First Quarter Results to March 31, 2011

Shire plc
April 28, 2011

Angus Russell
Chief Executive Officer

Michael Cola
President, Specialty Pharmaceuticals

Graham Hetherington
Chief Financial Officer

Sylvie Grégoire
President, Human Genetic Therapies

Dr. Jeffrey Jonas
SVP, Specialty Pharmaceuticals R&D

Shire

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, Shire'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 Shire's Specialty Pharmaceuticals and Human Genetic Therapies products, as well as the ability to secure new products for commercialization and/or development; government regulation of Shire's products; Shire's ability to manufacture its products in sufficient quantities to meet demand; the impact of competitive therapies on Shire's products; Shire's ability to register, maintain and enforce patents and other intellectual property rights relating to its products; Shire'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 Shire's filings with the Securities and Exchange Commission.

Agenda

- **Q1 2011 Highlights** | Angus Russell
- **Financial Review** | Graham Hetherington
- **VYVANSE® New Uses** | Dr. Jeffrey Jonas
- **Concluding remarks** | Angus Russell
- **Q & A** | All

Q1 2011 Highlights

Angus Russell
Chief Executive Officer

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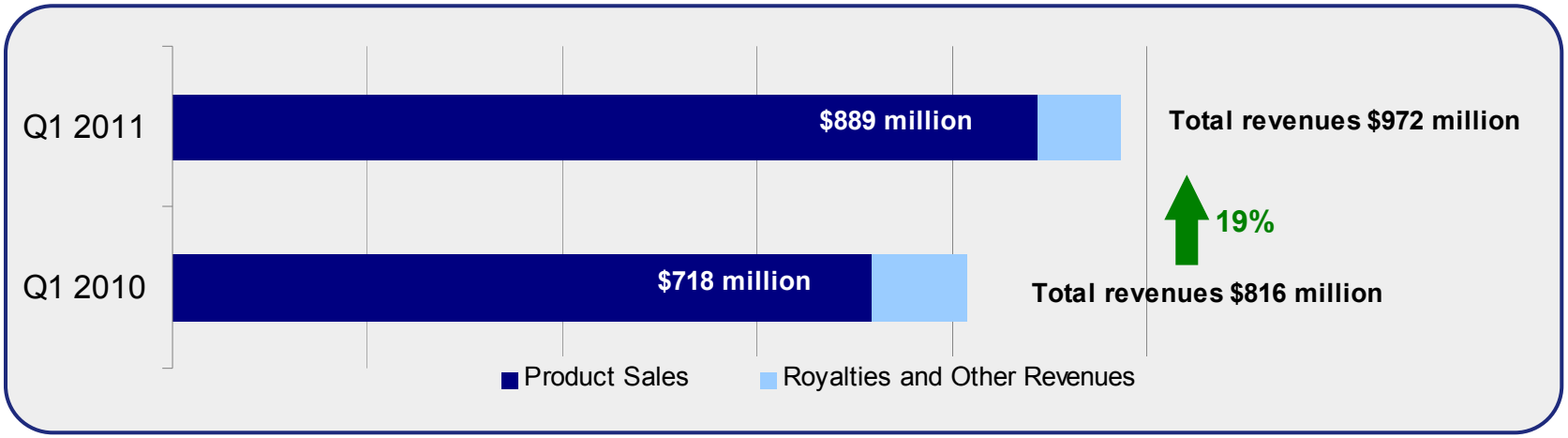
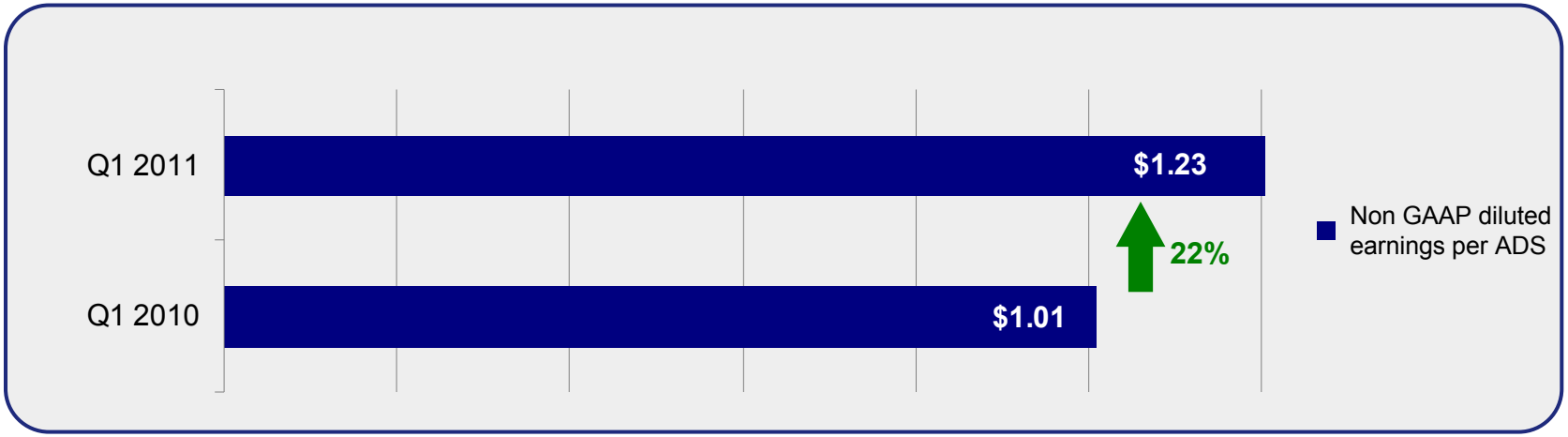
Strong top-line growth



Total revenues ↑ **19%** to $972 million

Product sales ↑ **24%** to $889 million

Product sales growth drives increase in Non GAAP earnings



Q1 2011 Non GAAP diluted earnings per **ADS: $1.23**

Q1 2011 Non GAAP operating income ↑ **15%** to $306 million

Specialty Pharma: Recent Highlights

- ✓ Adolescent indication launched in US
- ✓ Launching in Brazil as *VENVANSE*
- ✓ EU Pivotal Programs – progressing as planned
- ✓ Potential Non-ADHD indications – continued advancements

- ✓ 3%* US market share
- ✓ Launched Co-Admin Adjunctive Therapy with Stimulant indication
- ✓ EU Pivotal Programs – progressing as planned

- ✓ 20%* US market share

- ✓ Currently launched in UK, Germany and Belgium. Additional EU launches in 2011 & 2012 as pricing/reimbursement is secured
- ✓ Ongoing trial in men and initiation of Opioid Induced Constipation program (in non-cancer pain patients).

* IMS NPA (National Prescription Audit) March 2011

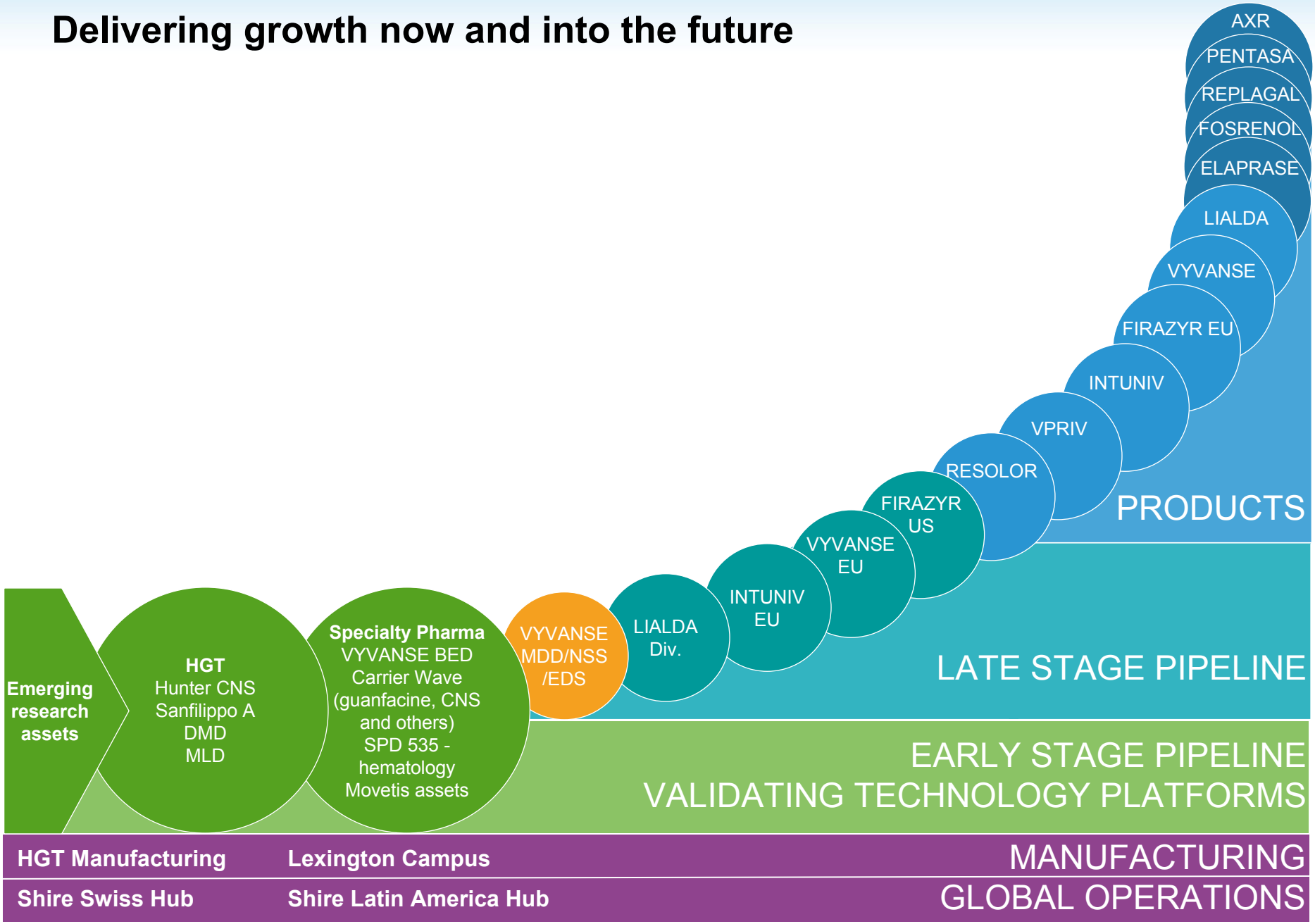
HGT: Recent Highlights

- ✓ Self-admin for acute HAE attacks approved by European Commission
- ✓ Complete response filed with the FDA; PDUFA date August 25
- ✓ Positive efficacy and safety demonstrated in US Phase 3 results

- ✓ 73% ex-US market share
- ✓ Filed for European approval in the new Lexington manufacturing facility
- ✓ Successful inspection of the new facility by European authorities

- ✓ 34% US market share; 18% global market share
- ✓ Continuing Process Validation Runs in new Lexington manufacturing facility

Delivering growth now and into the future



Financial Review

Graham Hetherington
Chief Financial Officer

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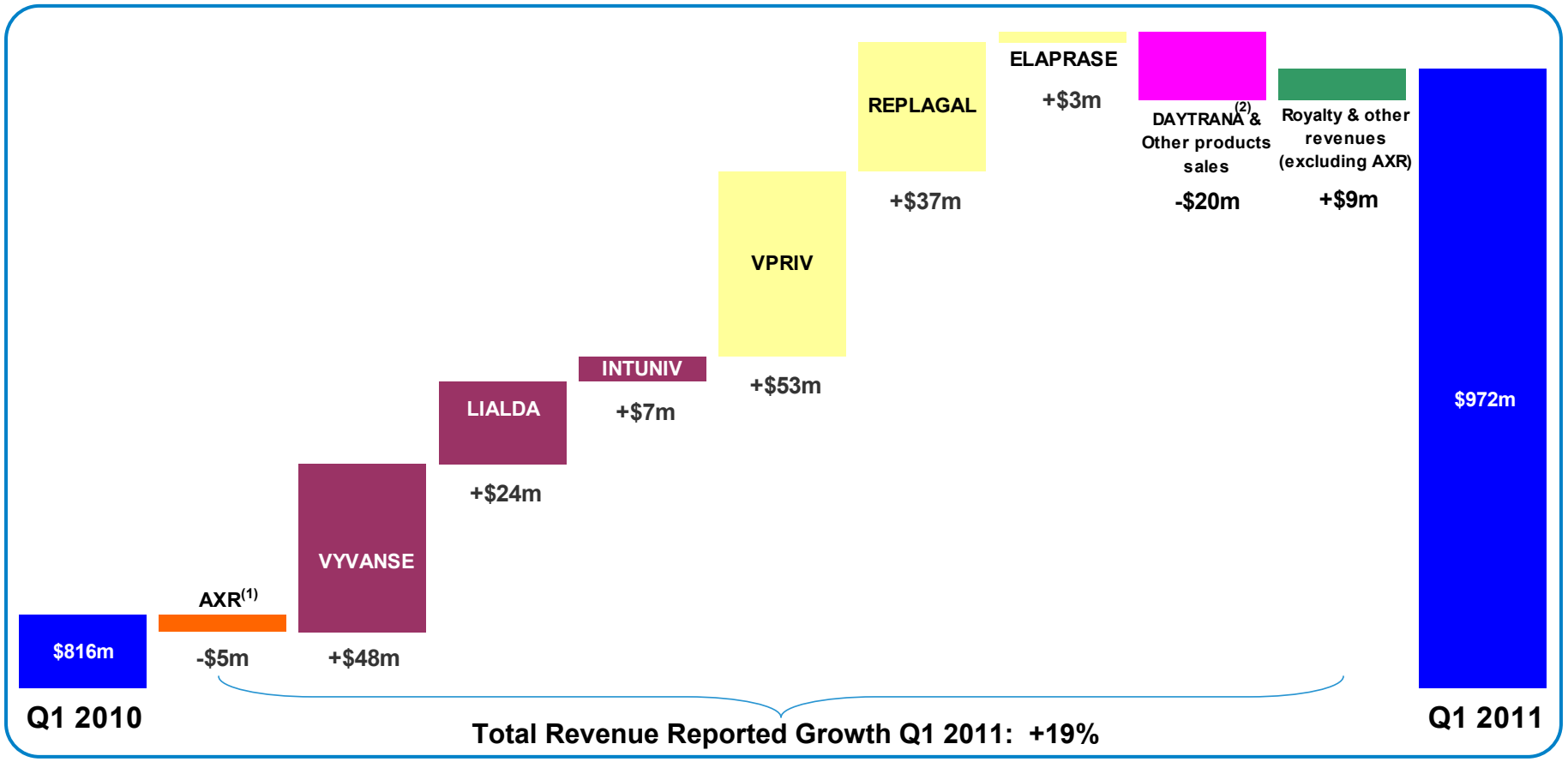
2011 Q1 Performance Summary

	Q1 2011 $m	Q1 2010 $m	Reported Growth	Like for Like Growth (1)
Product sales	889	718	+24%	+24%
Royalties and other revenues	83	98	-15%	-15%
Total revenues	972	816	+19%	+19%
EBITDA (2)	331	288	+15%	+17%
EBITDA % of product sales (2)(3)	28%	26%		
EPS - ADS (2)	$1.23	$1.01	+22%	
Cash generation (2)	208	276	-25%	

(1) 'Like for Like Growth' excludes movements in exchange rates by applying 2010 exchange rates to 2011 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.

Diverse product portfolio drives strong Q1 total revenue growth of over $150m



(1) Product sales and royalties.
(2) DAYTRANA was divested on October 1, 2010.

Operating leverage continuing – Key Financial Ratios

Year on Year:	Q1 2011	Q1 2010
Product sales	+24%	-5%
R&D(1)	+36%	+9%
SG&A(1)	+14%	+14%

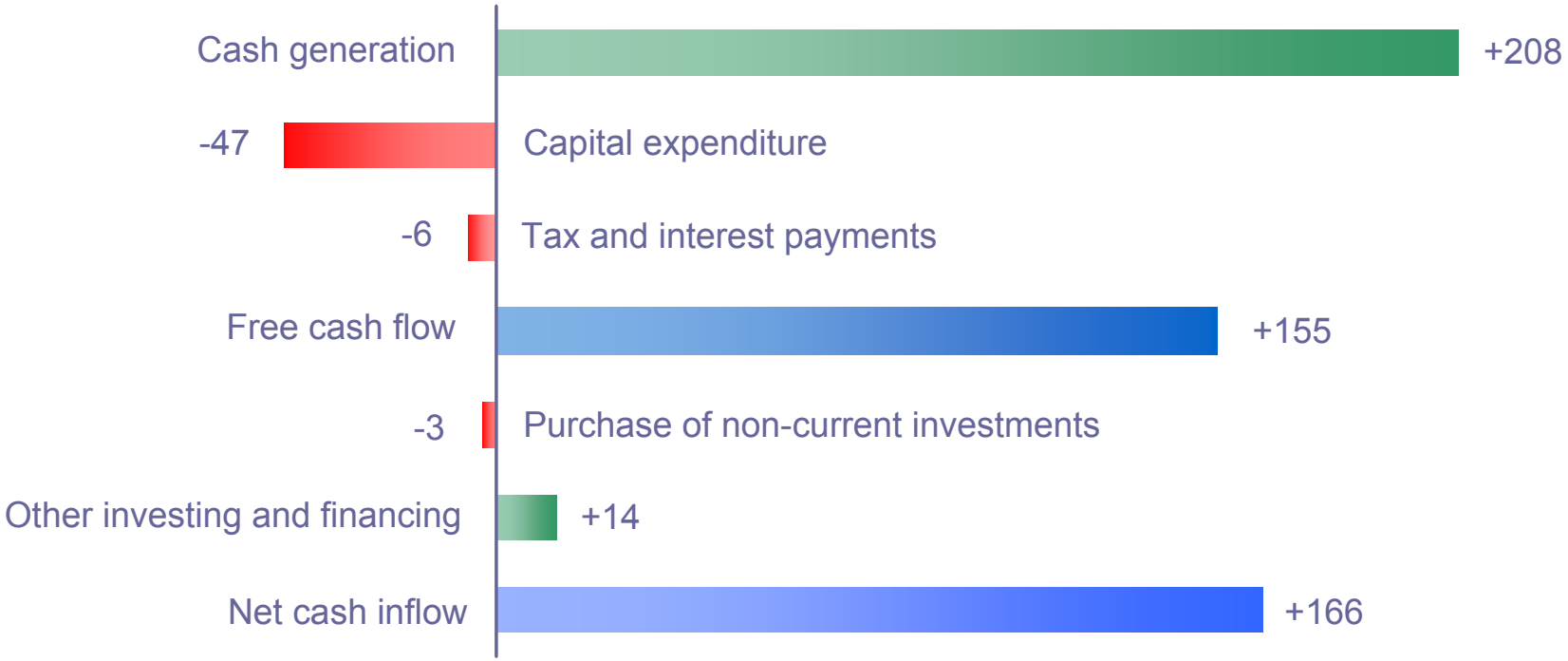
Ratios:

% of product sales		
Gross margin(1)	87%	87%
R&D(1)	19%	18%
SG&A(1)	40%	43%
EBITDA(1) (2)	28%	26%

(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.

Q1 2011 Cash flow

Millions of USD



Note: Shire has a revolving 5 year credit facility of $1.2bn, which matures in 2015, and remains undrawn.

Shire 2011 outlook

Full year 2011 dynamics	Direction versus FY 2010	
Product sales	↑	Growth continuing at 2010 rate
Royalties	↓	Generic erosion (total royalties & other revenue -10%)
Product gross margins	≈	
R&D and SG&A	↑	At the upper end of 10 to 13% growth
Tax rate	≈	22-24% tax rate
Reported EPS-ADS	↑	**Good Earnings growth**

VYVANSE® New Uses Update

Investigation of dopamine-norepinephrine modulation in

- ✓ Major Depressive Disorder (MDD)
- ✓ Excessive Daytime Sleepiness (EDS)
- ✓ Negative Symptoms in Schizophrenia (NSS)
- ✓ Binge Eating Disorder (BED)

Dr. Jeffrey Jonas
SVP, Specialty Pharmaceuticals R&D

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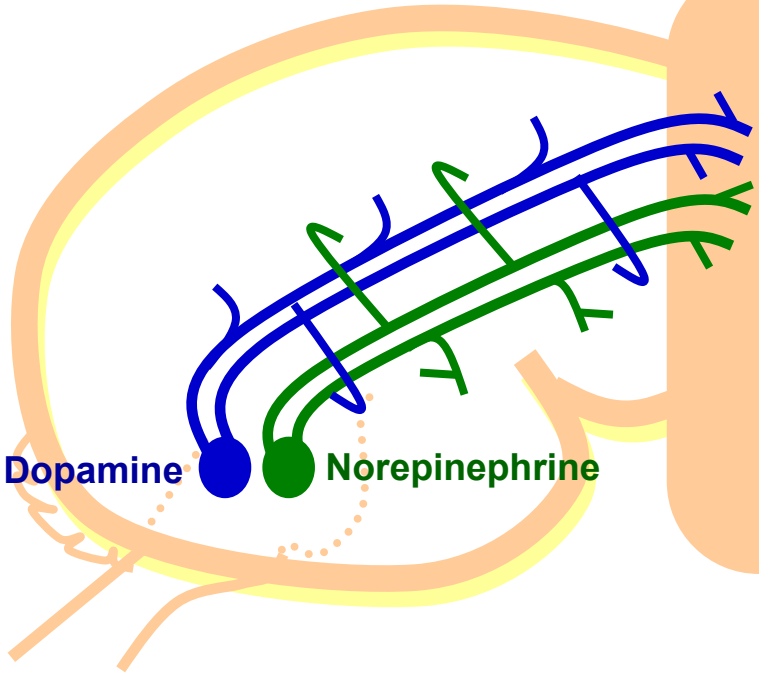
VYVANSE® New Uses Update

This communication describes investigational studies which evaluate the potential use of VYVANSE in treating non-ADHD conditions. These data are presented to inform the medical and financial communities about Shire development programs. No conclusions can be drawn regarding the safety or efficacy of VYVANSE in any of these other conditions without additional studies and review by regulatory authorities. VYVANSE is approved only for the treatment of Attention Deficit Hyperactivity Disorder. Shire does not recommend the use of its products in any way other than as described in the Prescribing Information.

VYVANSE NEW USES

Dopamine (DA) and norepinephrine (NE) dysregulation is implicated in many neuropsychiatric disorders

As VYVANSE impacts DA and NE transmission, therapeutic effects may be seen in symptomatic disorders involving these neural pathways



- MOOD
- COGNITION
- INTEREST
- INHIBITION
- ENERGY
- MOTIVATION
- WAKEFULNESS

- ADHD
- Major Depression
- Excessive Daytime Sleepiness
- Schizophrenia
- Binge Eating

Kessler RC et al. *Am J Psychiatry* 2006;163:716-723; Atlfas et al. *BMC Psychiatry* 2002;2:9; Hudson et al. *Biol Psychiatry* 2007;61:348-358; Ross et al. *Schiz. Res* 2006;88:90-95; Wingo et al. *J Clin Psychiatry*, 2007, 68:11:1776-1784; Walters et. al. *J Clin Sleep Med*, 2008, 4:6:591-600; Dunlop & Nemeroff *Arch Gen Psych* (2007); 64:327-37.

VYVANSE NEW USES
Approach to Managing Development Risk

- Clear Phase 2 signal finding studies
  - Clear, indication-based diagnostic criterion
  - Study designs to minimize multiple forms of bias
  - Pre-defined go/no-go criteria with suitable safety-efficacy balance
  - Value established early, including comparator data (as appropriate)
- Enriched or more homogeneous study populations/models
  - EDS (wakefulness model), MDD adjunctive (SSRI inadequate responders), NSS adjunctive (large schizophrenia subgroup with substantial unmet medical need)
- Reduced major Phase 3 investment risk
  - By making relatively small investments in clearly defined signal finding studies
  - By obtaining global regulatory guidance
  - Study indications with clear, valued and medically relevant endpoints

VYVANSE NEW USES (NSS)
Market Dynamics

Prevalence of Schizophrenia
6,645,156

Diagnosis rate = 95%

Diagnosed
6,312,899

Treatment rate = 73%

Treated
4,608,416

Negative Symptoms = 65%

Negative Symptom Patients
2,995,470

CAGR [2008-2018] of each rate = 1.04%

3.0 million candidates for treatment (G7 in 2010)

Estimated Total Societal Cost (G7)
~ $120 Billion per year

- Lifetime disability
- Multiple hospitalizations
- Dependence on public care

Medication Costs

Total Atypical Antipsychotic Market Value (2008)
$18.2 Billion per year

- No consensus of approved medication or medications for NSS

Potential NSS Market Value
>$1 Billion

Schizophrenia presents substantial societal costs to offset (G7)

WHO report, global burden of Disease 2004 (2008), www.who.int, Decision Resources Schizophrenia Report 1/2010, Sartorius N, Schiz. Bulletin: 21-34,1974;Knapp et al., Schiz. Bulletin (30), 2, p279-293, 2004; Wu et al, J Clin Psych 2005; Sources: Eurostatand US Census, Commercial Insight: Antipsychotics, October 2009; Decision Resources Shire Estimates

VYVANSE NEW USES (NSS) – study design

- Study 204: A blinded rater open-label, double blind withdrawal design
- 21 sites, mean age = 42, average dose = 52mg
- Entry into open label required SANS Total ≥ 55, CDSS ≤ 9, SAS Akinesia <2, and PANSS Positive subscore < 20

3 week screening (no VYVANSE)	10 week open label (augmentation with VYVANSE of atypical antipsychotics)	4 week double blind, randomised discontinuation
• Patients stable on atypical antipsychotic medication • Stability confirmed over three weeks • No depression (CDSS ≤ 9) • No EPS • Mild positive symptoms	• 10 week open label VYVANSE augmentation of atypical antipsychotics • 92 enrolled, 69 completed • Weekly BLINDED assessments • Optimised dose over 20 to 70 mg/d range	• 4 week double blind discontinuation • 35 patients switched to placebo • 34 patients continued VYVANSE • Weekly BLINDED assessments

Efficacy Measurements
- **Negative symptoms (1º endpoint)**
- **Positive symptoms**
- **Psychiatric symptoms, depression-anxiety**
- **Global Clinical Assessments**
- **Cognitive functioning**
- **Real-world functioning**

Safety Measurements
- **Movement disorder symptoms**
- **Suicidal thinking**
- **Amphetamine cessation symptoms**
- **Sleep quality**
- **Vital Signs, Adverse Events**
- **Fasting laboratories, ECG**

VYVANSE NEW USES (NSS) - Safety
No new issues in population expected to experience tolerability issues

Disposition

- All cause discontinuation: 25% in OL, 14% in DB (no group differences)
- Most common: 'withdrawal by subject' (12 –14%)
- Adverse event discontinuations: 5.4% in OL, 2.2% in DB

Treatment-emergent adverse events (≥ 5%)

- Headache 14.1%
- Insomnia 10.9%
- Decreased Appetite 10.9%
- Dizziness 8.7%
- Dry Mouth 6.5%
- Diarrhea 5.4%
- Across both phases, 'exacerbation of illness' in 3.2% of subjects receiving Vyvanse and 1.1% of subjects receiving placebo

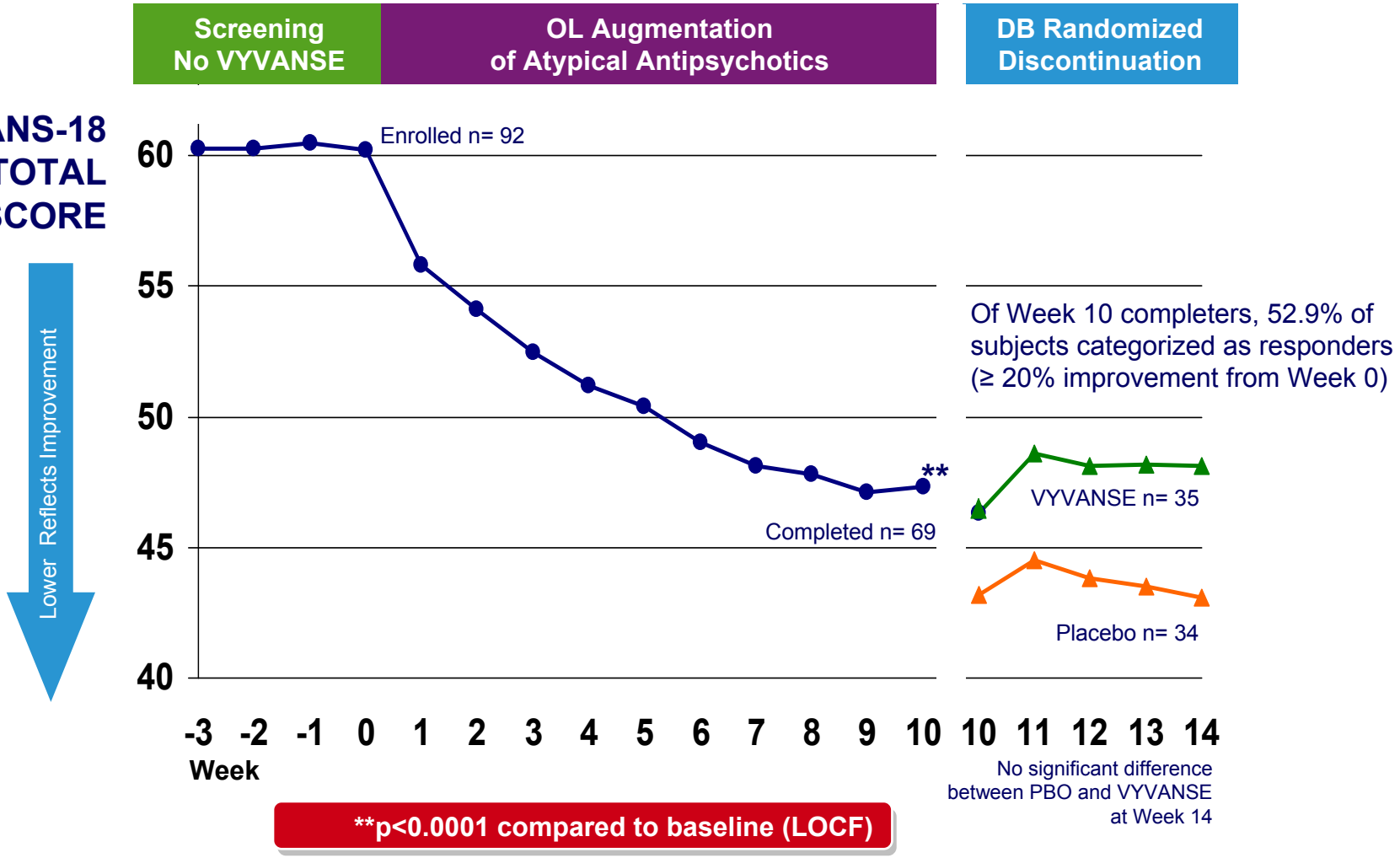
Vital Sign mean changes (Week 10)

• Systolic BP (mmHg)	2.6	Diastolic BP (mmHg)	2.5
• Pulse (bpm)	5.1	Weight (kg)	-0.46

No clinically significant changes in laboratories or ECG measurements

Data Source SPD489-204: Tables 4.2.2.1; 4.2.2.3; 4.6.6.1; 4.7.2 15-Mar-2011; Shire data on file

VYVANSE NEW USES (NSS) – Clinical Effect on Negative Symptoms
Improvement in open-label, no rebound in randomized discontinuation

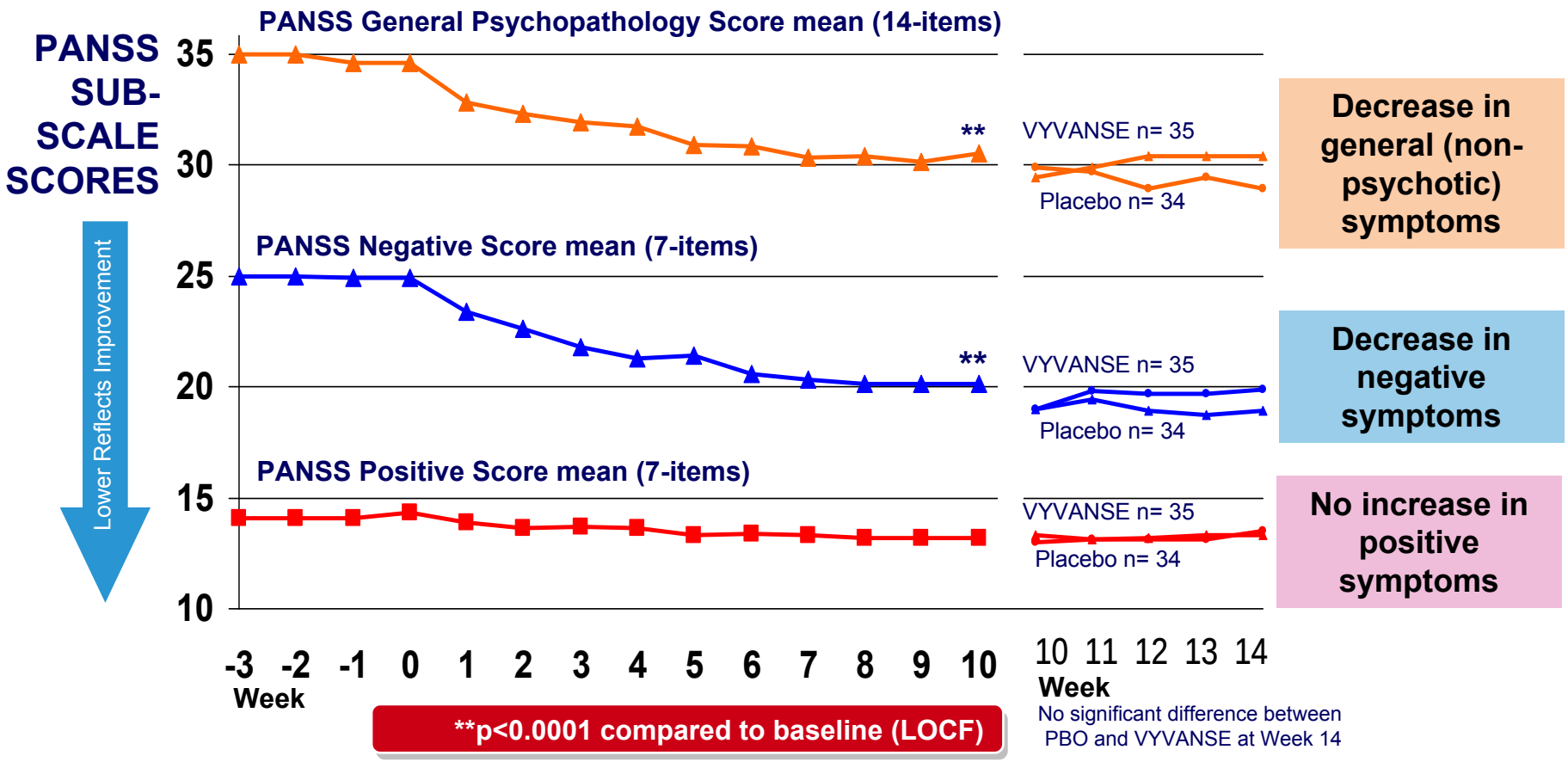


Shire To be as brave as the people we help.

Data Source SPD489-204: Tables 3.1.1.1, 3.1.2.4, 15-Mar-2011; Shire data on file

VYVANSE NEW USES (NSS) – Clinical Effect on Positive Symptoms
Mean PANSS Total and subscale scores

In the OL phase, mean PANSS Total Score decreased from 73.8 (Week 0) to 63.9 (Week 10), or *-9.8 points (95% CI: -11.7 to -8.0)***



Data Source SPD489-204: Tables 3.2.4.1 to 10, 15-Mar-2011; Shire data on file

VYVANSE NEW USES
Summary and Next Steps for VYVANSE in NSS

Summary

- Improvement with VYVANSE augmentation during OL-blinded rater phase; no worsening/rebound during short DB phase
  - Slow/little offset of activity over 4 weeks suggests conventional withdrawal designs may suffice
- No new or unexpected safety findings across psychiatric (positive symptoms, anxiety, depression) and medical (laboratories, vital sign, ECG) parameters
- Negative symptom improvements supported by collateral improvements in other clinical domains

Next Steps

- Schedule and complete health authority interactions in 2H11
- Establish potential/parameters for biomarkers for response, including commercially viable diagnostic and maintenance tools
- Potential to initiate Phase 3 by end 2011

Concluding remarks

Angus Russell
Chief Executive Officer

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

Key events for the rest of 2011

Lialda (mesalamine) 1.2g	Approval and launch for maintenance of remission in the US
Vyvanse (lisdexamfetamine dimesylate) capsules	File MAA in Europe Binge Eating Disorder Ph 2
firazyr icatibant	PDUFA August 25, 2011 & US launch
Carrier Wave	Guanfacine program update
	Lexington manufacturing plant validation and submission and potential approval

Strategy Continues to Deliver

Driving strong revenue growth through balanced product portfolio

Launching new indications and advancing our pipeline

Delivering value to patients, physicians, payors and policymakers

Questions and Answers

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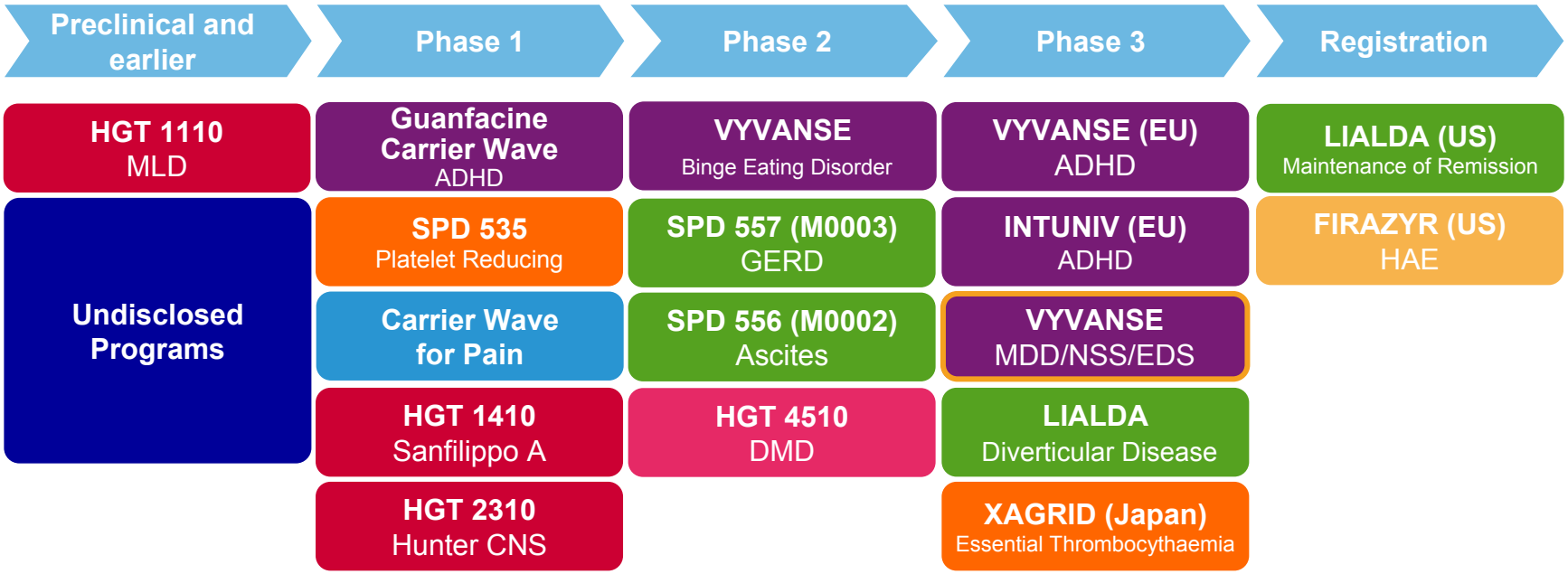
APPENDIX

Replenishing our pipeline



2011 Portfolio Strength and Diversity – Q1 Product Sales

	Q1 2011 $m	Q1 2010 $m	Reported Growth	Like for Like Growth(1)
VYVANSE	202	154	+31%	+31%
ADDERALL XR	111	92	+21%	+21%
REPLAGAL	105	68	+55%	+56%
ELAPRASE	104	101	+3%	+2%
LIALDA / MEZAVANT	87	64	+37%	+37%
PENTASA	65	58	+11%	+11%
VPRIV	59	6	+917%	+921%
INTUNIV	42	35(2)	+21%	+21%
FOSRENOL	41	47	-13%	-13%
FIRAZYR	5	2	+141%	+141%
RESOLOR	1	-	n/a	n/a
OTHER	67	91(3)	-27%	-28%
PRODUCT SALES	**889**	**718**	**+24%**	**+24%**

(1) 'Like for Like Growth' excludes movements in exchange rates by applying 2010 exchange rates to 2011 results.
(2) Includes $17.6m of revenue relating to initial stocking shipments which had previously been deferred.
(3) 2010 'Other' includes DAYTRANA net product sales of $18.4m.

2011 Emerging Shape of Shire Income Statement

	2010 Q1	2010 Q2	2010 Q3	2010 Q4	2010 FY	2011 Q1	Direction V. FY 10	2011 Dynamics
Total product sales	$718m	$764m	$794m	$852m	$3,128m	$889m	↑	Growth continuing at 2010 rate
versus prior year [1]	*-9%*	*+37%*	*+24%*	*+21%*	+16%	+24%		
Royalties	$95m	$83m	$77m	$73m	$328m	$74m	↓	Generic erosion (total royalties & other revenue - 10%)
versus prior year	+88%	+24%	+27%	-36%	+12%	-23%		
Gross margin [2] [3]	87%	86%	87%	86%	87%	87%	≈	
R&D [3]	$127m	$144m	$149m	$178m	$598m	$173m		
versus prior year	+$10m	+$26m	+$5m	+$34m	+$75m	+$46m	↑	At the upper end of 10 to 13% growth
SG&A [3]	$309m	$304m	$302m	$373m	$1,288m	$352m		
versus prior year	+$38m	+$19m	+$35m	+$58m	+$150m	+$43m		
Tax Rate [3]	26%	25%	24%	16%	23%	22%	≈	22-24% tax rate

(1) Product sales growth compared to 2009 product sales on a “normalized Medicaid rebate” basis
(2) Gross margin calculated as a percentage of product sales
(3) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalents used to calculate these measures.

2011 Q1 Royalties

	Q1 2011 $m	Q1 2010 $m	Reported Growth
3TC and ZEFFIX	36	37	-3%
ADDERALL XR	17	41	-59%
REMINYL	13	13	0%
Other	8	4	100%
Total Royalties	**74**	**95**	**-23%**

2011 Q1 Non GAAP cash flow measures

Non GAAP cash generation reconciliation	Q1 2011 $m	Q1 2010 $m
Net cash provided by operating activities	**202**	186
Tax and interest payments, net	**6**	90
Non GAAP cash generation[(1)]	**208**	276

Non GAAP free cash flow reconciliation	Q1 2011 $m	Q1 2010 $m
Net cash provided by operating activities	**202**	186
Capital expenditure	**(47)**	(44)
Non GAAP free cash flow[(2)]	**155**	142

(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 debt

	March, 31 2011 $m	December, 31 2010 $m
Cash and cash equivalents	712	550
Restricted cash	31	27
Convertible bonds	(1,100)	(1,100)
Building finance obligation	(8)	(8)
Net debt	**(365)**	**(531)**

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.
- Where applicable 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, and 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.

VYVANSE® new uses update

Appendix

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VYVANSE NEW USES
Negative Symptom Schizophrenia (NSS) – A Potential Paradigm Shift

- Long-held clinical belief that amphetamines and related agents inevitably exacerbate symptoms of schizophrenia
  - 'Excess' dopaminergic tone is a cornerstone belief in etiology of schizophrenia
- Little systematic data to dispute clinical belief
  - Anecdotal clinical and pre-clinical evidence suggest the biology of 'excess' dopaminergic tone may not be as straightforward as believed
- Substantial unmet medical need world-wide
  - Opportunity to shift scientific and clinical practice for patient-family, treatment professional, public health benefit
  - No consensus of approved medication or medications for NSS

Curran et al. Br J Psychiatry 2004; 185: 196-204

VYVANSE NEW USES - Clinical Symptoms and Disorder
Schizophrenia is heterogeneous and symptomatically wide-reaching

POSITIVE

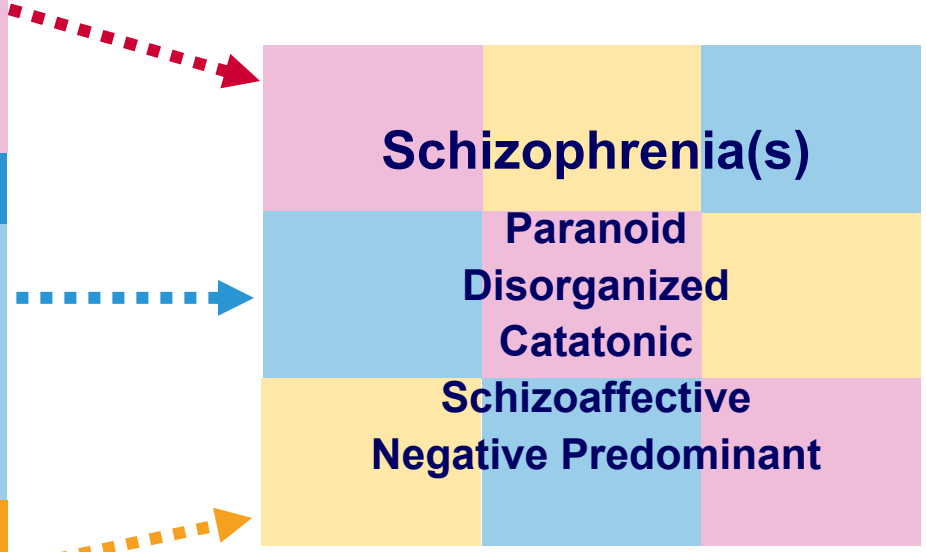
Delusions
Paranoia, bizarre
Hallucinations
Auditory common
Disorganization

NEGATIVE

Alogia (communication)
Affect (emotion)
Anhedonia (interest)
Apathy (motivation)
Asociality

COGNITIVE

Attention/Concentration
Working memory
Verbal, Spatial Learning
Social Cognition
Executive Function



Prevalence: Men = Women
Men present earlier (teens-20s)
Cause unknown

Buchanan R. *Schiz Bull* 2007: 33 (4): 1013-22; Buchanan R. Schiz Bull 2007: 33 (4): 1013-22; WHO report, global burden of Disease 2004 (2008), Sartorius N, Schiz. Bulletin: 21-34,1974;Knapp et al., Schiz. Bulletin (30), 2, p279-293, 2004; Shire Estimates

VYVANSE NEW USES - Demographics
Study 204 sample was representative of NSS population

Performed across 21 US sites

- Mean age = 42.3 years, 67% male, 34% Caucasian
- Nearly 95% unemployed
- 36% did not complete high school

Dosing

- VYVANSE average daily dose (Week 10 randomization) = 53 mg/d
  - Majority titrated to 60 or 70 mg/d

- Most common atypical anti-psychotics used:
  - Risperidone [RISPERDAL]: 32.6%
  - Paliperidone [INVEGA]: 9.8%
  - Quetiapine [SEROQUEL]: 23.9%
  - Olanzapine [ZYPREXA]: 19.6%
  - Aripiprazole [ABILIFY]: 14.1%

Data Source: Table 1.1-2.1; 4.1.2; 16-Mar-2011; Shire data on file

VYVANSE NEW USES
Summary of On-Going Programs

Parameter	MDD inadequate response	Excessive Daytime Sleepiness	Negative Symptom Schizophrenia	Binge Eating Disorder
Approach	Augmentation of anti-depressants	Monotherapy	Augmentation of atypical anti-psychotics	Monotherapy
Clinical data and planning	• Positive Ph 2 data presented 4Q10 • Ph 3 planned 2H11 start • MDD Cognition data 2Q11	• Positive Wakefulness model data presented 3Q10	• Completed longest, largest study of amphetamine conducted 1Q11	• Most common eating disorder (2% US; up to 20% patients with psychiatric disorders) • Ph 2 start 2H11

Swanson et al, *Arch Gen Psychiatry* (2011), McElroy et al *Affect Disord* 2011;128(3):191-8