Q3 2014: 83.6%).

(3) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Combined R&D and SG&A (Q3 2015: 9%, Q3 2014: 21%).

(4) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Net income Margin (Q3 2015: 27%, Q3 2014: 30%).

(5) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Tax rate (Q3 2015: -5%, Q3 2014: 11%).

(6) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is EPS-ADS (Q3 2015: \$2.29, Q3 2014: \$2.43).

(7) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Non GAAP cash flow measures

<b>Non GAAP cash generation <sup>(1)(2)</sup> and Non GAAP free cash flow <sup>(1)(2)</sup> reconciliation</b>	<b>Q3 2015 \$m<sup>(1)</sup></b>	<b>Q3 2014 \$m<sup>(1)</sup></b>
<b>Non GAAP cash generation<sup>(1)(2)</sup></b>	588	612
<b>Tax and interest payments, net</b>	(27)	(6)
<b>Up-front payments in respect of in-licensed and acquired products</b>	-	(13)
<b>US GAAP Net cash provided by operating activities</b>	561	593
<b>Capital expenditure</b>	(22)	(31)
<b>Up-front payments in respect of in-licensed and acquired products</b>	-	13
<b>Non GAAP free cash flow<sup>(1)(2)</sup></b>	539	575

(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).

(2) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# Non GAAP net (debt)/cash<sup>(1)(2)</sup>

	September 30, 2015 \$m	December 31, 2014 \$m
Cash and cash equivalents	45	2,982
Long term borrowings	(71)	-
Short term borrowings	(2,006)	(850)
Other debt	(13)	(13)
<b>Non GAAP net (debt)/cash<sup>(1)(2)</sup></b>	<b>(2,045)</b>	<b>2,119</b>

(1) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is Cash and Cash equivalents (Q3 2015: \$45m, FY 2014: \$2,982m).

(2) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

At September 30<sup>th</sup>, 2015 Shire had a \$2.1bn revolving credit facility that matures in December 2019. Shire also had a \$0.85bn term loan facility, of which \$0.75bn remains outstanding. This facility matures in January 2016, although the maturity date may be extended twice, at Shire's option, by six months on each occasion.

# Q3 2015 – Operating Income US GAAP and Non GAAP

	Q3 2015 \$m <sup>(1)</sup>	Q3 2014 \$m	Reported Growth
<b>Non GAAP Operating Income<sup>(2)(3)</sup> from continuing operations</b>	<b>725</b>	<b>717</b>	<b>+1%</b>
Intangible asset amortization	(133)	(63)	
Legal and litigation costs	(2)	(3)	
Acquisition and integration costs	(97)	(68)	
Gains on sale of product rights	1	46	
Reorganization costs	(31)	(28)	
Other	(7)	(29)	
<b>US GAAP Operating Income from continuing operations</b>	<b>456</b>	<b>572</b>	<b>-20%</b>

(1) Results include NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015).

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is US GAAP Operating income (see details above).

(3) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.

# YTD 2015 – Operating Income US GAAP and Non GAAP

	YTD 2015 \$m <sup>(1)</sup>	YTD 2014 \$m <sup>(1)</sup>	Reported Growth
<b>Non GAAP Operating Income<sup>(2)(3)</sup> from continuing operations</b>	<b>2,022</b>	<b>1,938</b>	<b>+4%</b>
Intangible asset amortization	(352)	(182)	
Impairment of IPR&D intangible assets	(523)	(188)	
Legal and litigation costs	(4)	(7)	
Acquisition and integration costs	24	(259)	
Gains on sale of product rights	13	86	
Reorganization costs	(60)	(123)	
Other	(57)	(48)	
<b>US GAAP Operating Income from continuing operations</b>	<b>1,063</b>	<b>1,217</b>	<b>-13%</b>

(1) Results from continuing operations including NPS Pharmaceuticals Inc. in 2015 (acquired on February 21, 2015) and ViroPharma Inc. in 2014 (acquired on January 24, 2014) and excluding DERMAGRAFT in 2014 (treated as a discontinued operation following divestment on January 17, 2014).

(2) This is a Non GAAP financial measure. The most directly comparable measure under US GAAP is US GAAP Operating income (see details above).

(3) See slide 33 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 Q3 2015 earnings release on pages 22 to 28.



# 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 gross margin; 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* (excluding royalties and other revenues). 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 directors.

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; and

#### *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; and
- 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 used by Shire for the nine months to September 30, 2015 were \$1.54:£1.00 and \$1.12:€1.00 (2014: \$1.67:£1.00 and \$1.36:€1.00). Average exchange rates used by Shire for the three months to Q3 2015 were \$1.56:£1.00 and \$1.11:€1.00 (2014: \$1.69:£1.00 and \$1.34:€1.00).

A reconciliation of Non GAAP financial measures to the most directly comparable measure under US GAAP is presented in Shire’s Q3 2015 earnings release on pages 22 to 28.