

Third Quarter Results to September 30, 2010

Shire plc
October 29, 2010

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



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 Pharmaceutical 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

- Opening remarks
Angus Russell
- Financial review
Graham Hetherington
- HGT update
Sylvie Grégoire
- Specialty Pharma update
Michael Cola
Dr. Jeffrey Jonas
- Concluding remarks
Angus Russell
- Q & A
All

Opening remarks

Angus Russell
CEO



Our purpose

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

Continued excellent performance in Q3

- Revenues up 31% to \$874 million
- Non GAAP diluted earnings per ADS: \$1.16
 - Up 138% versus Q3 2009
- Strong cash generation of \$271 million
- Increased full year non GAAP earnings guidance
 - Up to \$4.20 per ADS
 - 20% increase on 2009
- Progress supports our long term aspirational target
 - Mid-teens sales growth on average between 2009 - 2015

Q3 2010 highlights



- Approved in the EU



- Strong demand with over 330 patients added in Q3



- Rx's up 28% vs Q3 2009
- Q3 US ADHD market up 13% versus Q3 2009
- New uses - New value in pipeline



- Exclusive ex-North American rights to ActRIIB molecules to be used in muscular disorders



- Successful tender offer with over 99% acceptance



- Addresses symptomatic unmet need of chronic constipation
- Now launched in 3 countries

Financial Review

Graham Hetherington
CFO



Our purpose

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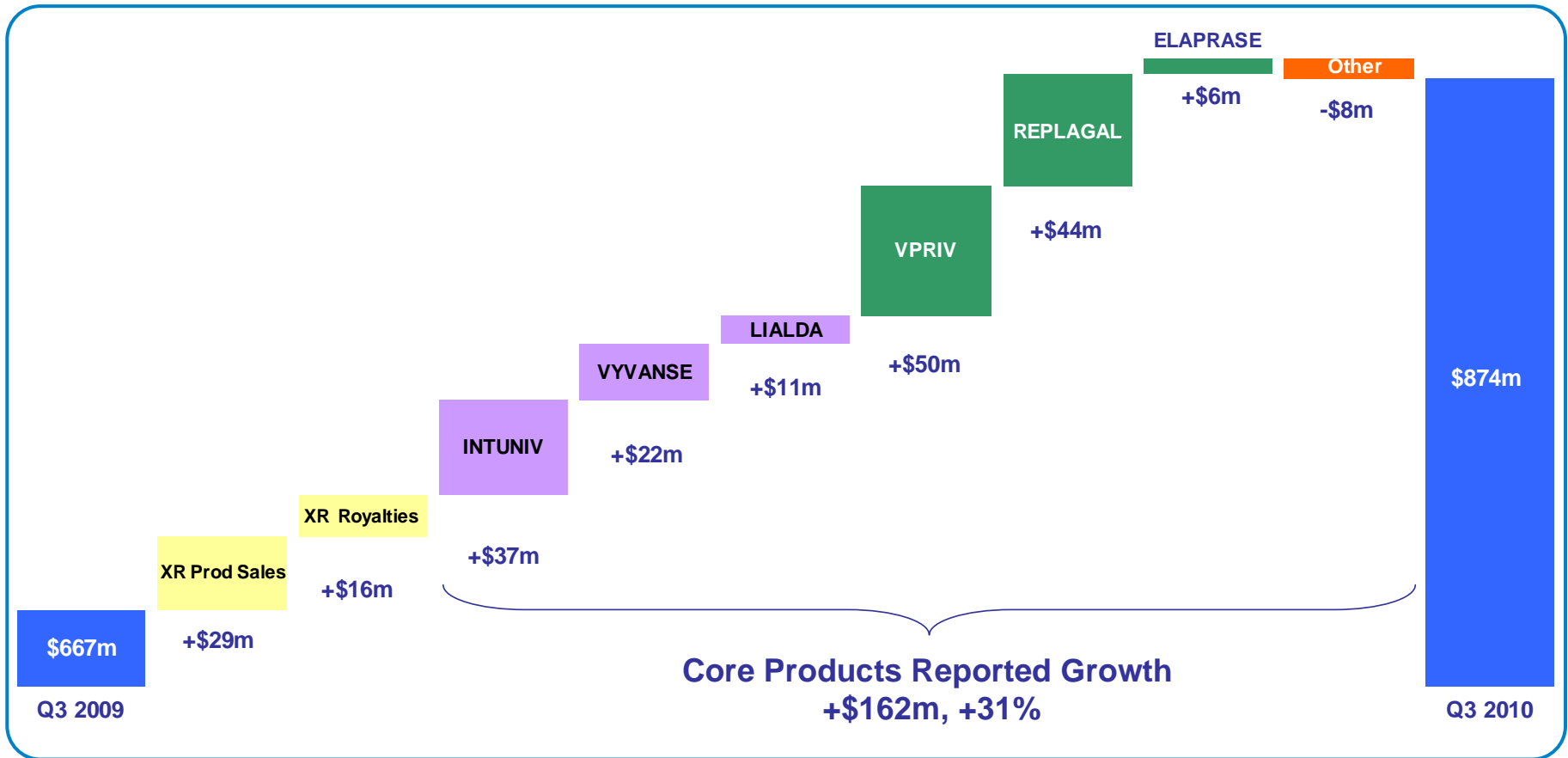
2010 Q3 Revenue summary

	Q3 2010 \$m	Q3 2009 \$m	Reported Growth	Like for Like Growth ⁽²⁾
Core Product Sales ⁽¹⁾	694	532	+31%	+34%
ADDERALL XR Sales	100	71	+41%	+40%
Total Product Sales	794	603	+32%	+35%
Royalties and Other Revenues	80	64	+24%	+25%
Total Revenues	874	667	+31%	+34%

(1) Core product sales represent Shire's product sales excluding ADDERALL XR.

(2) 'Like for Like Growth' excludes movements in exchange rates by applying 2009 exchange rates to 2010 results.

2010 Core products driving strong revenue growth



Operating leverage emerging – Key financial ratios

Year on Year percentage growth:

Q3 2010

Q3 2009

Total Product Sales

+32%

-15%

Core Product Sales

+31%

+20%

R&D⁽¹⁾

+3%

+23%

SG&A⁽¹⁾

+13%

-6%

Ratios:

% of Total Product Sales

Gross margin⁽¹⁾

87%



84%

R&D⁽¹⁾

19%



24%

SG&A⁽¹⁾

38%



44%

EBITDA^{(1) (2)}

30%



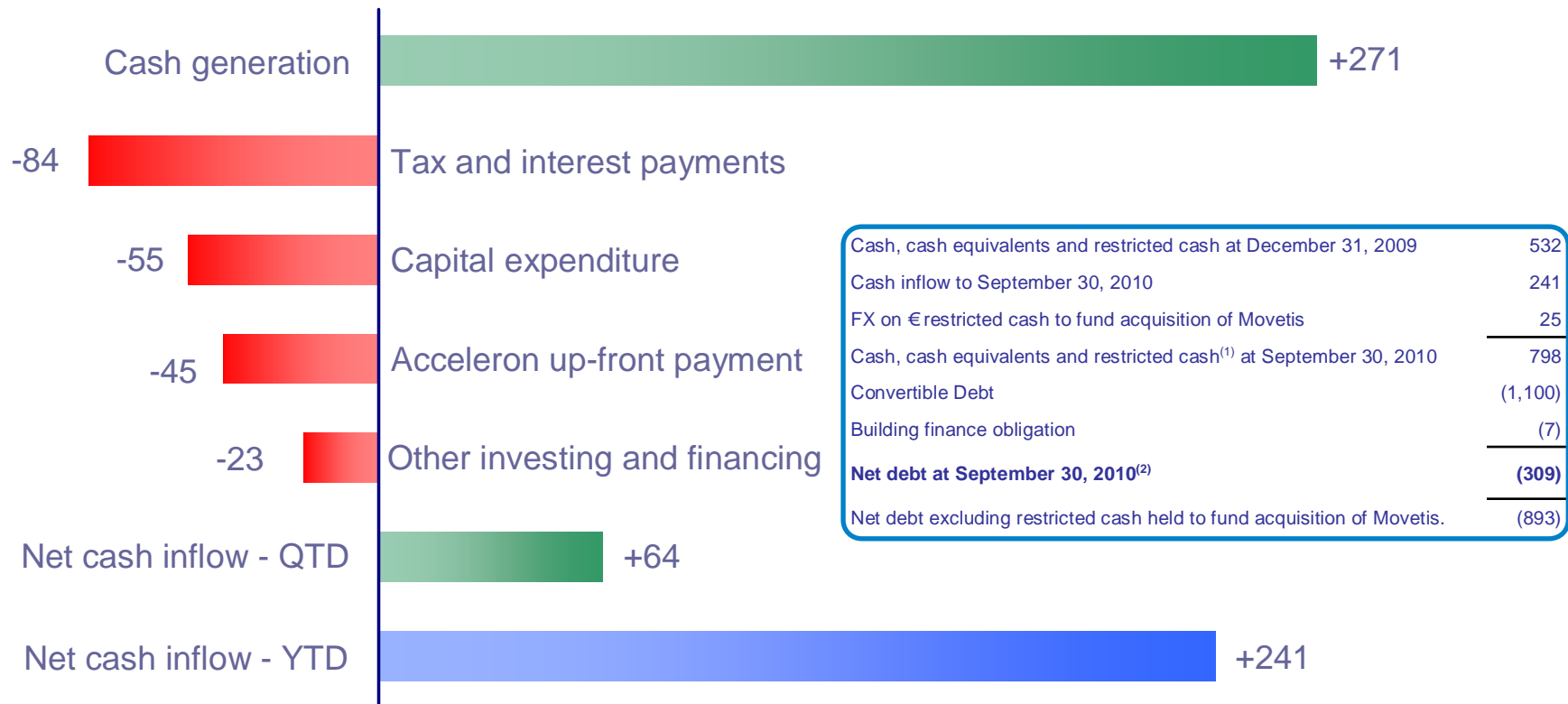
15%

(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

2010 Q3 - Cashflow

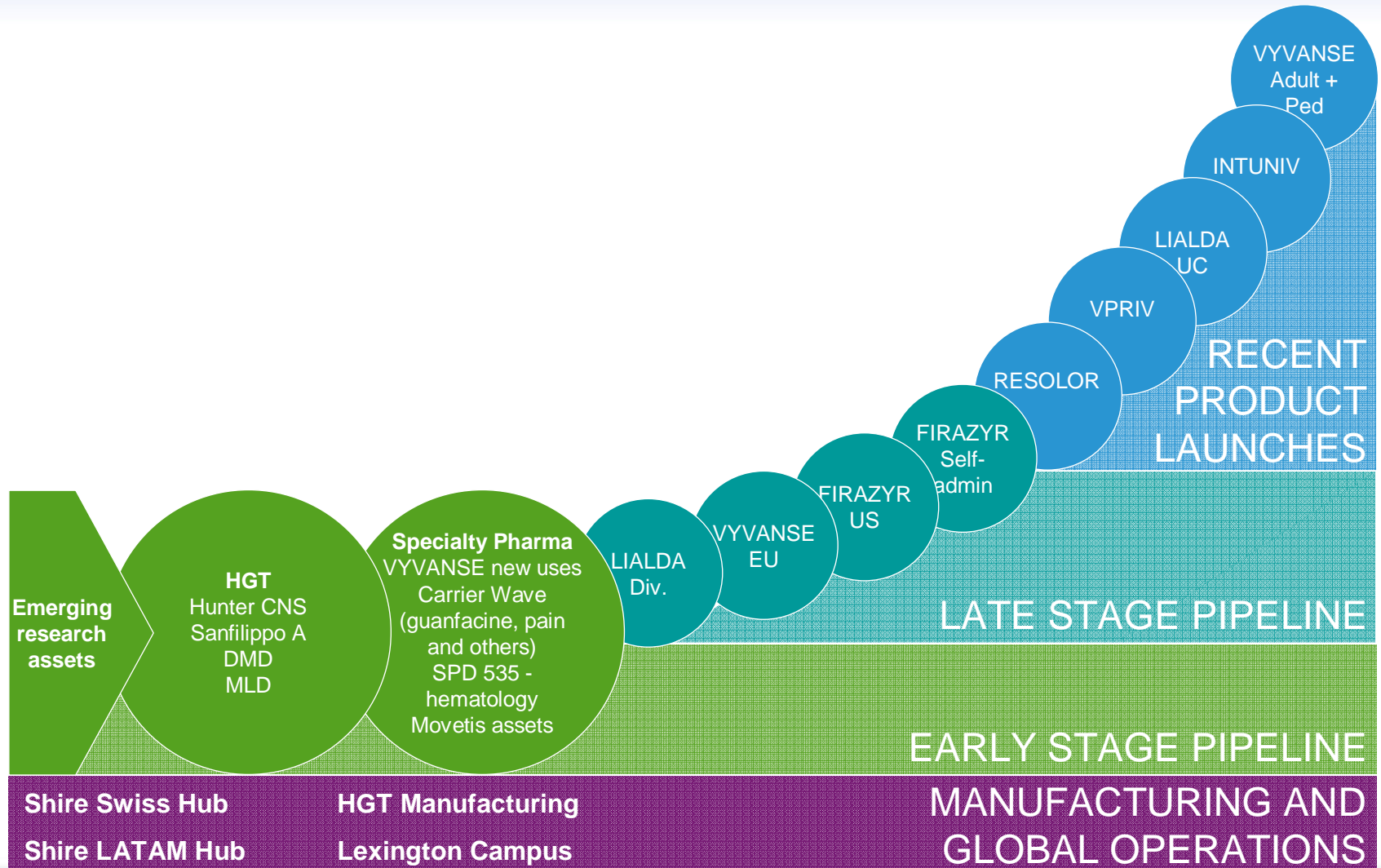
Millions of USD



(1) Restricted cash: \$605m. At September 30, 2010 includes restricted cash of \$584m related to the acquisition of Movetis

(2) Shire has a revolving credit facility of \$1.2bn which was undrawn at September 30, 2010.

Patient-focused investments driving sustained growth and returns



Shire 2010 Guidance raised

Full year 2010 Dynamics

Direction
Versus FY 2009

(see Appendix for more analysis)

ABSORBING THE IMPACT OF:

- US Healthcare reform
- European Pricing
- Foreign exchange rate movements to date
- Movetis acquisition
- DAYTRANA disposal
- Q4 dynamics of AXR product sales & royalties

Core Product Sales



- Continued growth against strengthening comparatives
- REPLAGAL year on year growth moderating

Total Product Sales



Core product growth > AXR decline

Royalties



AXR royalties offset declines in other royalties

Gross Margins



R&D and SG&A



- Continued operating leverage
- Increasing investment behind long term growth
- Marginally above 10% year on year growth

Tax rate



Reported EPS-ADS



FY 10 up to \$4.20 per ADS

Memo: Interest on convertible = \$34m pa



To be as brave as the people we help

Dynamics beyond 2010

DRIVERS

KEY ELEMENTS

SUSTAINED CORE PRODUCT SALES GROWTH

- Strong start to achieving aspiration of mid teen sales growth through 2015

INVESTING IN FUTURE GROWTH

- Progressing the pipeline
- Maximising the global reach of our products

ABSORBING THE IMPACT OF RECENT TRANSACTIONS

- Movetis acquisition
- DAYTRANA disposal

DELIVERING FINANCIAL PERFORMANCE

- Expanded operating margins
- Earnings growth
- Strong cash generation

HGT update

Sylvie Grégoire
President, Human Genetic Therapies

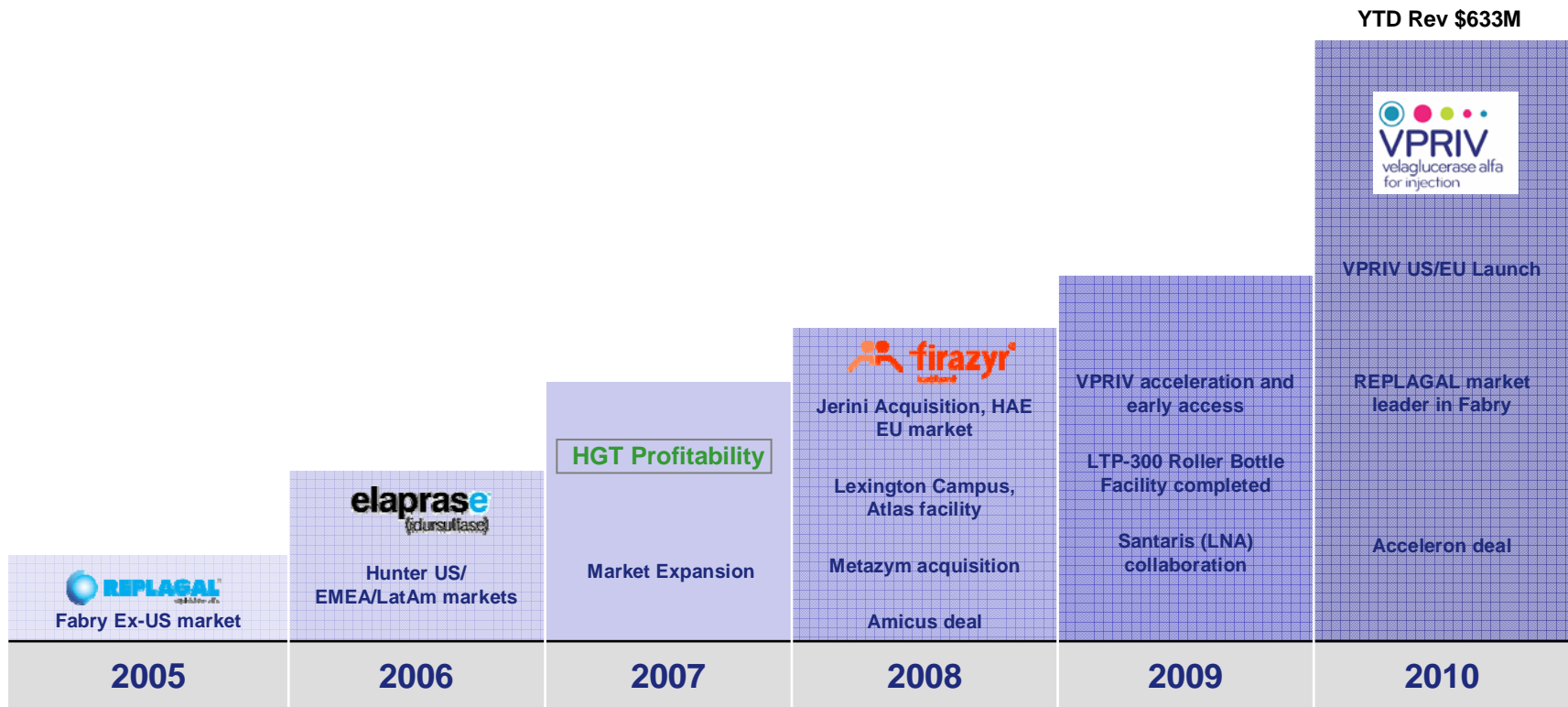


Our purpose

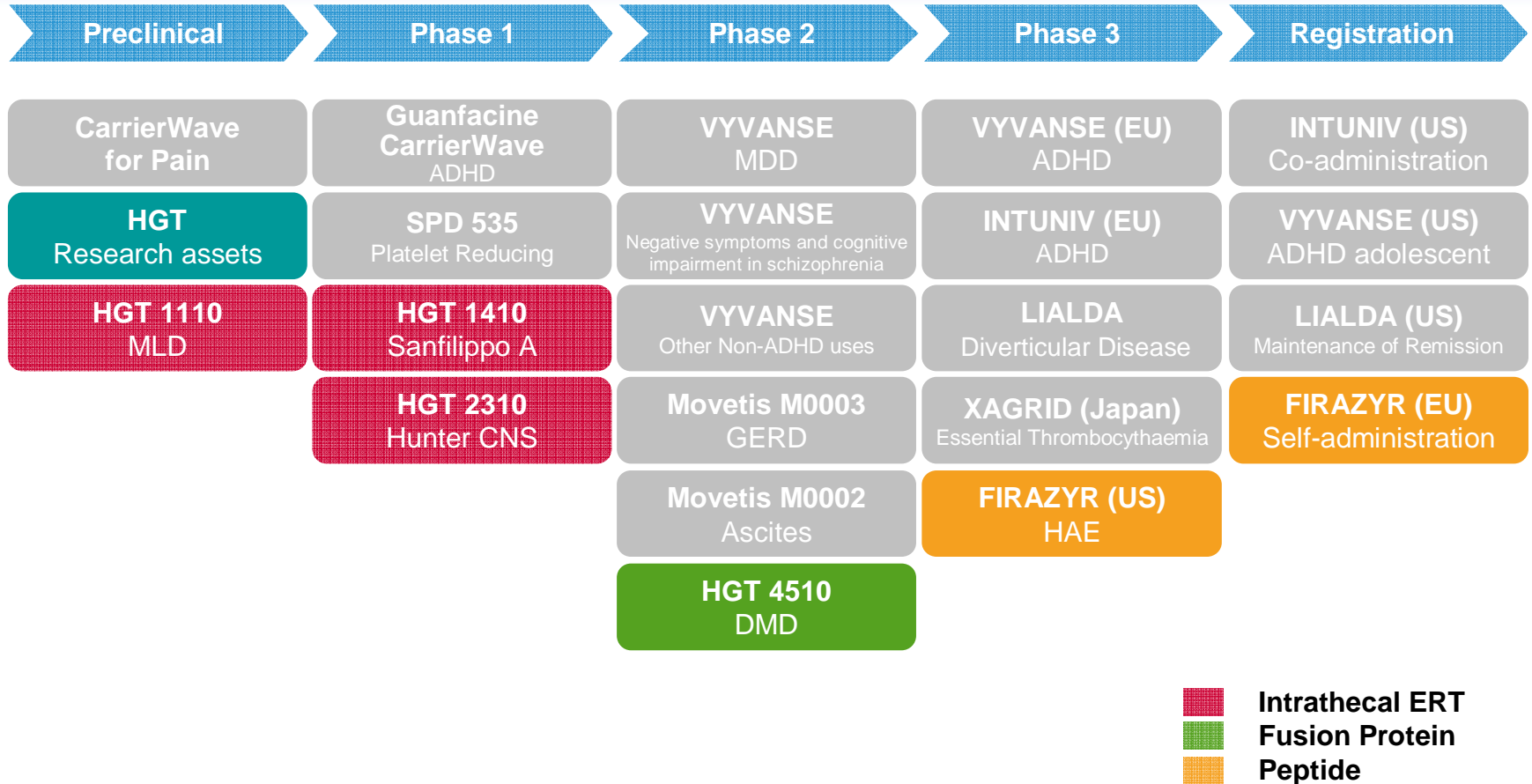
We enable people with life-altering conditions to lead better lives

Past year completes series of transformational events for Shire's rare disease business

HGT has transformed into a global business with leading marketed products and a focused pipeline



HGT R&D pipeline

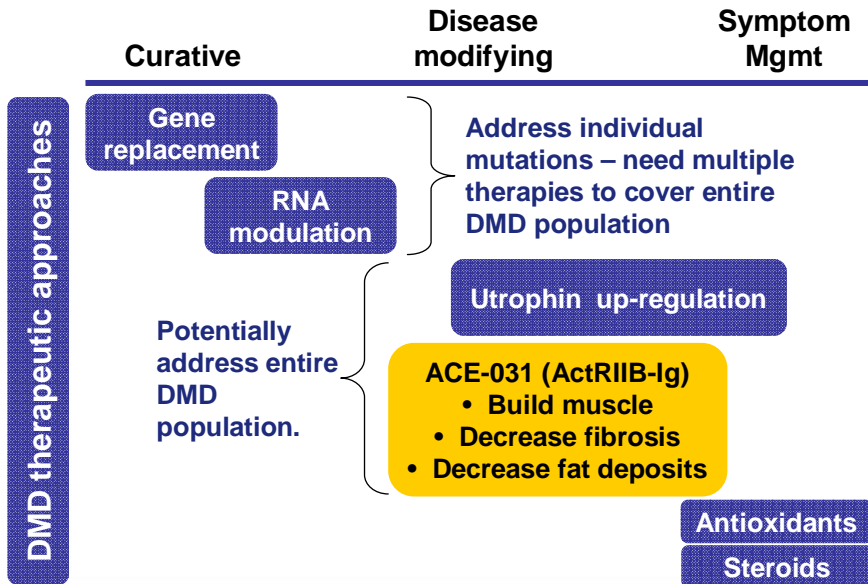


Duchenne Muscular Dystrophy – a fatal orphan muscle disease with no current treatment

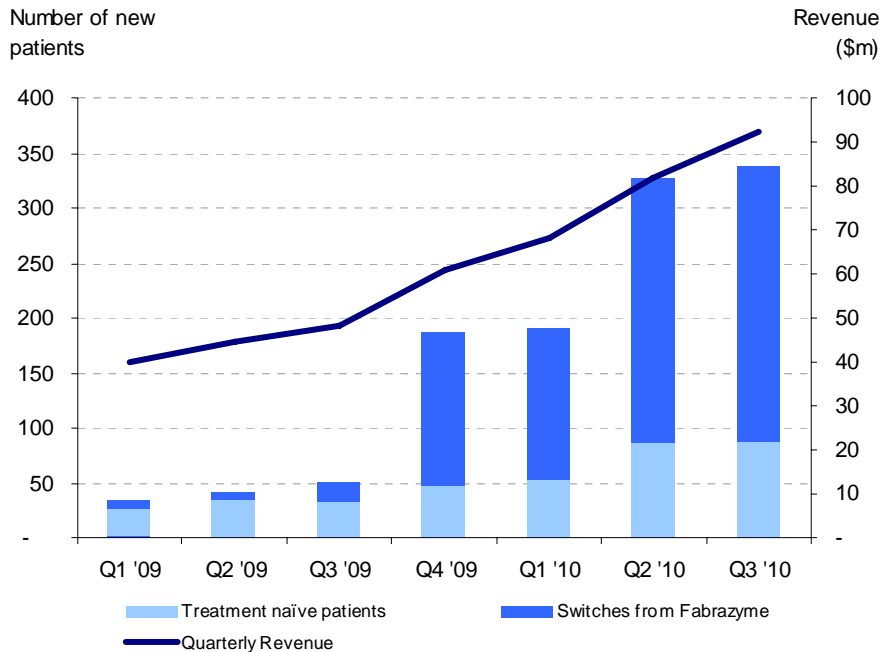


<http://www.cureduchenne.org/>

- DMD - Excellent strategic fit for HGT
 - Orphan disease
 - Est. 50,000 patients worldwide (38,000 ex-NA)
 - Leverages manufacturing expertise
- Partnership with Acceleron
 - Ex-North America license for activin receptor type IIB (ActRIIB) class of molecules
 - \$45m upfront, up to an additional \$165m of milestones payable for successful commercialisation of DMD
- HGT 4510 / ACE-031 is a fusion protein that increases muscle mass
 - An inhibitor of negative muscle regulators
 - DMD program currently in Phase 2a
 - Has the potential to treat a wide range of muscle wasting diseases

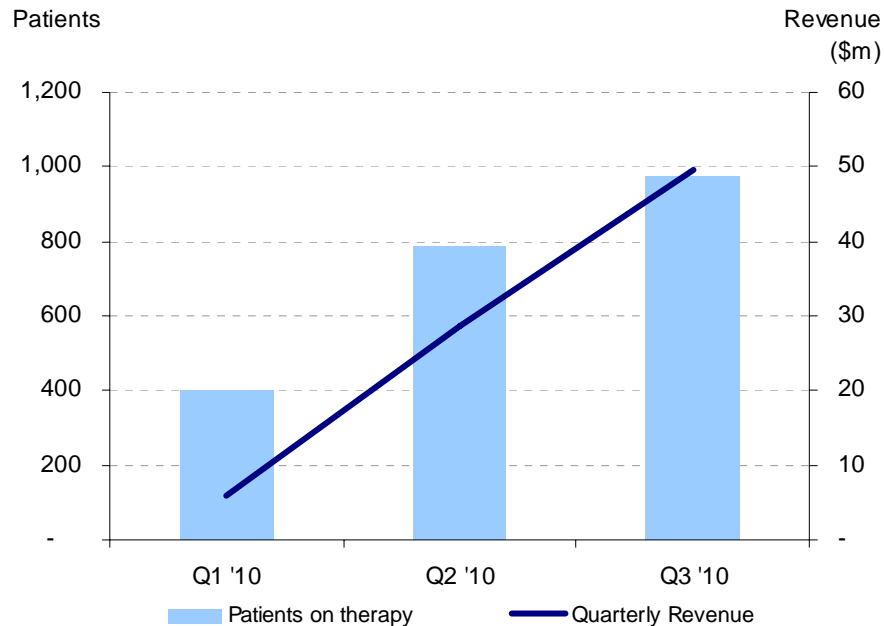


REPLAGAL is Fabry market leader in every region outside of the USA



- Approximately 80% market share in Western Europe and 70% ex-US
- Q3 Revenue of \$92m
 - 103% growth at constant exchange rates
- Over 330 patients added in Q3
 - Over 2,300 total patients on therapy
- Continuing to accommodate additional Fabry patients in 2010
- At least 300 patients could be added to meet additional patient demand in 2011, phased throughout the year

VPRIV now commands 31% US market share and 16% globally

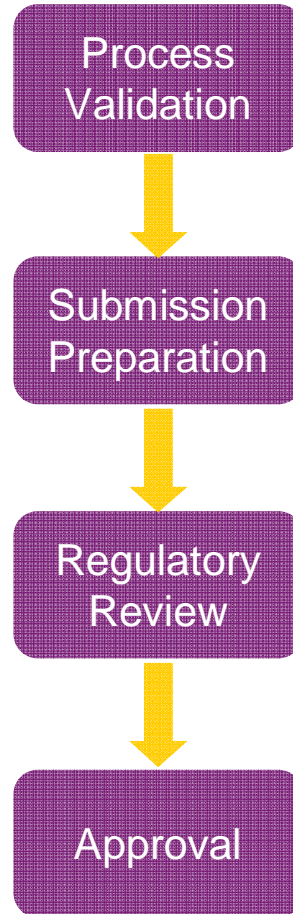


- VPRIV approved in EU
- Strong foundation for long term global success
- Q3 revenues of \$50m
 - 71% growth over Q2'10 at constant exchange rates
- Now over 1,000 total patients on therapy
- Can meet demand for approximately 200 additional Gaucher patients

Lexington Manufacturing – Discussions with agencies ongoing for REPLAGAL and VPRIV

REPLAGAL

- Downstream process validation only
- Q1 2012 approval under standard timelines
 - Exact timing of approval depends on discussions in Europe
- Earlier approval could add capacity for several hundred patients in 2011



VPRIV

- Upstream and downstream process validation
- Upstream scale up 3x and disposable technology
- H1 2012 approval under standard timelines
 - Any acceleration of approval will depend on further discussions

Specialty Pharma update

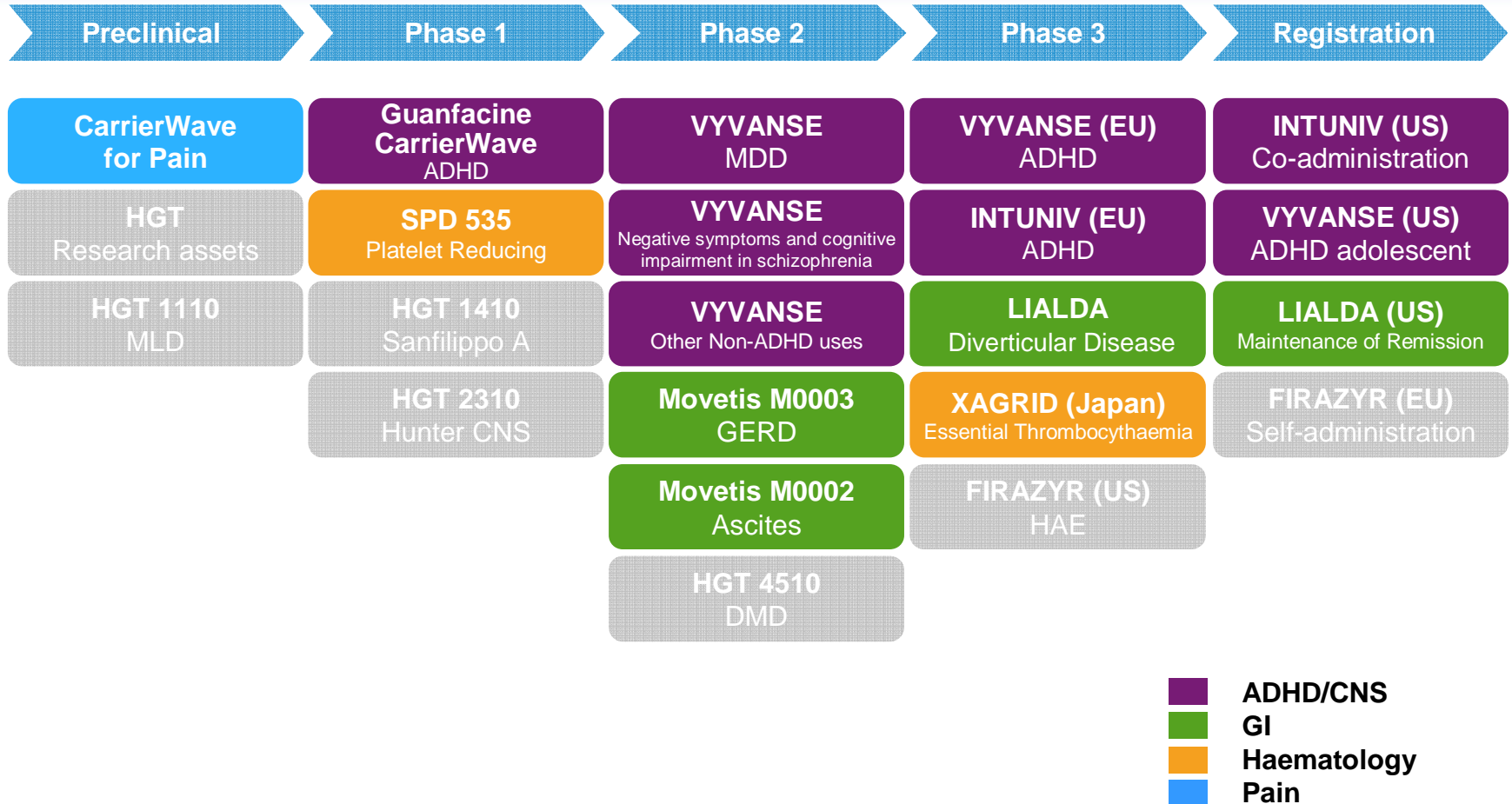
Michael Cola
President, Specialty Pharmaceuticals



Our purpose

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Specialty Pharma R&D pipeline



Vyvanse® New Uses -Clinical Update-

Investigation of dopamine modulation in Major
Depressive Disorder

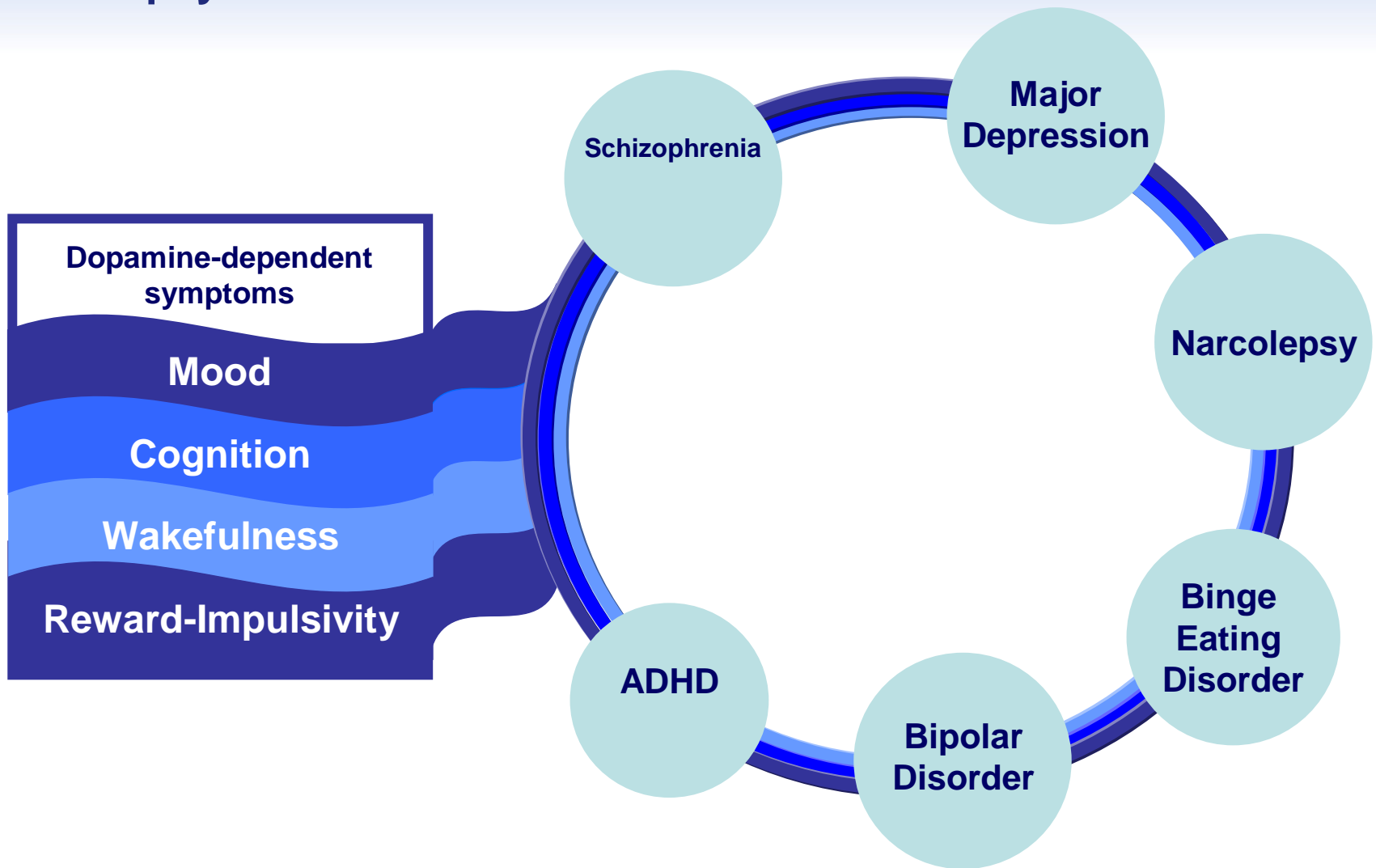
Dr. Jeffrey Jonas
SVP, Specialty Pharmaceuticals R&D



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Dopamine dysregulation implicated in many neuropsychiatric disorders



Major Depressive Disorder (MDD)

Role for dopamine-modulating agents

- **Brain circuitry underlying cognition, motivation, and reward are increasingly recognized as dopamine-dependent**
 - Clinical benefits from dopamine-modulating interventions supported by decades of clinical practice and research
 - Large number of clinical trials have documented treatment benefit with early, unrefined forms of amphetamine
 - Proof of principle inherent in approval of dopamine antagonists-partial agonists for 'inadequate response' in MDD (quetiapine, aripiprazole)
 - While depression burden reduced, approved treatments have minimal impact on symptoms of concentration, motivation, and interest
 - Well-described neurologic and metabolic safety concerns with antipsychotic medication class

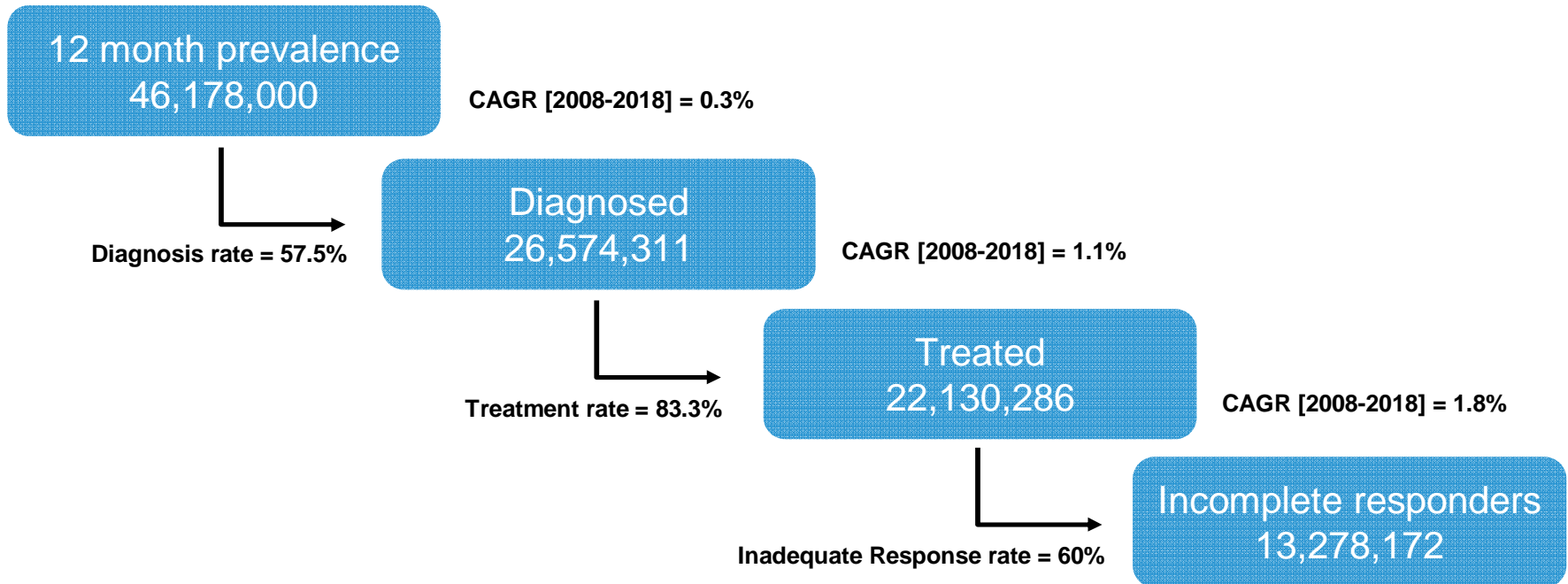
Inadequate response in MDD

Unmet medical needs

- **WHO estimates that MDD will be the 2nd leading cause of morbidity worldwide in all ages by 2020**
 - About 60% of patients with MDD do not achieve clinical remission
 - Residual symptoms include difficulties with concentration, motivation, interest and mood
 - Global regulatory pathways are established for augmentation of primary anti-depressants in patients with 'inadequate response' in MDD
- **VYVANSE (lisdexamfetamine dimesylate) being investigated as potential adjunctive therapeutic option**
 - Novel technology delivering erythrocyte-metabolized pro-drug
 - Known action of lisdexamfetamine on multiple dopamine pathways
- **VYVANSE is currently approved only as a treatment for ADHD**
- **Shire does not recommend use of VYVANSE in any medical condition other than ADHD**

Inadequate response in MDD

Market Dynamics in G7 in 2013



Over 13 million patients (2013) estimated as potential candidates for augmentation of primary anti-depressant therapy

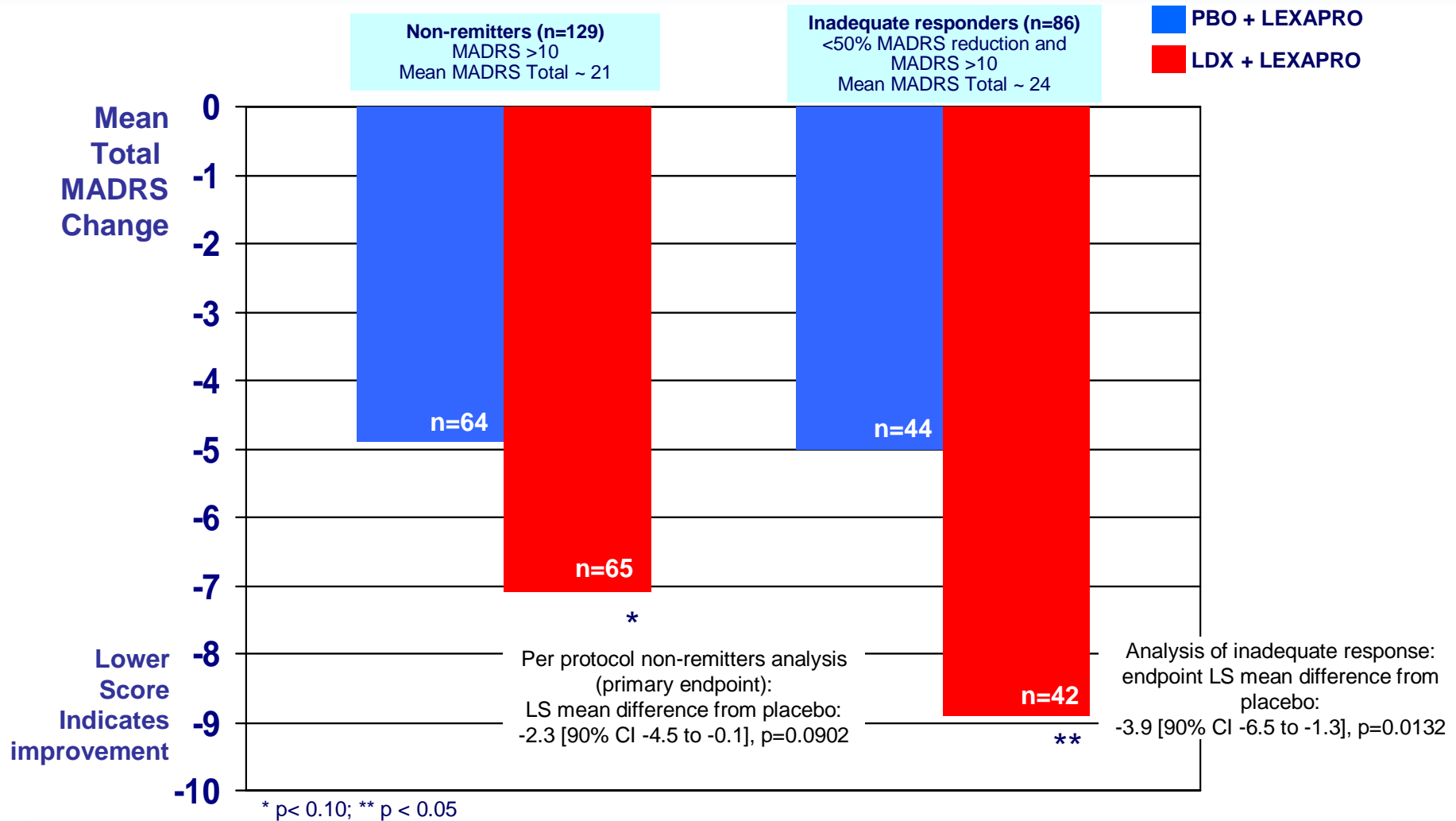
Inadequate response in MDD

Investigating the clinical signal

- **Study of subjects with inadequate response in MDD initiated in 2009**
 - Efficient design from hypothesis of improvement in particular domains of MDD, powered for overall effect, not individual MADRS items
 - Prospective assessment to identify inadequate responders to escitalopram (LEXAPRO) for 8 weeks (n=239)
 - Inadequate responders (< 50% response and MADRS >10) then randomized to escitalopram plus placebo or VYVANSE (Optimized over range: 20, 30 or 50 mg/day; n=129)
 - Primary endpoint: mean change in MADRS total score from augmentation baseline to endpoint
 - MADRS: well-established, validated, 10-item scale measuring symptoms of depression: sadness, tension, sleep, appetite, concentration, motivation, interest, and thought content (0 to 6 points, each item)
- **Study demographics representative of MDD trials - 15 US sites**
 - Mean age of 39 years, 61% female, 77% Caucasian
 - Mean daily dose of VYVANSE of 29.6 mg
 - Discontinuation (blinded phase) similar across treatment groups
 - **All causes: 10.2% Placebo, 12.4% VYVANSE**
 - **Adverse Event-related: 2.3% Placebo, 4.5% VYVANSE**

SPD489-203: MADRS Total Change

Improvement over placebo + LEXAPRO in both non-remitting and non-responding populations

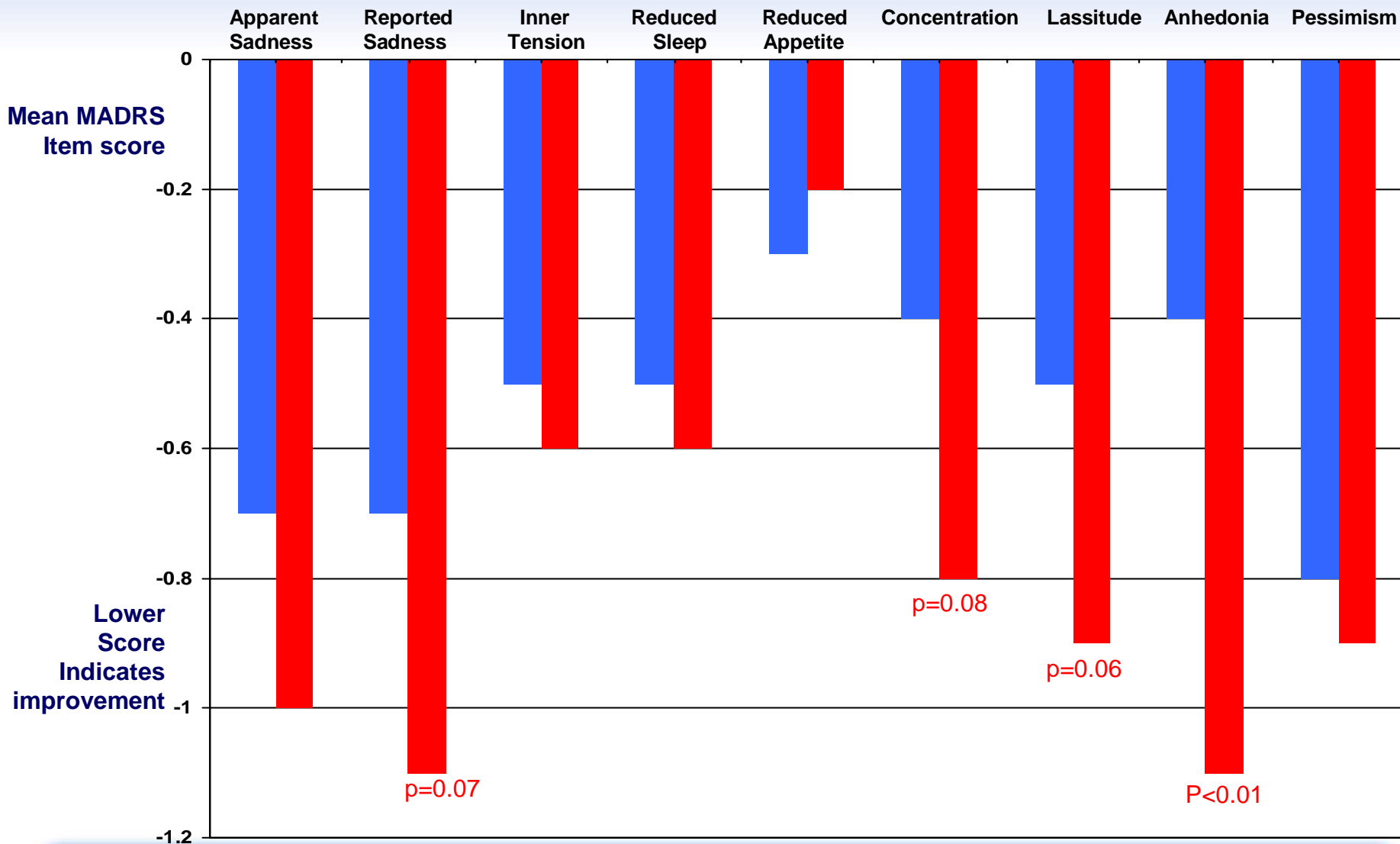


SPD489-203: MADRS Item Change

Improvement over placebo + LEXAPRO by item

PBO + LEXAPRO (n=64)

LDX + LEXAPRO (n=65)



To be as brave as the people we help

SPD489-203: Safety (Analysis set; n=173)

Findings aligned with known characteristics of VYVANSE

- Treatment-emergent adverse events reported were similar to the known, labeled profile of VYVANSE in ADHD
- Changes in blood pressure and heart rate consistent with known effects seen in previous studies of VYVANSE
- No clinically significant changes in ECG parameters
- Weight: Placebo increase of 0.32 kg, VYVANSE decrease of -1.2 kg
- BMI: Placebo increase of 0.12, VYVANSE decrease of -0.4
- No clinically significant changes in fasting liver or metabolic laboratory measures
- Amphetamines have a high potential for abuse and dependence
- Misuse of amphetamines may cause sudden death and serious cardiovascular events

VYVANSE in Inadequate response in MDD

Next steps

- Examine options for dosing and speed of titration
- Complete Phase 1 studies for drug-drug interactions and in elderly population (ongoing)
- Seek end of Phase 2 meetings with regulatory authorities to discuss future clinical development plans
- Gather additional insights from SPD489-205, a double-blind, placebo-controlled trial of VYVANSE in inadequate response in MDD focused on cognitive dysfunction

VYVANSE New Uses Update

Conclusions

- Supports hypothesis of dopamine-modulating effects in MDD
 - VYVANSE appears able to deliver improvement in common residual depressive symptoms
- Adverse event profile of VYVANSE in augmentation of anti-depressants similar to known adverse event profile in the treatment of ADHD
- Await data and interpretation from other signal finding studies
 - Negative Symptoms in Schizophrenia (actively enrolling)
 - Inadequate response in MDD with cognitive impairment (actively enrolling)
 - Wakefulness model (for Narcolepsy and Shift Work Sleep Disorder, data under analysis)
- Shire does not recommend use of VYVANSE in any medical condition other than ADHD.

Concluding remarks

Angus Russell
CEO



Our purpose

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

Delivering growth now and into the future

- Strong financial performance
 - Revenues up 31%
 - 2010 full year Non GAAP earnings per ADS of up to \$4.20
- Executing on our strategy
 - Delivering value to patients, physicians, & payors
 - Driving growth from our balanced portfolio
 - Progressing our pipeline
 - Increasing our global footprint
- Delivering sustainable growth
 - Well positioned to absorb industry macro challenges
 - Aspiration to grow sales in the mid-teens range on average between 2009 and 2015

Questions and Answers



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APPENDIX



Our purpose

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Future key events next 18 months

- VYVANSE
 - Brazil - Launch for treatment of ADHD in pediatrics
 - Data from Ph 2 proof-of-concept trial for treatment of negative symptoms associated with schizophrenia
 - Discuss with regulatory authorities clinical development program in major depressive disorder
- INTUNIV
 - Approval and launch of co-administration with stimulants
- LIALDA - approval and launch for maintenance of remission in the US
- CarrierWave pain program - Initiation of formal Ph 1 clinical program
- CarrierWave guanfacine – Ph 1 program update
- SPD 535 – initiation of Ph 2 proof-of-concept clinical trials
- FIRAZYR
 - Complete Response filed to FDA
 - Self-admin label in EU
 - US launch
- Lexington manufacturing plant validation and submission and potential approvals

2010 Q3 Performance summary

	Q3 2010 \$m	Q3 2009 \$m	Reported Growth	Like for Like Growth ⁽²⁾
Total Revenues	874	667	+31%	+34%
EBITDA ⁽¹⁾	320	157	+104%	+108%
EPS - ADS ⁽¹⁾	\$1.16	\$0.49	+138%	
Cash generation ⁽¹⁾	271	220	+23%	

(1) These are Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalent used to calculate these measures.

(2) 'Like for Like Growth' excludes movements in exchange rates by applying 2009 exchange rates to 2010 results.

2010 Q3 Portfolio Strength and Diversity – Core product sales

	Q3 2010 \$m	Q3 2009 \$m	Reported Growth	Like for Like Growth ⁽²⁾
VYVANSE	151	129	+17%	+17%
ELAPRASE	97	91	+7%	+11%
REPLAGAL	92	48	+91%	+103%
LIALDA / MEZAVANT	76	65	+16%	+17%
PENTASA	57	51	+11%	+11%
VPRIV	50	-	n/a	n/a
FOSRENOL	45	48	-5%	-1%
INTUNIV	37	-	n/a	n/a
FIRAZYR	3	2	+61%	+73%
OTHER	86	98	-11%	-8%
CORE PRODUCT SALES ⁽¹⁾	694	532	+31%	+34%

(1) Core product sales represent Shire's product sales excluding ADDERALL XR.

(2) 'Like for Like Growth' excludes movements in exchange rates by applying 2009 exchange rates to 2010 results.

2010 Q3 Key financial ratios

FINANCIAL RATIOS	Q3 2010	y-o-y Growth	Q3 2009	y-o-y Growth
Product sales	\$794m	32%	\$603m	-15%
Gross margin	87%		84%	
R&D	19%	3%	24%	23%
SG&A	38%	13%	44%	-6%
EBITDA ⁽¹⁾ (% of product sales)	30%		15%	
EBITDA ⁽²⁾ (% total revenue)	37%		23%	
% of core product sales				
Core product sales	\$694m	31%	\$532m	20%
R&D	21%		27%	
SG&A	44%		50%	

(1) Excluding royalties and other revenues.

(2) Including royalties and other revenues.

This slide contains Non GAAP financial measures. See appendix for a list of items excluded from the US GAAP equivalent used to calculate these measures.

2010 Emerging shape of Shire income statement

	2009 Q1	2009 Q2	2009 Q3	2009 Q4	2009 FY	2010 Q1	2010 Q2	2010 Q3	FY 2010 Dynamics	
									Direction V. FY 09	Explanations
Core product sales	\$459m	\$491m	\$532m	\$585m	\$2,067m	\$626m	\$684m	\$694m	↑	<ul style="list-style-type: none"> Continued strong growth, against strengthening comparatives REPLAGAL year on year growth moderating
versus prior year	+24%	+20%	+20%	+36%	+25%	+36%	+39%	+31%		
Total product sales	\$756m	\$558m	\$603m	\$777m	\$2,694m	\$718m	\$764m	\$794m	↑	Core product growth > AXR decline
versus prior year	+20%	-21%	-15%	+10%	-2%	-5%	+37%	+32%		
Royalties	\$51m	\$67m	\$60m	\$115m	\$293m	\$95m	\$83m	\$77m	↑	AXR royalties offset declines in other royalties
versus prior year	-22%	+3%	-1%	+109%	+19%	+88%	+24%	+27%		
Gross margin ^{(1) (2)}	89%	84%	84%	87%	86%	87%	86%	87%	=	
R&D ⁽²⁾	\$117m	\$118m	\$144m	\$144m	\$523m	\$127m	\$143m	\$149m	↑	<ul style="list-style-type: none"> Continued operating leverage Increasing investment behind long term growth Marginally above 10% year on year growth
versus prior year	+\$9m	-\$9m	+\$27m	+\$21m	+\$48m	+\$10m	+\$25m	+\$5m		
SG&A ⁽²⁾	\$271m	\$285m	\$267m	\$315m	\$1,138m	\$309m	\$304m	\$302m		
versus prior year	-\$27m	-\$14m	-\$16m	+\$26m	-\$31m	+\$37m	+\$19m	+\$35m		
Tax Rate ⁽²⁾	24%	2%	33%	31%	25%	26%	25%	24%	=	

(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.

2010 Emerging shape of Shire income statement

- Normalised Medicaid Rebate

	2009	2009	2009	2009	2009	2010	2010	2010	FY 2010 Dynamics	
	Q1	Q2	Q3	Q4	FY	Q1	Q2	Q3	Direction V. FY 09	Explanations
Core product sales	\$459m	\$491m	\$532m	\$585m	\$2,067m	\$626m	\$684m	\$694m	↑	<ul style="list-style-type: none"> Continued strong growth, against strengthening comparatives REPLAGAL year on year growth moderating
versus prior year	+24%	+20%	+20%	+36%	+25%	+36%	+39%	+31%		
<i>Total product sales</i>	<i>\$793m</i>	<i>\$557m</i>	<i>\$641m</i>	<i>\$703m</i>	\$2,694m	\$718m	\$764m	\$794m	↑	Core product growth > AXR decline
<i>versus prior year</i>	<i>+26%</i>	<i>-21%</i>	<i>-10%</i>	<i>+0%</i>	-2%	<i>-9%</i>	<i>+37%</i>	+24%		
Royalties	\$51m	\$67m	\$60m	\$115m	\$293m	\$95m	\$83m	\$77m	↑	AXR royalties offset declines in other royalties
versus prior year	-22%	+3%	-1%	+109%	+19%	+88%	+24%	+27%		
<i>Gross margin</i> ^{(1) (2)}	<i>90%</i>	<i>84%</i>	<i>85%</i>	<i>86%</i>	86%	87%	86%	87%	=	
R&D ⁽²⁾	\$117m	\$118m	\$144m	\$144m	\$523m	\$127m	\$143m	\$149m	↑	<ul style="list-style-type: none"> Continued operating leverage Increasing investment behind long term growth
versus prior year	+\$9m	-\$9m	+\$27m	+\$21m	+\$48m	+\$10m	+\$25m	+\$5m		
SG&A ⁽²⁾	\$271m	\$285m	\$267m	\$315m	\$1,138m	\$309m	\$304m	\$302m	↑	Marginally above 10% year on year growth
versus prior year	-\$27m	-\$14m	-\$16m	+\$26m	-\$31m	+\$37m	+\$19m	+\$35m		
Tax Rate ⁽²⁾	24%	2%	33%	31%	25%	26%	25%	24%	=	

(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.

2010 Q3 Royalties

	Q3 2010 \$m	Q3 2009 \$m	Reported Growth
3TC and ZEFFIX	41	42	-3%
ADDERALL XR	18	2	+718%
REMINYL	11	12	-8%
Other	7	4	+75%
Total Royalties	77	60	+27%

2010 Q3 Cash generation reconciliation

	Q3 2010 \$m	Q3 2009 \$m
Net cash provided by operating activities	142	134
Tax and interest payments (net)	84	86
Payments for acquired and in-licensed products	45	-
Non GAAP cash generation	271	220

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, and fair value adjustments on contingent consideration and acquired inventory; and
- Costs associated with the integration of companies.

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.