Third Quarter Results to September 30, 2012

Shire plc
October 25, 2012

Matthew Emmens
Chairman

Angus Russell
Chief Executive Officer

Graham Hetherington
Chief Financial Officer

Sylvie Grégoire
President, Human Genetic Therapies

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

THE "SAFE HARBOR" STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

Statements included herein 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, the Company's results could be materially adversely affected. The risks and uncertainties include, but are not limited to, risks associated with: the inherent uncertainty of research, development, approval, reimbursement, manufacturing and commercialization of the Company's Specialty Pharmaceuticals, Human Genetic Therapies and Regenerative Medicine products, as well as the ability to secure new products for commercialization and/or development; government regulation of the Company's products; the Company's ability to manufacture its products in sufficient quantities to meet demand; the impact of competitive therapies on the Company's products; the Company's ability to register, maintain and enforce patents and other intellectual property rights relating to its products; the Company's ability to obtain and maintain government and other third-party reimbursement for its products; and other risks and uncertainties detailed from time to time in the Company's filings with the Securities and Exchange Commission.

Agenda

- **Management succession** | Matthew Emmens
- **Financial highlights & growth drivers** | Angus Russell
- **SP and RM business updates** | Angus Russell
- **HGT business update** | Sylvie Grégoire
- **Financial review** | Graham Hetherington
- **Concluding remarks** | Angus Russell
- **Q & A** | All

Management succession

Matthew Emmens

Chairman

Our purpose

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

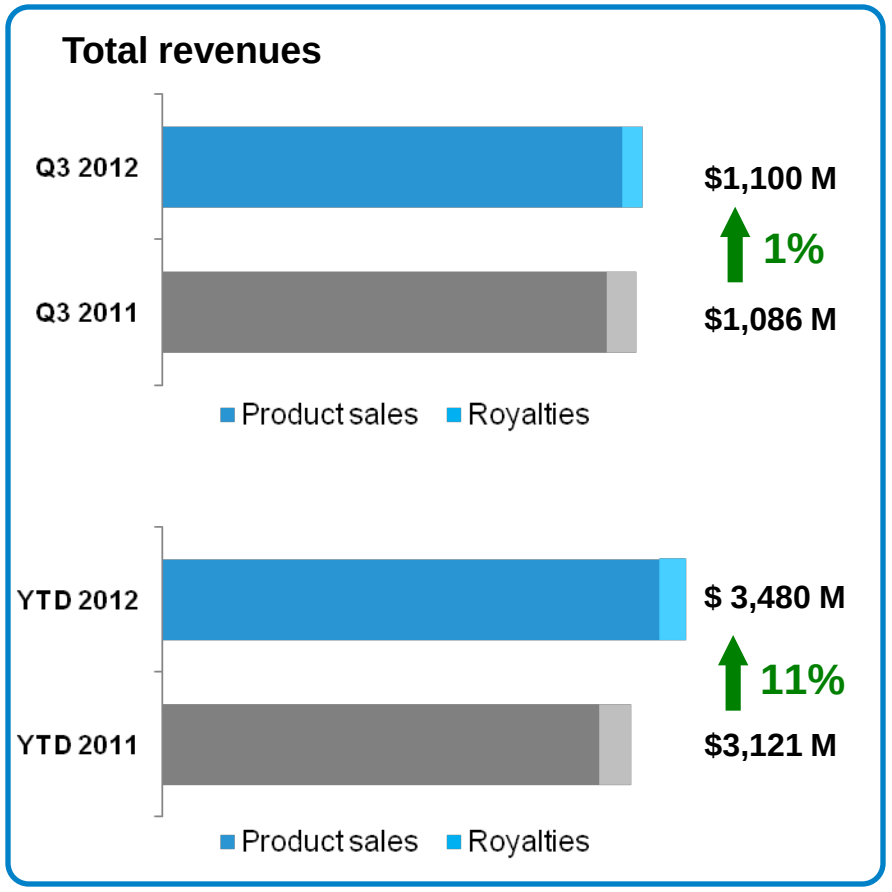
Shire on track for double digit full year earnings growth

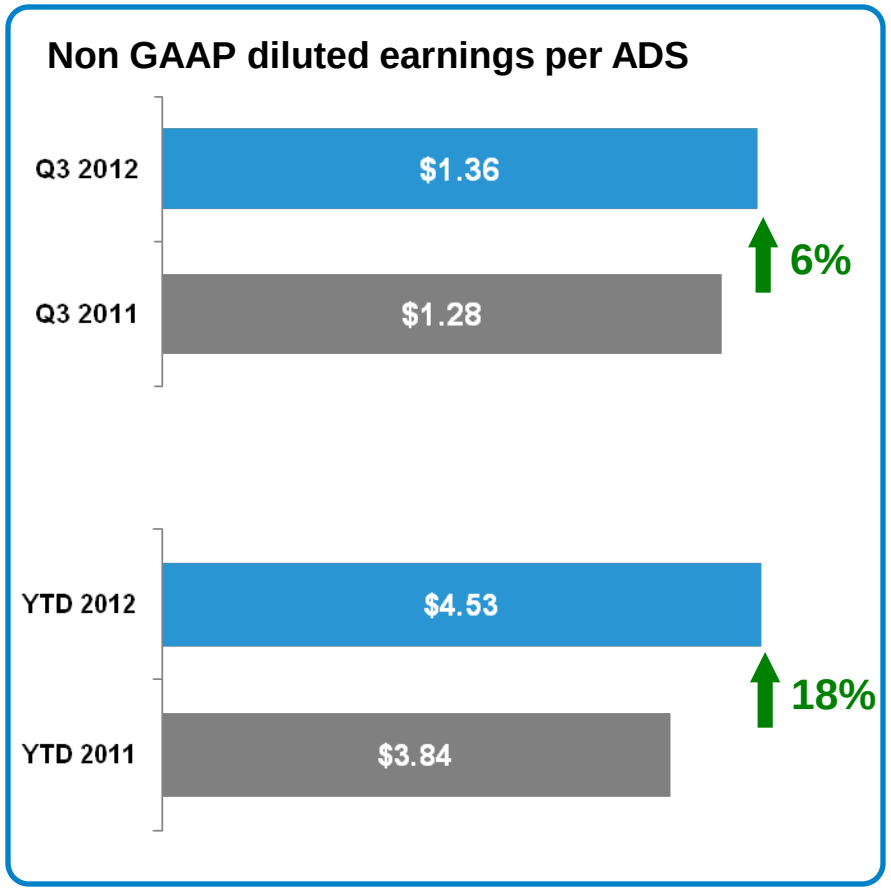
Advancing late stage pipeline of new growth opportunities

Angus Russell
Chief Executive Officer

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

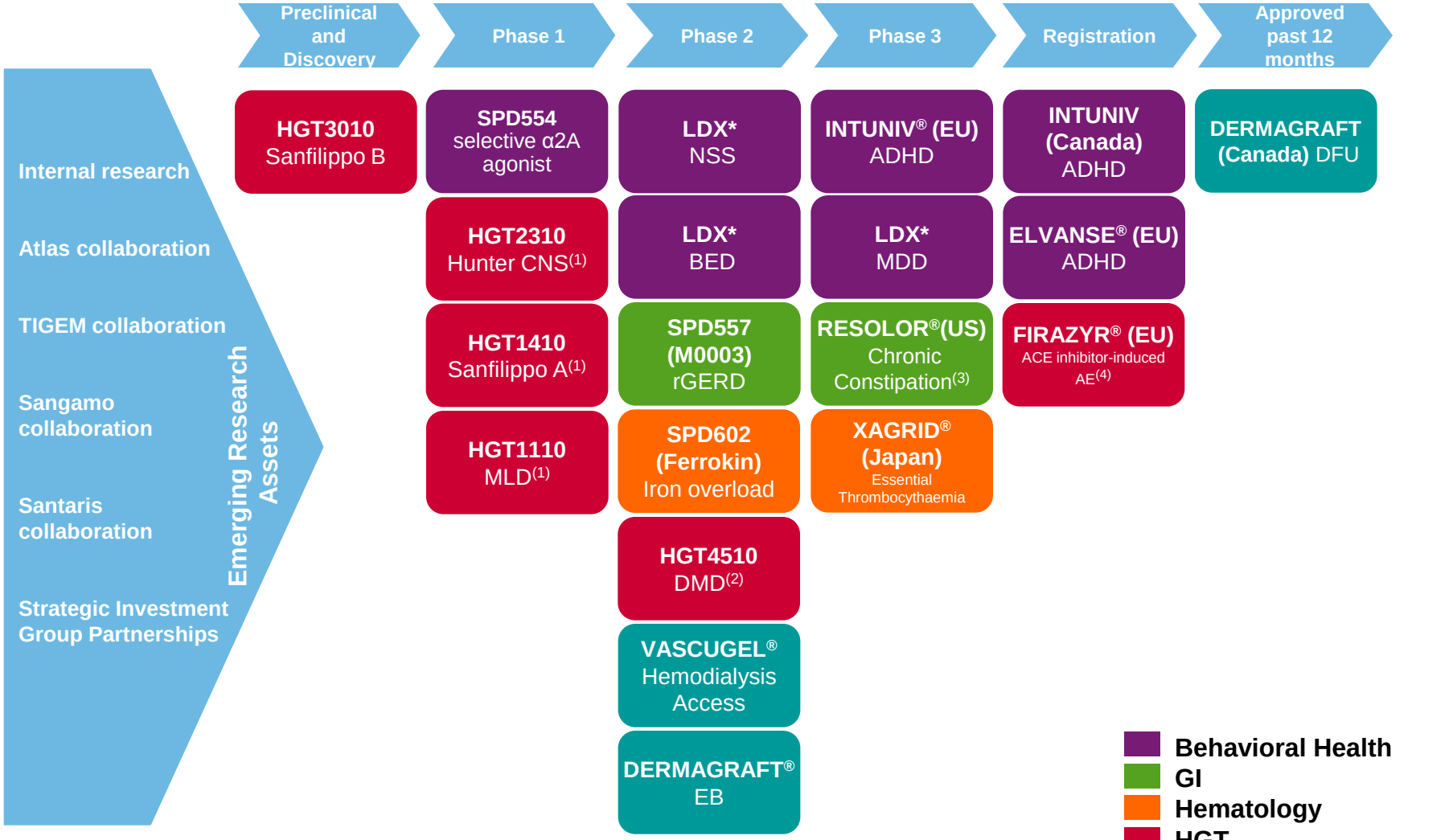
On track for double digit full year earnings growth





Non GAAP earnings per ADS up 6% after increasing our investment in R&D by over 20% to fund our increasingly late stage pipeline

Increasing number of growth opportunities



Notes

* Lisdexamfetamine dimesylate, active ingredient in VYVANSE®.

(1) HGT1410 , HGT2310 and HGT1110 are currently in Phase 1/2 clinical trials.

(2) Currently on clinical hold.

(3) Phase 3 ready.

(4) Filing in the EU planned for December 2012.

Specialty Pharma Q3 highlights

- US Rx's grew 16% versus Q3 11. Achieved 16.9%(1) market share – a gain of 1% versus last year. Strong "back to school" season
- ADHD Phase 1 completed for Japan program(2)
- sNDA filed for ADHD maintenance treatment in children & adolescents ages 6 to 17 years
- Awaiting European approval
- Progressing H2H trial versus Concerta(3)

- 27% increase in Q3 Rx's versus prior year. Increase in both Rx's and market share primarily driven by use as adjunctive therapy with stimulant
- Phase 1 study in Japan completed; enrolling EU pivotal Phase 3 programs
- Patent settlement with Anchen; trial completed with Actavis and Teva

SP Pipeline

- LDX(4) – three non-ADHD Phase 3 programs progressing (details on next slide)
- SPD602 (FBS-0701) - Orphan Drug designation by the EMEA and the FDA for the treatment of chronic iron overload requiring chelation therapy
  - Second Phase 2 trial initiated to evaluate the safety and efficacy in adults with transfusional iron overload
  - Opportunities exist in both Hereditary and Acquired Anemias
  - Anticipate improved safety and tolerability profile vs. currently marketed products

(1) IMS NPA (National Prescription Audit) Sept 2012.
(2) S-877489 ADHD-US - Shionogi development product in Japan.
(3) trade mark of ALZA corporation.
(4) Lisdexamfetamine dimesylate, active ingredient in VYVANSE.

LDX* New Uses – significant opportunities to benefit patients

Program	Patients	Program Status
MDD	• ~ 60% of patients do not experience clinical remission • >5 MM patients have inadequate control of symptoms (US)	• Ph3 ongoing • H/L data anticipated 2H 2013
BED	• No approved medical treatments • ~ 4 MM adults with BED (US)	• Initiation of Ph3 Q4 2012/Q1 2013
NSS	• No pharmacotherapy available • Unique and complex market with hospitals, community mental health centers at core • ~ 1.5 MM patients (US)	• Initiation of Ph3 Q4 2012/Q1 2013 following completion of final discussions with Regulatory authorities

* Lisdexamfetamine dimesylate, active ingredient in VYVANSE

Regenerative Medicine - Building a foundation for future growth

Strategic focus on diabetes complications and dermal repair

Enhancing management and leadership capabilities

Implementing a new commercial model

Increasing manufacturing capacity

Building a pipeline and becoming the partner of choice

Delivering Value through Regenerative Medicine Solutions

Epidermolysis Bullosa (EB) – Potential new orphan indication for DERMAGRAFT

- Rare genetic disorder that is painful and can lead to disability, disfigurement & early death
  - There is no approved therapy
  - EB makes the skin so fragile that the slightest friction causes blisters and skin tears
- As patients get older; malnutrition increases; recurrent wounds cause fibroblasts to become exhausted and senescent: leading to the development of stalled chronic wounds
- DERMAGRAFT target indication: Initiation and Continuation of Healing of Stalled Chronic Cutaneous Wounds in Generalized EB
- Starting a pivotal EB trial around the end of 2012

HGT business update

Sylvie Grégoire

President, Human Genetic Therapies

Our purpose

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

HGT Q3 highlights

firazyr® icatibant

- Continue to add patients worldwide; > 800 US patients are treated with FIRAZYR
- Per-patient utilization is high, driven by FIRAZYR's benefits, including self-administration
- Irregular HAE attack frequency and number of new patient starts drives Q-on-Q revenue variability

REPLAGAL® agalsidase alfa

- Continues to maintain its strong leadership position, despite return of competition
- Vast majority of new naïve patients initiate therapy with REPLAGAL
- We expect the Fabry market to grow ~5% per year

VPRIV velaglucerase alfa for injection

- Global market share ~24%; US market share ~39%
- Regulatory submissions targeted by year end to update label to include bone data
- Can meet all anticipated demand for VPRIV
- After positive interactions with FDA filed a Complete Response for Lexington plant

Development Pipeline

- Worldwide license from IGAN to develop treatment for IgA nephropathy
- TIGEM Alliance signed, further broadening research strength in Rare Diseases

HGT Intrathecal Programs – developing therapies where none currently exist for severe rare neurological diseases

Program	Disease Characteristics
Hunter CNS *HGT2310*	• Incidence of ~1:243,000(1) • Hunter CNS therapy designed to be administered in Elaprase IV treated pts
Sanfilippo A *HGT1410*	• Incidence of ~1:114,000(1) • Childhood rapidly progressive CNS disease
MLD *HGT1110*	• Incidence of ~1:100,000(1) • Infantile form onset at 2-3 yrs of age • Rapid disease progression

- Ph 1/2 trials fully enrolled
- Expect top line data by year end
- All eligible patients in extension studies
- No drug-related SAEs observed
- Planning for next phase clinical studies in 2013

- First patient dosed in Ph 1/2 trial in Q3 2012

(1) There is limited information on the incidence of these rare disease states; information is sourced from various scientific publications.

FIRAZYR (icatibant) in ACE Inhibitor-Induced Angioedema

- Rare, potentially life-threatening side effect of ACE inhibitor therapy
- Bradykinin is normally degraded by ACE, but this is blocked by inhibitors
- Represents significant potential upside to HAE
- Positive data from investigator-sponsored trial
- Planning for EU label extension filing in December 2012
- FDA meeting in late October to determine US pathway

Important Note

No conclusions should be drawn regarding the safety or efficacy of FIRAZYR in the treatment of ACE inhibitor-induced angioedema prior to its review by regulatory authorities. FIRAZYR is only approved for the treatment of acute attacks of Hereditary Angioedema in adults 18 years of age and older.

Financial review

Graham Hetherington
Chief Financial Officer

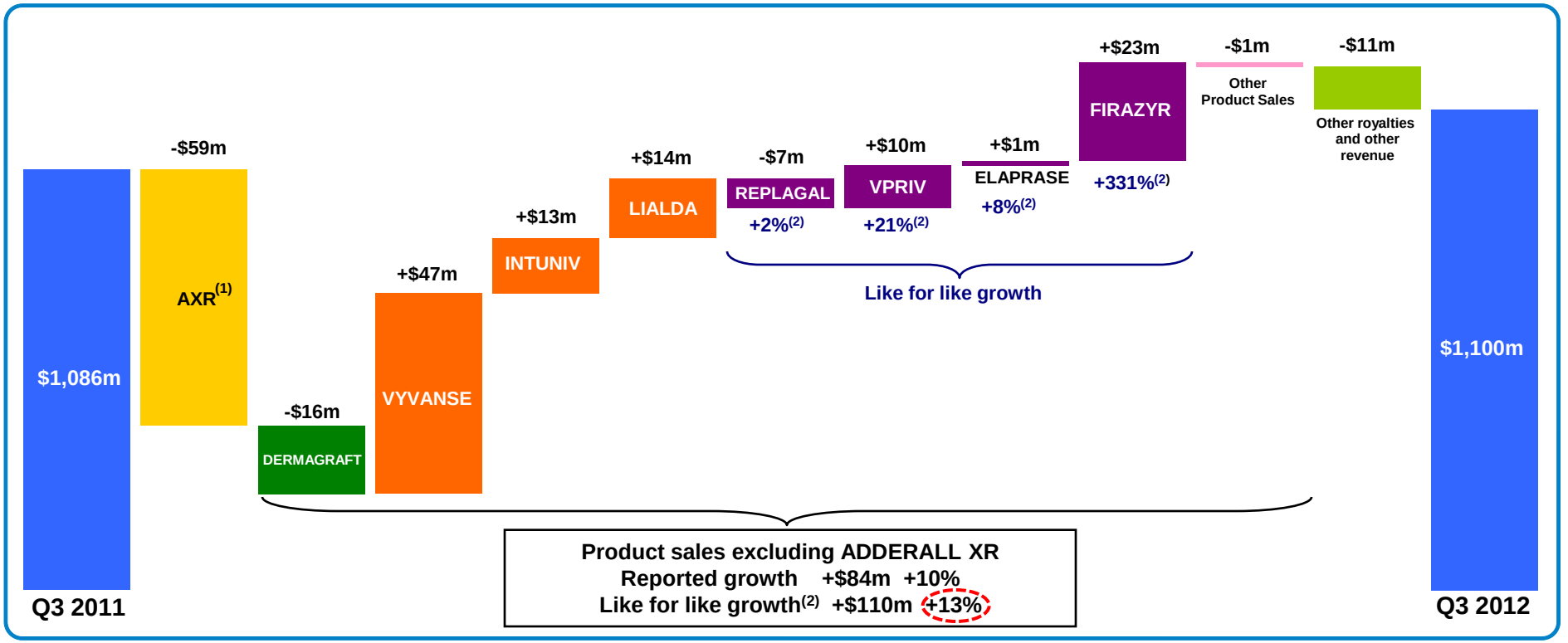
Our purpose
We enable people with life-altering conditions to lead better lives.

Q3 2012 performance summary

	Q3 2012 $m	Q3 2011 $m	Reported Growth	Like for Like Growth[1]
Product sales	1,055	1,018	+4%	+6%
Product sales excluding ADDERALL XR®	952	868	+10%	+13%
Royalties and other revenues	45	68	-32%	-31%
Total revenues	1,100	1,086	+1%	+4%
EBITDA[2]	354	372	-5%	-3%
EBITDA % of product sales[2][3]	29%	30%	-71bp	
EPS - ADS[2]	$1.36	$1.28	+6%	
Cash generation[2]	355	296	+20%	

(1) 'Like for Like Growth' excludes movements in exchange rates by applying Q3 2011 exchange rates to Q3 2012 results.
(2) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalent used to calculate these measures.
(3) Excluding royalties and other revenues.

Drivers of future product sales growth support Q3 performance despite FX headwinds



(1) Underlying product sales (-$21m), royalties (-$12m) and Q3 2011 one-time retail pipeline adjustment (-$26m).
(2) 'Like for Like Growth' excludes movements in exchange rates by applying Q3 2011 exchange rates to Q3 2012 results.

Operating leverage – Key financial ratios

Year on Year:	2012 YTD	2011 YTD
Product sales	+14%	+27%
Product sales excluding ADDERALL XR	+19%	+24%
R&D(1)	+17%	+25%
SG&A(1)	+8%	+23%
Combined R&D and SG&A(1)	+11%	+24%

Ratios:

% of product sales			
Gross margin(1)	86.2%	◀	86.4%
R&D(1)	19%	◀	18%
SG&A(1)	37%	◀	39%
EBITDA(1) (2)	31%	◀	29%

(1) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalents used to calculate these measures.
(2) Excluding royalties and other revenues.

Shire 2012 outlook

Full year 2012 dynamics	Direction versus FY 2011	
Product sales	↑	Growth of around 12%
Royalties and Other Revenues	↓	Down 15-20%, reflecting lower AXR royalties and the recent settlement reached with GSK
Gross margins	≈	Marginal dilution from full year contribution of DERMAGRAFT
R&D and SG&A	↑	Continued investment for sustained future growth, trending towards the lower end of our previous guidance of 10-12%
Tax rate	↓	18-20% tax rate
Reported EPS-ADS	↑	Double digit earnings growth

Concluding remarks

Angus Russell
Chief Executive Officer

Shire progressing well

- On track to deliver double digit full year earnings growth in 2012
- Broad based product portfolio delivering sustainable growth
- Advancing late stage pipeline opportunities
- Investing in promising early technologies
- Confident in delivering sound earnings growth in 2013

Questions and Answers

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

APPENDIX

2012 Portfolio strength and diversity – Q3 product sales

	Q3 2012 $m	Q3 2011 $m	Reported Growth	Like for Like Growth(1)
VYVANSE	247	200	+24%	+24%
REPLAGAL	122	129	-6%	+2%
ELAPRASE	111	110	+1%	+8%
LIALDA / MEZAVANT®	104	90	+16%	+17%
VPRIV	75	65	+16%	+21%
INTUNIV	69	56	+23%	+23%
PENTASA®	67	56	+20%	+20%
FOSRENOL®	38	41	-6%	-1%
DERMAGRAFT	34	50	-33%	-33%
FIRAZYR	30	7	+321%	+331%
OTHER	55	64	-16%	-11%
Product sales excluding ADDERALL XR	**952**	**868**	**+10%**	**+13%**
ADDERALL XR	103	150	-32%	-32%
PRODUCT SALES	**1,055**	**1,018**	**+4%**	**+6%**

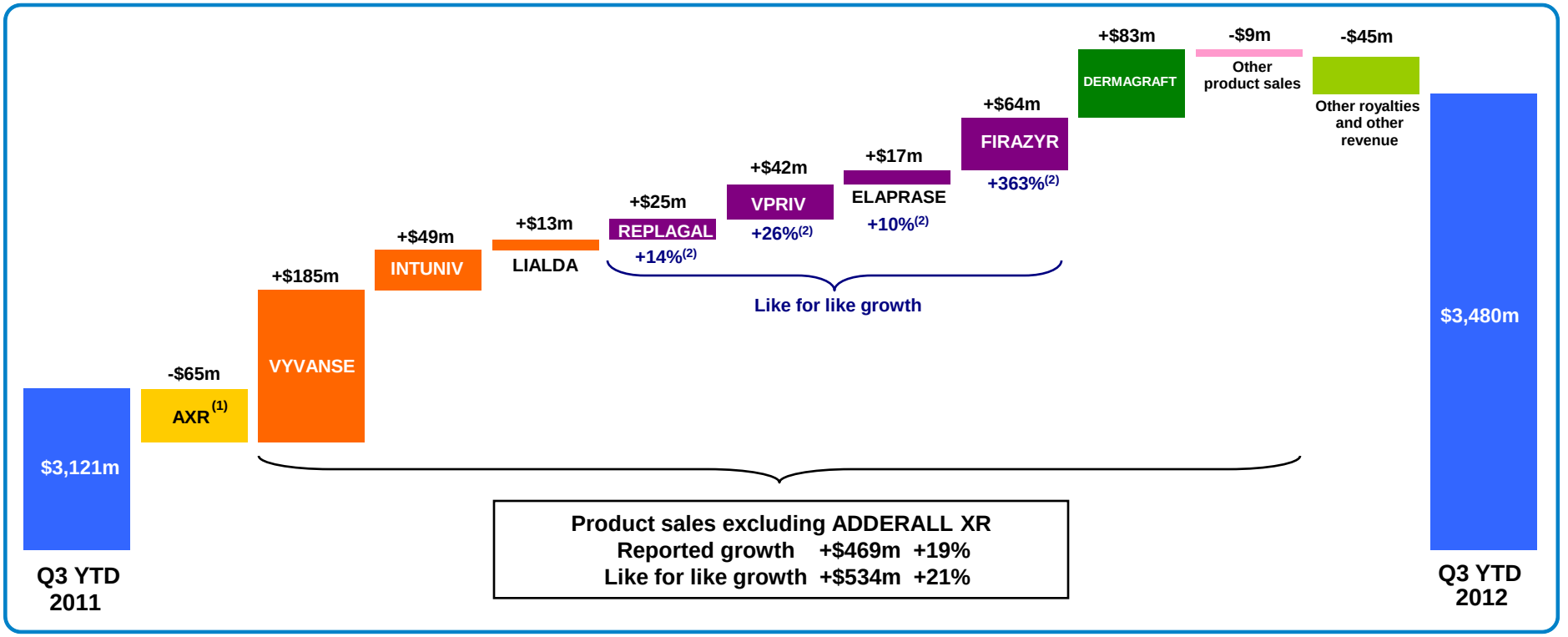
(1) 'Like for Like Growth' excludes movements in exchange rates by applying Q3 2011 exchange rates to Q3 2012 results.

Q3 2012 Royalties & Other revenues

	Q3 2012 $m	Q3 2011 $m	Reported Growth
FOSRENOL	14	11	+28%
ADDERALL XR	11	23	-51%
3TC® and ZEFFIX®(1)	11	17	-39%
REMINYL®(2) & Other	6	12	-49%
Royalties	**42**	**63**	**-33%**
Other revenues	3	5	-16%
Royalties & other revenues	**45**	**68**	**-32%**

(1) Trade mark of GSK.
(2) Trade mark of Johnson & Johnson.

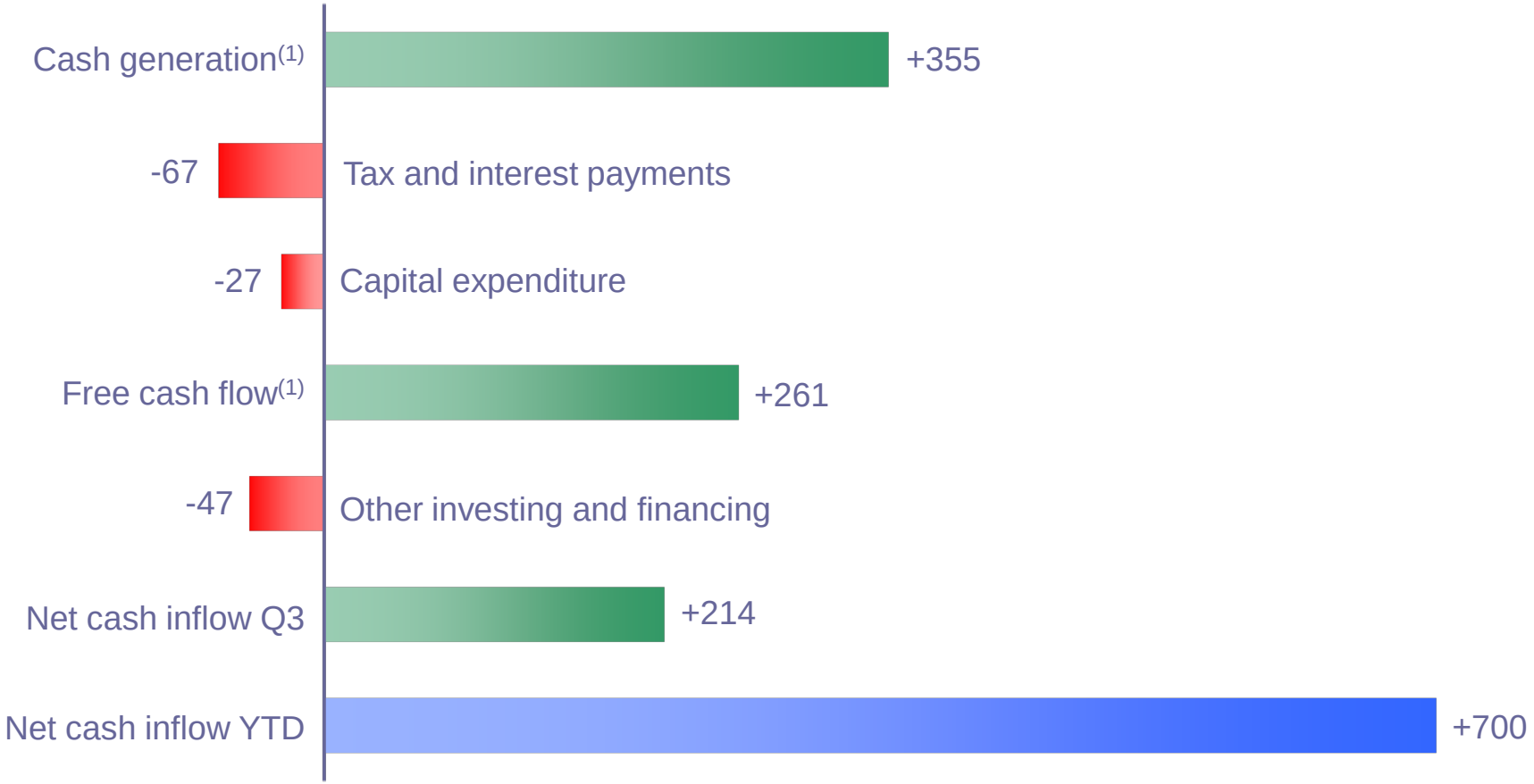
YTD growth across portfolio drives $359m increase in total revenues



(1) Underlying product sales (-$34m), royalties (-$5m) and Q3 2011 one-time retail pipeline adjustment (-$26m).
(2) 'Like for like growth' excludes movements in exchange rates by applying Q3 2011 exchange rates to Q3 2012 results.

Strong cash generation will support Shire's future growth

Millions of USD



Note: Shire has a revolving 5 year credit facility of $1.2bn signed in November 2010 which remained undrawn at September 30, 2012.
(1) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalents used to calculate these measures.

2012 Emerging shape of Shire income statement

	2011 Q1	2011 Q2	2011 Q3	2011 Q4	2011 FY	2012 Q1	2012 Q2	2012 Q3	FY 2012 Dynamics: Direction V. FY 11	FY 2012 Dynamics: Explanations
Product Sales	$890m	$993m	$1,018m	$1,049m	$3,950m	$1,107m	$1,148m	$1,055m	↑	Growth of around 12%
versus prior year	+24%	+30%	+28%	+23%	+26%	+24%	+16%	+4%		
Royalties & Other revenues	$82m	$70m	$68m	$93m	$313m	$65m	$60m	$45m	↓	Down 15 - 20%, reflecting lower AXR royalties and the recent settlement reached with GSK
versus prior year	-15%	-18%	-15%	+17%	-9%	-22%	-14%	-32%		
Total Revenues	$972m	$1,063m	$1,086m	$1,142m	$4,263m	$1,172m	$1,208m	$1,100m		
versus prior year	+19%	+25%	+24%	+23%	+23%	+21%	+14%	+1%		
Gross Margin (1) (2)	87%	87%	86%	87%	87%	86%	87%	85%	≈	Marginal dilution from full year contribution of DERMAGRAFT
R&D (2)	$172m	$171m	$180m	$206m	$729m	$191m	$205m	$219m	↑	Continued investment for sustained future growth, trending towards the lower end of our previous guidance of 10-12%
versus prior year	+$45m	+$27m	+$31m	+$28m	+$131m	+$19m	+$34m	+$39m		
SG&A (2)	$353m	$388m	$389m	$393m	$1,523m	$441m	$410m	$369m		
versus prior year	+$44m	+$84m	+$87m	+$20m	+$235m	+$88m	+$22m	-$20m		
Tax Rate (2)	22%	23%	25%	19%	22%	20%	20%	18%	↓	18-20% tax rate
EPS - ADS (2)	$1.23	$1.33	$1.28	$1.51	$5.34	$1.48	$1.68	$1.36	↑	Double digit earnings growth
versus prior year	+22%	+29%	+10%	+47%	+26%	+20%	+26%	+6%		

(1) Gross margin calculated as a percentage of product sales.
(2) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalents used to calculate these measures.

2012 Non GAAP cash flow measures

Non GAAP cash generation and free cash flow reconciliation	Q3 2012 $m	Q3 2011 $m	YTD 2012 $m	YTD 2011 $m
Non GAAP cash generation[(1)]	**355**	296	**1,185**	944
Tax and interest payments, net	**(67)**	(117)	**(151)**	(280)
Up-front payments in respect of in-licensed and acquired products	-	-	**(23)**	-
US GAAP Net cash provided by operating activities	**288**	179	**1,011**	664
Capital expenditure	**(27)**	(41)	**(91)**	(136)
Up-front payments in respect of in-licensed and acquired products	**-**	**-**	**23**	-
Non GAAP free cash flow[(2)]	**261**	138	**943**	528

(1) Non GAAP cash generation represents net cash provided by operating activities, excluding upfront and milestone payments for in-licensed and acquired products, tax and interest payments.

(2) Non GAAP free cash flow represents net cash provided by operating activities, excluding upfront and milestone payments for in-licensed and acquired products, but including capital expenditure in the normal course of business.

Non GAAP net cash/(debt)

	September 30, 2012 $m	December 31, 2011 $m
Cash and cash equivalents	1,322	620
Convertible bonds	(1,100)	(1,100)
Other	(9)	(8)
Net cash/(debt)	**213**	**(488)**

Non GAAP measures

- This presentation contains financial measures not prepared in accordance with US GAAP.
- These Non GAAP financial measures are used by Shire's management to make operating decisions because they facilitate internal comparisons of the Company's performance to historical results and to competitors' results. They should not be considered in isolation from, as substitutes for, or superior to financial measures prepared in accordance with US GAAP.
- The following items are excluded from these Non-GAAP financial measures:

Amortization and asset impairments:

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

Acquisitions and integration activities:

- Upfront 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
- Non-controlling interest in consolidated variable interest entities.

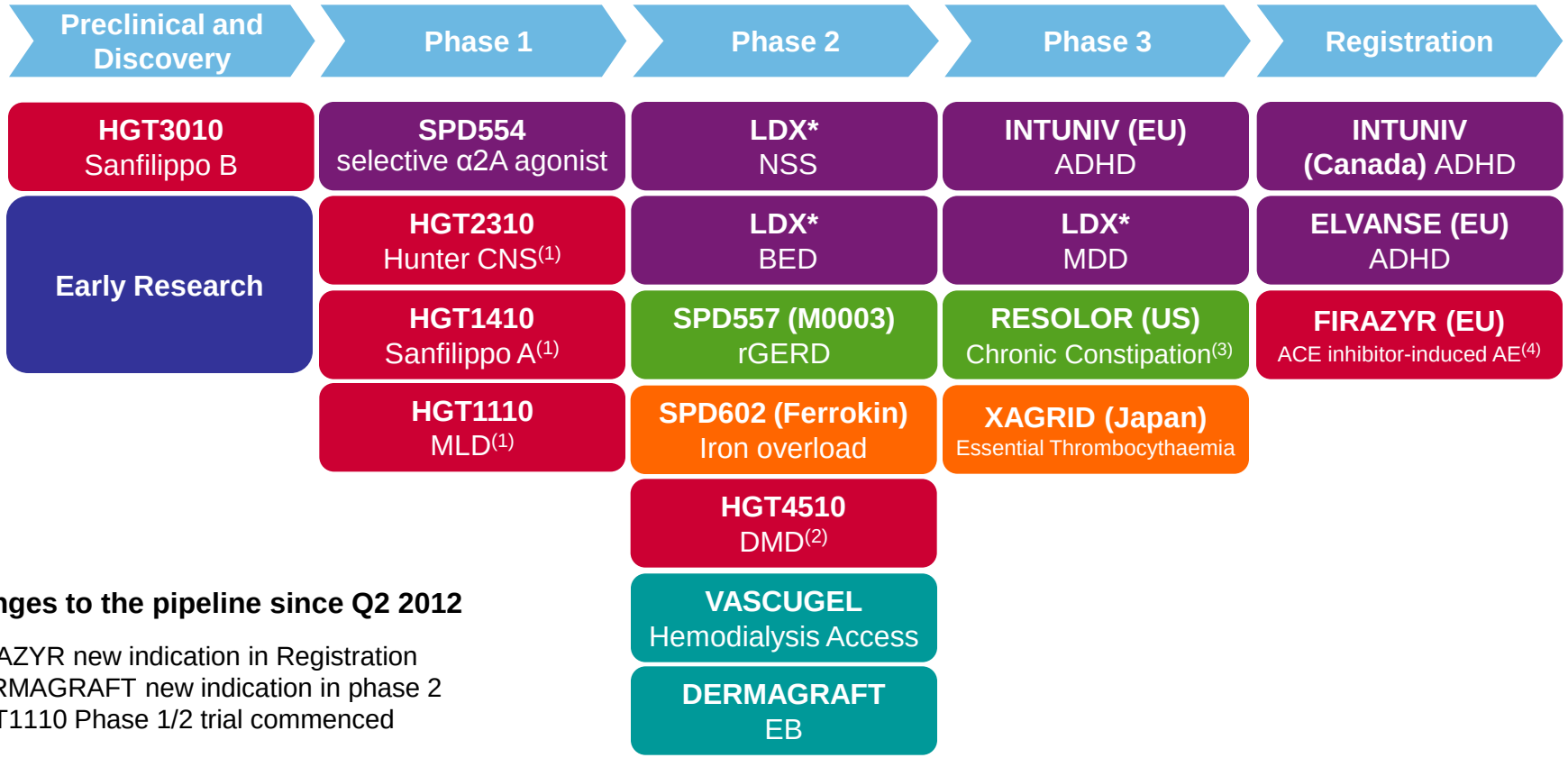
Divestments, re-organizations and discontinued operations:

- Gains and losses on the sale of non-core assets;
- Costs associated with restructuring and re-organization 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).

Expanding the pipeline



Changes to the pipeline since Q2 2012

- FIRAZYR new indication in Registration
- DERMAGRAFT new indication in phase 2
- HGT1110 Phase 1/2 trial commenced

De-prioritized

- SPD535

Approved

- DERMAGRAFT (Canada)

Behavioral Health
GI
Hematology
HGT
Regenerative Medicine

Notes

* Lisdexamfetamine dimesylate, active ingredient in VYVANSE
(1) HGT1410 , HGT2310 and HGT1110 are currently in Phase 1/2 clinical trials
(2) Currently on clinical hold
(3) Phase 3 ready
(4) Filing in the EU planned for December 2012.