







### R&D Seminar: Late-stage Pipeline Review

3 December 2012

Sir Andrew Witty Dr Moncef Slaoui Dr Patrick Vallance Strategy to maximise growth and returns to shareholders

Grow a diversified global business

Deliver more products of value

Simplify the operating model

### Reshaped R&D to deliver sustainable new revenue contributions

Grow a diversified global business

Deliver more products of value

Simplify the operating model

Re-engineered drug discovery organisation

Built late stage pipeline while improving efficiency

Enhanced returns on R&D investment

Restructured commercial & manufacturing to support the pipeline

# Sustainable pipeline with potential for around 15 launches in the next three years

Wave 1: 2011-2012 Wave 2: 2013-2014 Wave 3<sup>+</sup>: 2015+ ~ 50 clinical NMEs 15 PhIII data 1 ready to file 14\*PhIII data, 2 approved 3 filed 8 commit to 3 to file PhIII decisions

<sup>\*</sup> Includes some assets from Wave 1

Disciplined allocation of capital in R&D and Commercial for success

#### R&D

Returns driven investments behind generation of global, evidence rich data packages in R&D

# Commercial Capability

Returns driven global allocation of selling and promotional resource behind our key assets

### A new phase of significant launch potential requiring a different commercial model

Mix of geographic opportunities changing

US remains key

Europe more fragmented

EMAP and Japan more important

Use global evidence

Maximise quality of data packages for launch

Restructure commercial organisation

Share of voice reduced importance

Need strong evidence base

#### Recent launch history







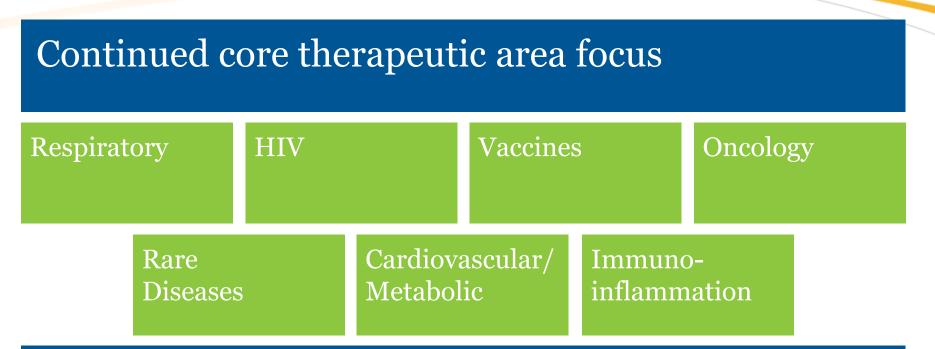








#### Focused on R&D value creation



Allocating capital to maximise returns

Flexible on monetising assets

#### R&D Journey Video

Available to view on www.gsk.com



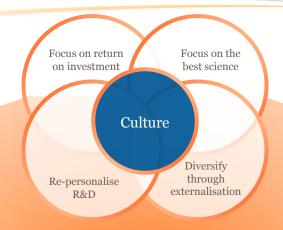






#### Dr Moncef Slaoui Chairman of R&D

#### Transforming R&D - How did we do it?



Disciplined decision making

Focus on Culture

Enhanced focus on evidence generation

### Unprecedented progress of the late stage pipeline in 2012

new vaccines (Nimenrix, Menhibrix, QIV) 1 launched,1 to launch,1 filed

new indications approved (Promacta Hep C, Votrient aSTS)

1 launched,1 to launch

- new drugs filed (Relvar /Breo\*, dabrafenib, trametinib)
- to file around end 2012 (albiglutide, UMEC/VI\*\*, dolutegravir)
- new phase III starts
  (dabrafenib / trametinib combination,
  sirukumab, mepolizumab)

<sup>\*</sup> Relvar/Breo is the proposed trade name for fluticasone furoate/vilanterol; \*\*UMEC/VI is umeclidinium/vilanterol

### We will apply the learnings from R&D to support Global launches



### Disciplined decision making

Focussed launch strategy

Allocation of investment

Franchise model

### Focus on Culture

Individual accountability

Leadership

Consistency of approach

Key talent

#### Enhanced focus on evidence generation

Global evidence
Data for key markets
(not just US, EU)

Our Wave 1 portfolio will be launched into both primary care and specialist therapeutic areas

#### Assets

Highly prevalent disease areas

Unmet need

Differentiated profile

### Expertise

Launching into therapy areas we know and where we have capability

# Therapy Area Reviews: Focus on 6 assets which completed Phase III in 2012

Oncology

Diabetes

HIV

Respiratory

dabrafenib
trametinib

UMEC/VI\*\*

<sup>\*</sup> Relvar/Breo is the proposed tradename for fluticasone furoate/vilanterol

<sup>\*\*</sup> umeclidinium/vilanterol

#### Patient Video

Available to view on www.gsk.com







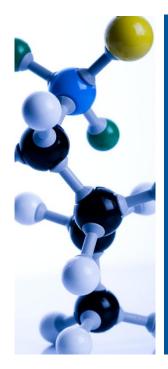


### Oncology

BRAF inhibitor - dabrafenib MEK inhibitor - trametinib

Dr Moncef Slaoui

#### Focus on the best science



Precision medicine delivering targeted therapies to appropriate patients

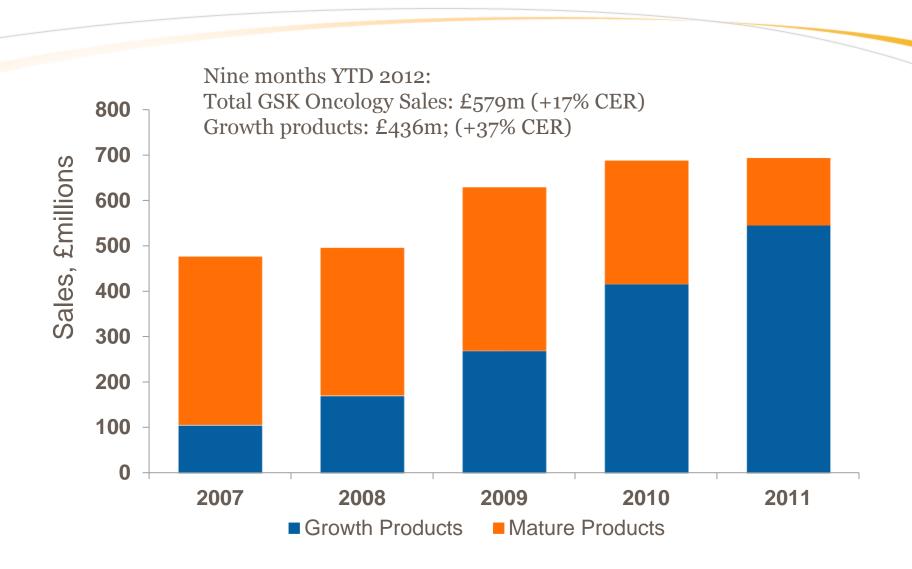




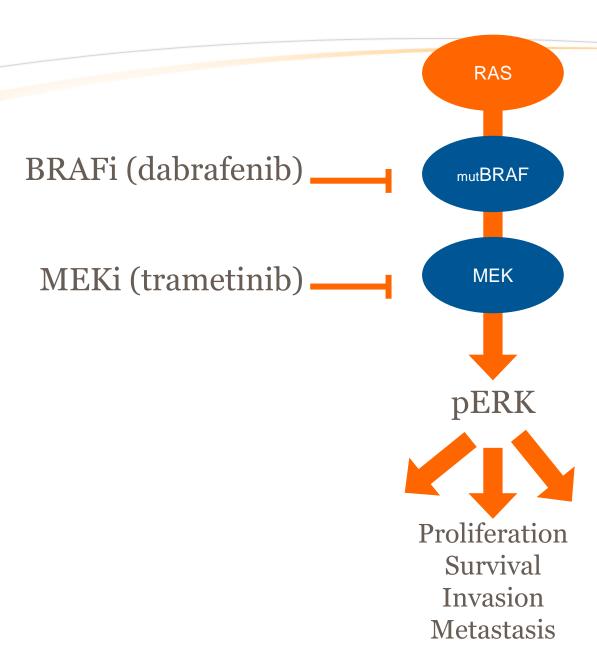




#### Innovation is the key driver of growth



#### Focus on interrupting tumour signalling pathways



#### Melanoma is the fastest growing cancer worldwide

#### Melanoma

**about 50%** of melanomas have a BRAF mutation

incidence rate has more than **doubled** since **1973**  people under the age of **45 years** account for **25%** of all melanoma cases

incidence is the highest in N. America, EU & Australia

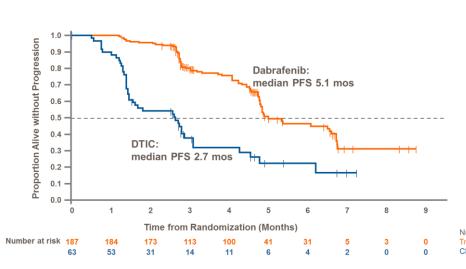
estimated
4-5000 new
cases of
metastatic
melanoma will
be diagnosed in
the US this year

until recently, no treatment proven to improve survival in advanced melanoma

#### Two highly active monotherapy agents

#### dabrafenib (BRAFi)

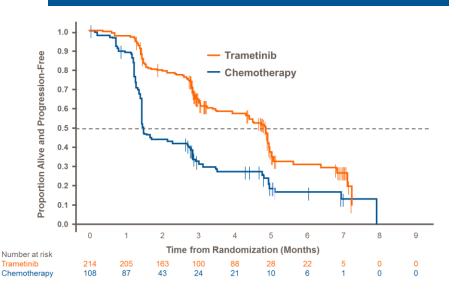
(70% reduction in risk of progression or death)



	dabrafenib N=187	Chemotherapy N=59
Median PFS	5.1 months	2.7 months
HR (95% CI) P-value	0.30 (0.18,0	0.51); <0.0001

#### trametinib (MEKi)

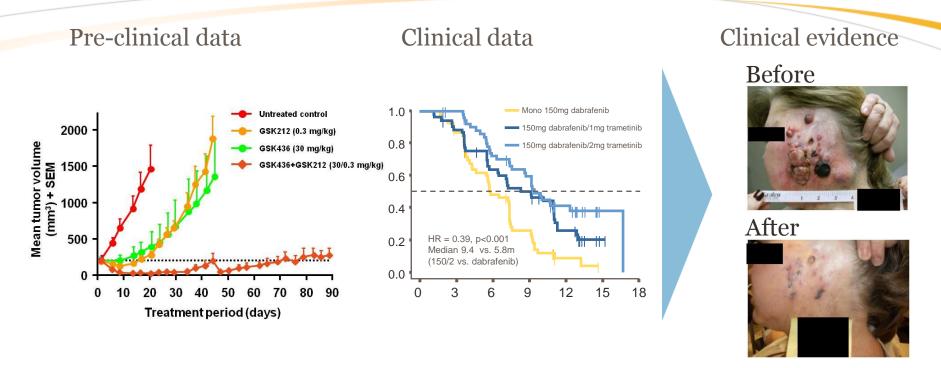
(55% reduction in risk of progression or death)



	trametinib N=214	Chemotherapy N=108	
Median PFS	4.8 months	1.5 months	
HR (95% CI) P-value	0.45 (0.33,	0.63); <0.0001	

The full data including the safety profiles of these investigational assets were presented at ASCO2012

#### Translating preclinical science into patient benefit with the combination of dabrafenib & trametinib



#### Goals of combination therapy

- more complete blockade of critical pathway
- prevent or delay emergence of resistance
- Phase III combination trials ongoing; Phase III adjuvant programme to commence imminently

Compared to dabrafenib monotherapy, **combination therapy** results in more fever/fever-related events & adverse events associated with MEK inhibition, such as peripheral oedema, hypertension, decreased ejection fraction and ocular events while reporting a lower incidence of BRAF inhibitor-associated skin effects

### Melanoma: targeted approach with dabrafenib & trametinib

High unmet need

Scientific advances & precision medicine

Fastest growing & highly competitive marketplace

Changing regulatory & payer environment

Deadly disease if not caught early

From "Untreatable Cancer" to potential medicines

Innovative and efficient development

Evidence-based value proposition









### Diabetes

GLP1 agonist - albiglutide

Dr Moncef Slaoui

#### Diabetes: an enormous public health burden

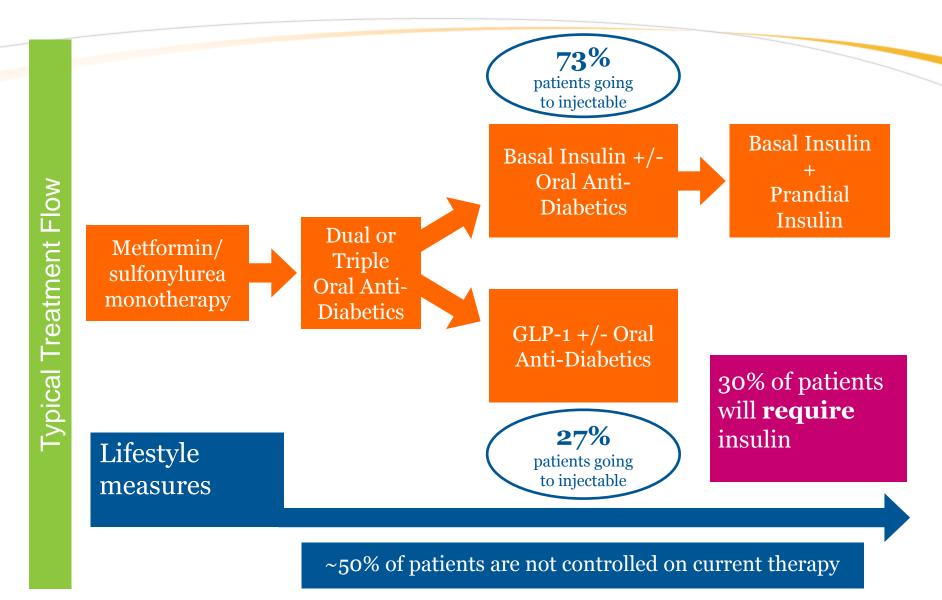
Factors include urbanisation, economic development, dietary changes & lack of physical activity

8% of adult population live with diabetes in developed markets (rising to 1:10 adults worldwide by 2030)

Incidence of Type 2 diabetes increasing at a rapid pace worldwide

By 2030, 7 of the top 10 countries with diabetes will be in Asia. India and China expected to be the largest diabetic-prevalent countries in the world

Diabetes is a chronic, progressive and generally irreversible condition; 30% of patients will end up on insulin therapy over time



#### The GLP-1RA class is forecast to grow

Current global market for diabetes is ~£26b including ~£1.3b for GLP-1RA class¹

GLP-1RA class has significant growth potential due to efficacy (reduction in HbA1c), modest weight loss & probable CV outcome

Professional acceptance of GLP-1RAs may increase with the availability of once-weekly injections, and the potential to delay insulin initiation

GLP-1RA use recommended earlier in disease progression in latest ADA/EASD guidelines (April 2012)

#### Albiglutide: the most comprehensive GLP1 clinical registration programme in Type 2 diabetes

24 studies, including 8 large pivotal PhIII studies with up to 3 years of treatment in ~6500 patients (HARMONY) & studied in combination with and vs. a range of active comparators

3 studies completed; overall registration package complete and supports filing around end of 2012

**Harmony 6:** albiglutide vs prandial insulin added on to insulin glargine; both produced clinically significant reductions in HbA1c from baseline; weight loss greater with albiglutide and maintained through 52 weeks

Harmony 7: liraglutide and albiglutide clinically and **statistically reduced HbA1c** from baseline; treatment difference did not meet non-inferiority criteria vs. liraglutide; nausea and vomiting lower with albiglutide and weight loss greater with liraglutide

Harmony 8: Clinically and statistically significant reductions in HbA1c and superiority versus sitagliptin in patients with severe renal impairment, weight loss greater with albiglutide

Safety profile supports filing; most common AEs were gastro-intestinal, hypoglycaemic events and injection site reactions

### Albiglutide profile is emerging, support plans to submit regulatory file around YE 2012

Superior to sitagliptin in renally impaired diabetic patients Opportunity to delay use of basal insulin and or avoid prandial insulin

24 studies, including 8 large pivotal studies with up to 3 years treatment in ~6500 patients (HARMONY) AE profile and GI tolerability profile supportive of potential sustained use, with no weight gain

First once weekly fully humanised GLP-1RA Administered in a pen device for reconstitution by the patient using a fine-gauge needle









#### HIV

Integrase Inhibitor - dolutegravir





#### Latest UNAIDS global estimates for HIV in 2011

34 million people living with HIV

2.5 million new HIV infections

1.7 million deaths due to AIDS

3.3 million of them are children

72% of those eligible for treatment do not have access

Overall, the number of people accessing HIV treatment increased by 63% from 2009 to 2011

24% fewer deaths than in 2005

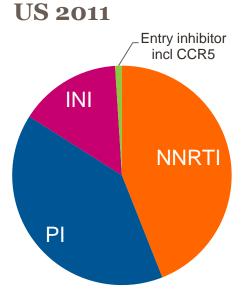
However, majority (1.2m) of deaths were in in Sub-Saharan Africa



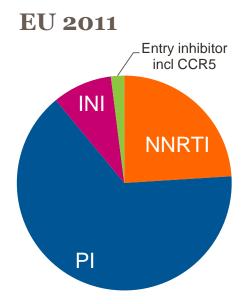


#### Current HIV Treatment Paradigm

- The majority of people on treatment receive a combination of three anti-retrovirals
- A backbone of 2 NRTIs + a third agent (NNRTI, PI, INI or CCR5 Inhibitor)
- Third agent choice varies according to patient characteristics and physician/patient preference



Source: Synovate patient monitor



Source: RP Therapy Watch patient monitor

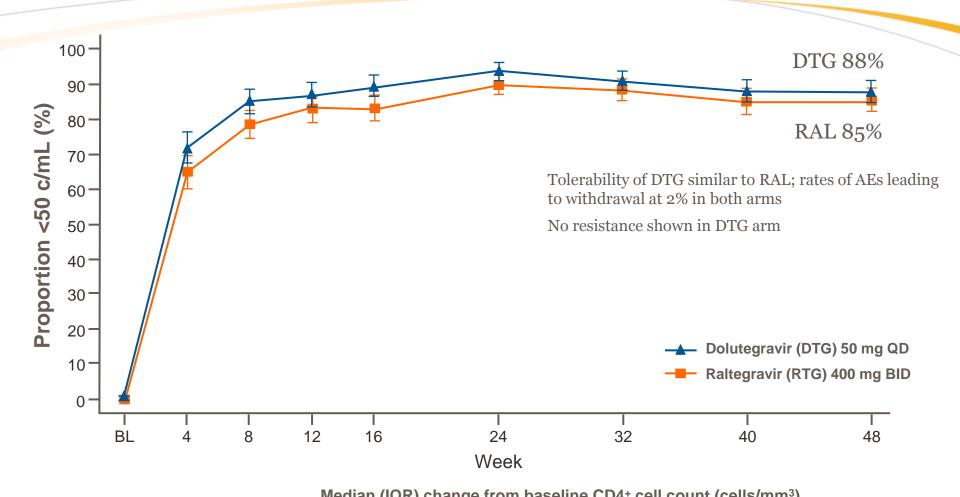
NRTI: Nucleoside Reverse Transcriptase Inhibitors , NNRTI: Non- Nucleoside Reverse Transcriptase Inhibitors, PI: Protease Inhibitors, INI: Integrase Inhibitors

#### Global HIV treatment trends

- Treatment is starting earlier at higher CD4+ T-cells counts
- Patients are aging and diversifying
- Naïve patients stay on therapy longer
- Trade-offs exist in the early or long-term with all 3rd agents **currently** used first line

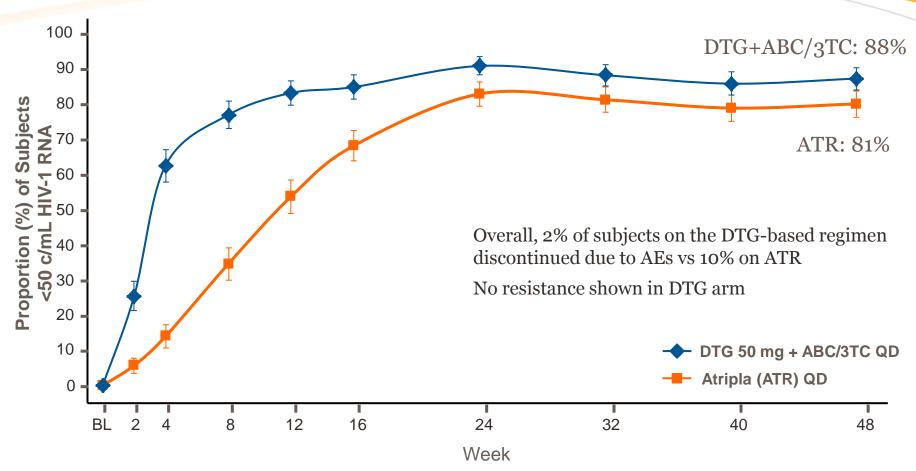


# Once-daily dolutegravir was non-inferior to twice-daily raltegravir over 48 weeks



median (learly change from baseline OD+ cen count (cens/inin )						1	
	W4		W24			W48	
DTG 50 mg QD	87	(26, 149)	183	(100, 295)		230	(128, 338)
RAL 400 mg BID	88	(32, 163)	182	(94, 296)		230	(139, 354)

# Dolutegravir 50mg +ABC/3TC QD was non-inferior & statistically superior to Atripla at Week 48



Subjects receiving DTG+ABC/3TC achieved virologic suppression faster than those receiving Atripla, median time to HIV RNA<50c/mL of 28 days (DTG+ABC/3TC) vs 84 days (Atripla), p<0.001

Full data on this investigational asset including safety data have been presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) 2012

# Pivotal phase 3 studies cover full spectrum of adults with HIV; support plans to submit regulatory file before YE 2012

	Study design	Results
SPRING <sup>2</sup>	Treatment naïve DTG 50mg OD vs. RAL 400mg BID	Non-inferior to RAL
SINGLE	Treatment naive DTG 50mg + ABC/3TC OD vs. Atripla	Superior to Atripla*
VIKING-3	Treatment experienced INI-resistant DTG 50mg BID	63% virologically suppressed at wk 24 3% discontinued due to AEs
	Treatment experienced, INI-naïve	Results in house
SAILING	DTG 50mg once daily	Presentation at future scientific meetings
FLAMINGO	Treatment naïve DTG 50mg OD vs DRV/r 800mg/100mg OD	Data expected in 2013 (not part of initial regulatory package)

<sup>\*</sup>The SINGLE study was designed to demonstrate non-inferiority of the dolutegravir-based regimen versus Atripla, and the primary analysis met this criterion. Statistical superiority was concluded as part of a subsequent, pre-specified testing procedure.







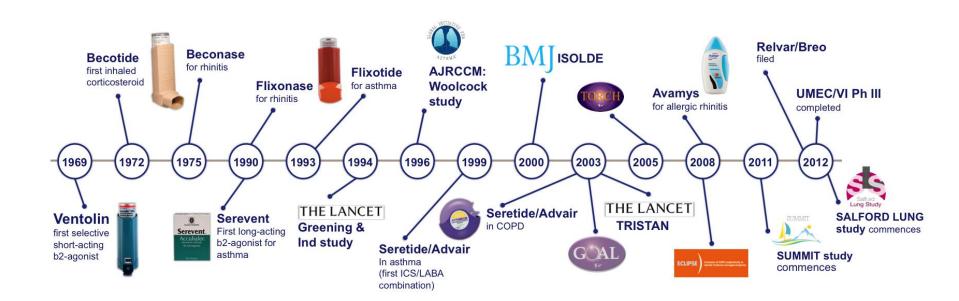


### Respiratory

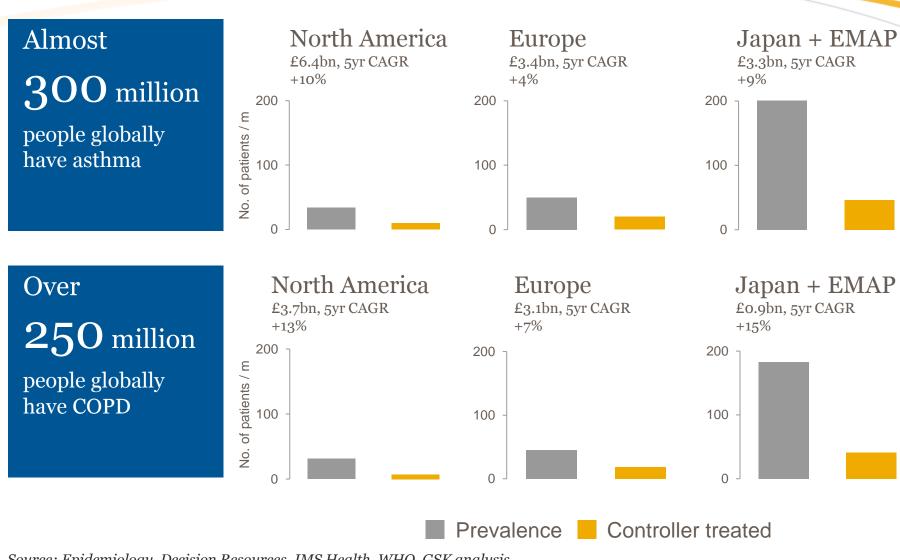
ICS/LABA – Relvar, Breo LAMA/LABA - UMEC/VI

Dr Patrick Vallance

### GSK's Respiratory heritage – the story so far



### Both Asthma and COPD have significant unmet need



 $Source: Epidemiology, Decision \ Resources, IMS\ Health, WHO, GSK\ analysis$ 

### Broad respiratory portfolio targets existing and new areas

	SABA	ICS	LABA	ICS/ LABA	LAMA	LAMA/ LABA	MABA	ICS/ LAMA	Anti- IL 5	р38	FLAP
<b>gsk</b> GlaxoSmithKline	<b>✓</b>	✓	✓	✓	<b>√</b>	<b>✓</b>	<b>√</b>	<b>✓</b>	<b>√</b>	✓	<b>√</b>
Company 1			✓	✓	✓	✓					
Company 2			✓		✓	✓					
Company 3			✓	✓	✓	✓	✓				
Company 4			✓	✓	✓	✓					
Company 5		✓	✓	✓	✓		✓		<b>✓</b>		
Company 6										<b>✓</b>	

£2.3bn: rescue£4.7bn: maintenance bronchodilator£7.8bn: ICS/LABA£0.6bn: biological severe asthma£2.7bn: steroid£2.9bn: oral asthma

Source: GSK R3 Model based on IMS Health MAT June 2012.

Includes marketed and development products for GSK and other companies

# Relvar/Breo extensive data package supported filings in asthma and COPD



Once daily FF well tolerated and efficacious at lower doses compared to FP

Addition of VI to FF significantly reduced risk of severe asthma exacerbations

Significantly greater improvements in lung function v FF or FP

FF/VI had generally similar safety profile to FF

FF/VI 100/25mcg significantly reduced annual rate of moderate & severe COPD exacerbations vs. VI alone

FF/VI 200/25mcg confers no additional benefit compared with FF/VI 100/25mcg in terms of reduced risk of COPD exacerbations

FF/VI 100/25mcg demonstrated superiority vs. Advair 250/50mcg in one of two studies

Overall rates of serious and fatal AEs were similar across 4treatment groups. The increase in risk of pneumonia with FF is consistent with previous studies of ICS in COPD. Pneumonia occurred approximately twice as often in the FF/VI groups than in the VI group.\*

2012 Filings	Asthma	COPD
US	Additional PhIII study ongoing	✓Breo 100/25mcg
EU & Japan	✓ Relvar 100/25mcg & 200/25mcg	√Relvar 100/25mcg

<sup>\*</sup>There were 6 cases of fatal pneumonia and one case of fatal COPD exacerbation with concurrent pneumonia in the FF/VI 200/25mcg group, all of which occurred in the HZC871 study and the majority of these cases were reported from one site; one case of fatal pneumonia occurred in the FF/VI 100/25 group of the HZC970 study. Full data on this investigational asset including safety data were presented at ERS2012

# Relvar/Breo - an innovative approach to evidence generation



- Relvar/Breo being studied in the COPD and asthma populations in Salford, England
- Unique pre-approval open-label controlled, minimum intervention trial to mimic real-world usage
- Paperless, fully integrated electronic records allowing capture of real time data to assess total impact on healthcare utilisation



- Study to Understand Mortality and MorbidITy in COPD
- Extensive global study of 16,000 patients to assess the potential for FF/VI to improve survival in those with COPD and a history of, or at risk from, cardiovascular disease
- Secondary objectives will evaluate the effect of FF/VI compared with placebo on the rate of decline in lung function, as well as on cardiovascular endpoints including cardiovascular death, heart attacks and strokes

## UMEC/VI profile is emerging, support plans to submit regulatory file before YE 2012

Global regulatory
filings to
commence from
end of 2012; data
supports UMEC
monotherapy
filings in 2013

Once daily
LAMA/LABA for
COPD;
potentially first in
class in the US

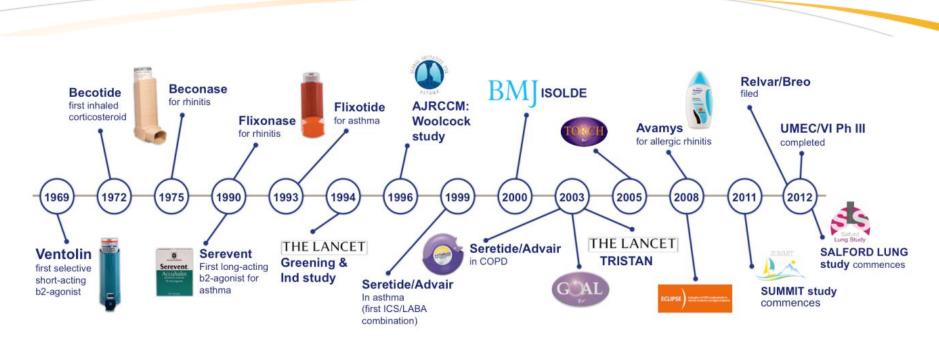
Global
development
programme,
programme,
provotal studies
investigating
62.5/25mcg &
125/25mcg doses
in ~6000 patients

Statistically significant improvements over placebo & individual components on trough FEV1

Incidence of CV events and all other serious AEs similar across all treatment groups

Administered in the investigational Ellipta device

#### We continue to progress our Respiratory portfolio



#### Advanced portfolio

LAMA mono - COPDLABA mono - COPDmepolizumab - asthmaMABA - COPDFF monotherapy (ICS) - asthmaLAMA / ICS - asthma









## Pipeline Sustainability

Dr Patrick Vallance

Re-engineered drug discovery delivers sustainable flow

#### Wave 1: 2011-2012

- 15 PhIII data
- **2** approved
- 3 filed
- $\overline{3}$  to file

#### Wave 1 delivered with accelerated cycle times

#### dabrafenib

Fastest cycle time for an NCE in history of GSK: Less than 5 years from CS to planned launch (vs. industry bench mark of 8.8 years)

#### trametinib

From FTIH to Ph III results in just over 3 years

#### **UMEC/VI**

Commit to Ph III to decision to file in 2 years

#### dolutegravir

FTIH to completion of registration programme in 5 years

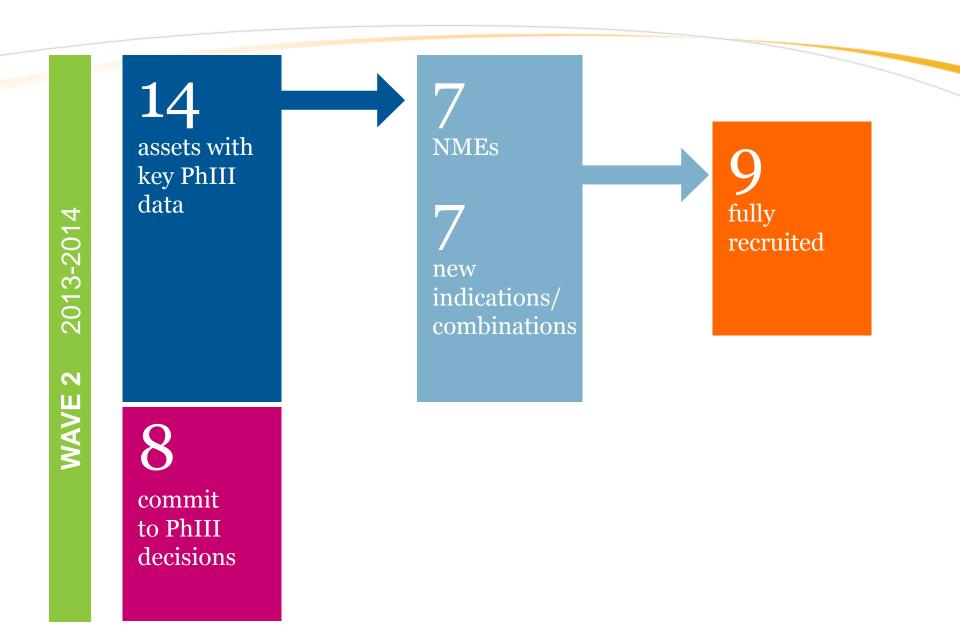
CS: Candidate selection; FTIH: First time in humans

### Re-engineered drug discovery delivers sustainable flow

### Wave 1: 2011-2012 Wave 2: 2013-2014 15 PhIII data 1 ready to file 14\*PhIII data, 2 approved 3 filed 8 commit to 3 to file PhIII decisions

<sup>\*</sup> Includes some assets from Wave 1

### Visibility of multiple waves of pipeline delivery



Wave 2: Key PhIII data delivery in 2013-2014

Respiratory	FF monotherapy (asthma) mepolizumab (severe asthma)
Oncology	Arzerra (CLL, DLBCL) MEK/BRAF combo (melanoma) Tykerb (H&N, gastric) Votrient (ovarian)
Vaccines	MAGE-A3* (therapeutic vaccines) Zoster* (shingles)
HIV	dolutegravir/Trii (HIV)
HIV Immuno- inflammation	dolutegravir/Trii (HIV)  Benlysta subcut (SLE) vercirnon (Crohn's)
Immuno-	Benlysta subcut (SLE)

<sup>\*</sup> Event driven

### Re-engineered drug discovery delivers sustainable flow

## Wave 1: 2011-2012

Wave 2: 2013-2014

Wave **3**<sup>+</sup>: **2015**+

 $\sim 50 \ {\rm clinical \ NMEs}$ 

1 ready to file

14\*PhIII data,

&

8 commit to PhIII decisions

15 PhIII data

2 approved

3 filed

3 to file

<sup>\*</sup> Includes some assets from Wave 1









## Thank you

Q&A

# Reference Guide to Wave 1 Key Clinical Data in 2012: Medical Conferences and Press Releases

#### **Oncology**

- Trametinib: METRIC phase III (ASCO)<sup>1,2</sup>
- Dabrafenib: Break 3 phase III (ASCO) 1,2

and-mek-inhibitors-dabrafenib-and-trametinib-at-asco.html

- Combination Trametinib/Dabrafenib phase II (ASCO, ESMO) 1,2,3
- Votrient: Comparz phase III H2H vs sunitinib (ESMO) 3,4
- 1: http://www.gsk.com/content/dam/gsk/globals/documents/pdf/ASCO-Investor-Meeting-June-2012.pdf 2: http://www.gsk.com/media/press-releases/2012/gsk-presents-positive-results-for-investigational-braf-
- 3: http://www.gsk.com/content/dam/gsk/globals/documents/pdf/Investors/presentations/2012/ESMO-number of the property of the content of the property of the p
- analyst-presentation-1-oct-2012.pdf
  4: http://www.gsk.com/media/press-releases/2012/head-to-head-study-of-gsks-votrient---pazopanib--vs-
- sunitinib-in.html

#### **Diabetes**

- Albiglutide: Harmony 6 phase III add on to insulin glargine (ADA, EASD)<sup>1,2,3</sup>
- Albiglutide: Harmony 7 phase III H2H vs liraglutide (ADA)<sup>2,3</sup>
- Albiglutide: Harmony 8 phase III renal impairment 4
- 1: http://www.gsk.com/media/press-releases/2012/gsk-receives-further-data-from-phase-III-studies-of-albiqlutide-in-type-2-diabetes.html
- 2: http://www.gsk.com/content/dam/gsk/globals/documents/pdf/ADA-Investor-Meeting-June-2012.pdf 3: http://www.gsk.com/media/press-releases/2012/gsk-announces-new-52-week-data-from-phase-iii-study-of-once-weekly-albiglutide-in-type-2-diabetes.html
- 4: http://www.gsk.com/media/press-releases/2012/gsk-announces-positive-data-from-harmony-8-and-completion-of-clinical-registration-package-for-albiglutide-in-type-2-diabetes.html

#### HIV

- Dolutegravir: Spring 2 phase III vs raltegravir (IAC)<sup>1,3,4</sup>
- Dolutegravir: SINGLE phase III vs Atripla (ICAAC)<sup>2,4</sup>
- Dolutegravir: VIKING-3 phase III integrase resistant (HIV-11)<sup>5</sup>
- 1: http://www.gsk.com/media/press-releases/2012/shionogi-viiv-healthcare-announces-initial-data-from-pivotal-phase-iii-study-of-dolutegravir-in-hiv.html
- 2: http://www.gsk.com/media/press-releases/2012/shionogi-viiv-healthcare-announces-positive-initial-data-from-phase-iii-study-of-dolutegravir-based-regimen-vs-atripla-in-hiv.html
- $3.\ http://www.gsk.com/media/press-releases/2012/once-daily-dolutegravir-is-non-inferior-to-twice-daily-raltegrav.html$
- 4: http://www.gsk.com/content/dam/gsk/globals/documents/pdf/media/presentations/ViiV-Presentation-27-July-2012.pdf
- 5: http://www.gsk.com/media/press-releases/2012/ViiV-healthcare-presents-phase-III-data-from-viking-3-study-dolutegravir-hiv-infected-integrase-inhibitor-resistant-adults.html

#### Respiratory

- Relvar/Breo: Asthma phase III exacerbation and FEV-1(ERS)<sup>1,3</sup>
- Relvar/Breo: COPD phase III exacerbation and FEV-1 (ERS)<sup>3</sup>
- LAMA/LABA: Headline results from four phase III trials <sup>2</sup>
- Umeclidinium: Phase II dose ranging (ERS, CHEST)<sup>3,4</sup>
- Mepolizumab (Wave 2): DREAM phase II (ERS)<sup>3</sup>
- 1: http://www.gsk.com/media/press-releases/2012/gsk-and-theravance-announce-completion-of-the-relovair-registrational-programme-and-topline-results-from-relovair-vs-advair-phase-iii-studies-incord html
- 2: http://www.gsk.com/media/press-releases/2012/gsk-and-theravance-announce-positive-results-from-four-pivotal-phase-iii-studies-for-once-daily-lamalaba-umecvi-in-copd.html
- 3: http://www.gsk.com/content/dam/gsk/globals/documents/pdf/media/presentations/GSK-Analyst-meeting-ERS-Sept-2012.pdf
- 4: Presented at CHEST 2012. Oct 20-25, 2012. Poster No 2076

# CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this document, are subject to risks and uncertainties that may cause actual results to differ materially from those projected.

Factors that may affect GSK's operations are described under 'Risk factors' in the 'Financial review & risk' section in the company's Annual Report 2011 included as exhibit 15.2 to the company's Annual Report on Form 20-F for 2011.

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