Innovative Pipeline

Sir Andrew Witty

3 November 2015

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This presentation contains forward-looking statements. Forward-looking statements give the Group's current expectations or forecasts of future events. An investor can identify these statements by the fact that they do not relate strictly to historical or current facts. They use words such as 'anticipate', 'estimate', 'expect', 'intend', 'will', 'project', 'plan', 'believe', 'target' and other words and terms of similar meaning in connection with any discussion of future development, operating or financial performance. In particular, these include statements relating to future actions, prospective products or product approvals, future performance or results of current and anticipated products, sales efforts, expenses, the outcome of contingencies such as legal proceedings, and financial results.

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Innovation is critical to maximising the potential of GSK in the current environment

Pharmaceuticals
Vaccines
Consumer

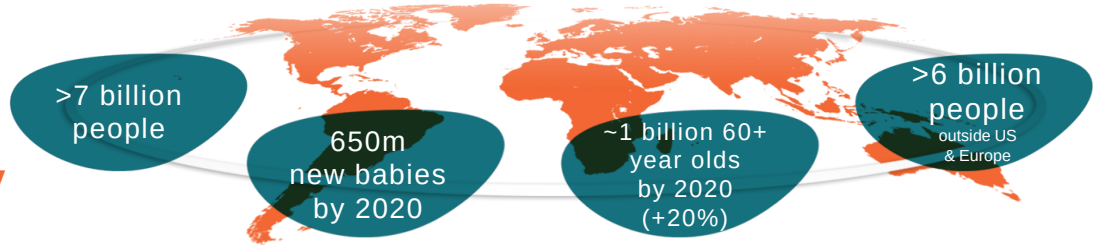
Future R&D innovation

+

Broad portfolio offering

Global footprint + regulatory and quality competence

Clear volume opportunity



But pricing environment uncertain

R&D Strategy: Reliable fill & flow with greater novelty and improved return on investment

Accelerate Discovery output

- Now have 30 DPUs, of which two thirds are from the original 2009 set. Average 20% turnover every 3 year cycle
- 65% of NMEs* in the clinic were either discovered or worked on by the DPUs
- Average of 60-65 publications annually in world class journals across pharma and vaccines

Focus where science is innovative

- Of the ~40 assets profiled today, 80% of new molecules, biologicals and vaccines are potentially 1st in class
- Almost 50% of clinical stage NMEs* are biopharm, CGT, or oligos. i.e. non-traditional white pill
- Competitive advantage through epigenetics, cell & gene technology, adjuvants, self amplifying RNA, inhaled technology, chimp adenovector

Improve balance internal vs external

- 60% of NMEs* in the clinic are home-grown, 40% partnered or in-licensed
- >1,500 collaborations inclusive of academic, public-private partnerships, biotech and pharma

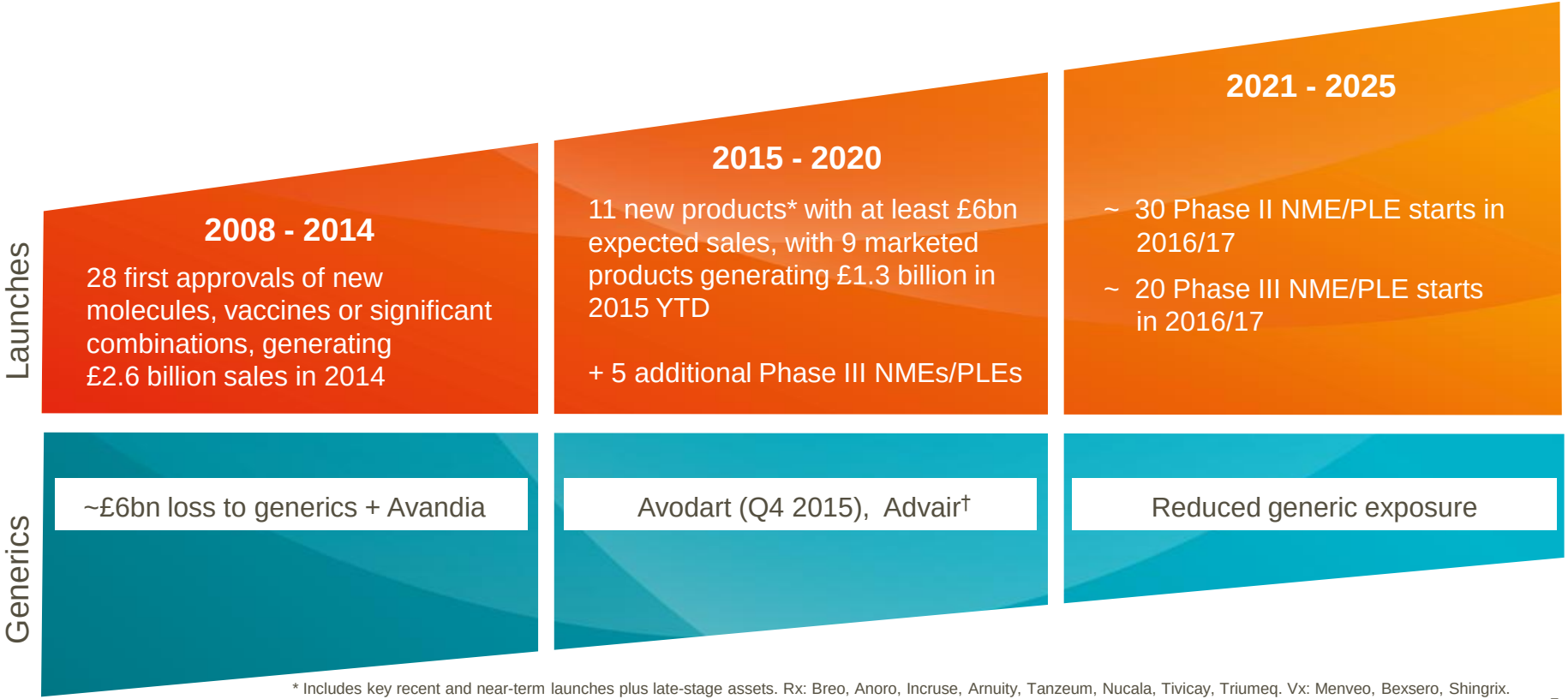
Reduce fixed cost and improve ROI

- 20% faster study execution times^
- Pharma R&D headcount reduced from 12,000 to 8,500 since 2008, reduced to 2 global pharma R&D hubs
- Balance discovery and development (pharma split 38% Discovery; 62% Development)
- Divested marketed oncology portfolio for $16bn

To deliver multiple launches per year

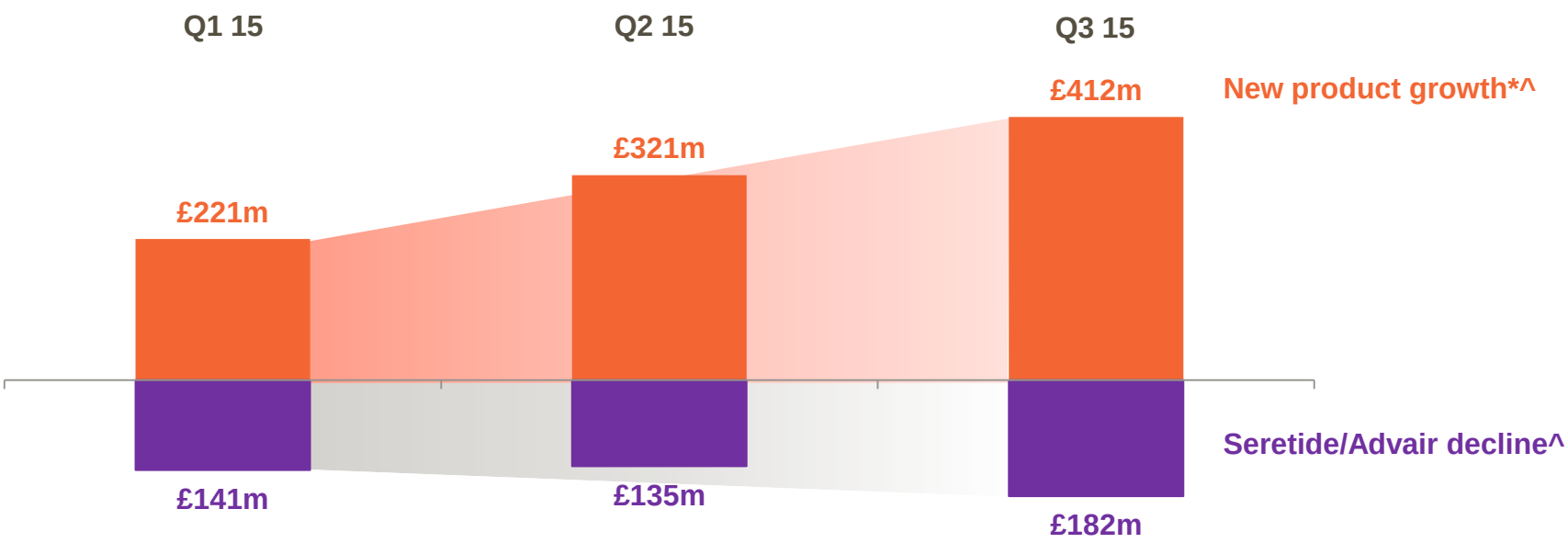
*NMEs: Phase I – III/submitted, per pipeline chart; † Pipeline = Phase I-III/submitted; ^ comparison vs peers based on CMR data.

New product contribution increasing as generic exposure reduces



* Includes key recent and near-term launches plus late-stage assets. Rx: Breo, Anoro, Incruse, Arnuity, Tanzeum, Nucala, Tivicay, Triumeq. Vx: Menveo, Bexsero, Shingrix.
† A number of assets in the portfolio will face generic competition in this time frame, the most significant of which is Advair PLE= New formulations or combinations

New product growth more than offsets Advair decline



* New products defined as: Rx: Breo, Anoro, Incruse, Arnuity, Tanzeum, Tivicay, Triumeq. Vx: Menveo, Bexsero
^ Growth and decline in the respective quarters on a Sterling basis

Assets profiled at R&D day by planned filing date

2014 to 2017: 7 NMEs & 5 PLEs

Nucala (mepolizumab) *IL-5 mAb* **Severe Asthma**	sirukumab *IL-6 mAb* **Rheumatoid Arthritis**
mepolizumab *IL-5 mAb* **COPD**	GSK2696273 *Ex-vivo stem CGT* **ADA-SCID**
mepolizumab *IL-5 mAb* **EGPA**	GSK2696274 *Ex-vivo stem CGT* **Metachromatic Leukodystrophy**
fluticasone furoate+vilanterol +umeclidinium *ICS/LABA/LAMA* **COPD**	GSK2696275 *Ex-vivo stem CGT* **Wiscott-Aldrich Syndrome**
dolutegravir + rilpivirine *Integrase inhibitor + NNRTI* **HIV**	GSK2998728† *TTR production inhibitor* **FAP**
Benlysta Subcutaneous *BLyS mAb* **SLE**	Shingrix **Herpes Zoster prophylaxis**

2018 to 2020: 11 NMEs & 5 PLEs

mepolizumab *IL-5 mAb* **Nasal Polyposis**	tarextumab† *Notch 2/3 mAb* **Pancreatic Cancer, SCLC**	GSK2398852+ GSK2315698 *SAP mAb + SAP depleter* **Amyloidosis**
mepolizumab *IL-5 mAb* **HES**	GSK525762 *BET inhibitor* **Solid Tumours, Haematological Malignancies**	GSK2998728† *TTR production inhibitor* **TTR Cardiomyopathy**
dolutegravir + lamivudine FDC *Integrase inhibitor+NRTI* **HIV**	GSK2879552 *LSD1 inhibitor* **Acute Myeloid Leukaemia, SCLC**	daprodustat* *Prolyl hydroxylase inhibitor* **Anaemia of CKD**
cabotegravir *Long acting integrase inhibitor* **HIV, HIV PrEP**	GSK3174998 *OX40 agonist mAb* **Solid tumours, Haematological Malignancies**	MenABCWY US filing **Meningococcal A,B,C,W and Y disease prophylaxis**
gepotidacin *Type 2 topoisomerase inhibitor* **Bacterial Inf.**	GSK3377794† # *NY-ESO-1 TCR* **Sarcoma, Mult. Myel., Melanoma Ovarian, NSCLC**	
sirukumab *IL-6 mAb* **Giant Cell Arteritis**	GSK3359609 *ICOS agonist mAb* **Solid tumours, Haematological Malignancies**	

2021 to 2025: 21 NMEs & 5 PLEs

sirukumab *IL-6 mAb* **Severe Asthma**	GSK3008348 *Alpha V beta 6 integrin antagonist* **IPF**	GSK525762 *BET inhibitor* **Therapy Resistant RA**	GSK3196165 *GM-CSF mAb* **RA, OA**	RSV paediatric **Respiratory syncytial virus prophylaxis**
danirixin *CXCR2 antagonist* **COPD**	*Long acting IL-5 mAb (NBE)* **Asthma, Others**	GSK2330811 *OSM mAb* **Systemic Sclerosis**	GSK2696277†^ *Ex-vivo stem CGT* **Beta Thalassemia**	COPD ◊ **COPD vaccine**
GSK2269557 *PI3 kinase delta inhibitor* **COPD, Asthma**	*IL5/13 bispecific antibody* **Asthma**	GSK2618960 *IL-7 receptor mAb* **Sjogren's Syndrome**	daprodustat* *Prolyl hydroxylase inhibitor (topical)* **Wound Healing**	
GSK2862277 *TNFR1 dAb* **Acute Lung Injury**	GSK2878175 *NS5B inhibitor* **HCV**	GSK2831781 *LAG-3 mAb* **Autoimmune Diseases**	mepolizumab *IL-5 mAb* **Severe Atopic Dermatitis**	
GSK2245035 *TLR7 agonist* **Asthma**	GSK3228836† *Antisense oligonucleotide* **HBV**	GSK2982772 *RIP1 kinase inhibitor* **Psoriasis, RA, UC**	RSV maternal **Respiratory syncytial virus prophylaxis**	
GSK3191812 *TSLP dAb* **Asthma**	belimumab + CD20 *BLyS+CD20* **Sjogren's Syndrome**	GSK3050002 *CCL20 mAb* **Psoriatic Arthritis**	GBS maternal **Group B streptococcus prophylaxis**	

- Respiratory
- HIV / Infectious Diseases
- Immuno-Inflammation
- Oncology
- Rare Diseases
- Other Pharma
- Vaccines

† Subject to exercise of option
# Subject to collaborator agreement
^ EU filing
* USAN, INN approval pending
◊ Planned to be filed post 2025

See www.gsk.com for full clinical pipeline

Focus on delivering innovative and sustainable presence in 6 key areas

Focus for today: Innovation to deliver products of value

Patrick Vallance
President, Pharmaceuticals R&D

Moncef Slaoui
Chairman of Vaccines

Patrick Vallance

President, Pharmaceuticals R&D

GSK R&D: what is important to us

Innovative science

- Average of 35 publications annually in worlds-class journals (Nature, Cell, Science)
- In 2014 and 2015 to date, GSK scientists listed as co-authors in more than 1,600 publications
- 80% of pre-clinical to Phase II assets have a novel mechanism of action
- Target sciences initiative with EBI/Sanger & Altius Institute in Seattle

Patient need

- 5 *Breakthrough Designations* since 2013
- 3 FDA *Priority Reviews* since 2010
- Focus on preventative and curative medicines
- Strong focus on patient input
- Quality of life study endpoints

Quality

GSK achieved highest number of FDA approvals, 2010-15 **14**

- All first cycle approvals since 2012
- 10% faster in time to file approval than industry average
- Clinical study cycle times 20% faster than average
- Cost per patient visit 30% less than 2008
- Molecule quality focus

Partnership

Collaborations with academia, biotechs, pharmaceutical companies and regulators

Recruiting and developing the best scientists

We're committed to ensuring GSK remains the best place to develop medicines

World-class leaders

External talent sourcing

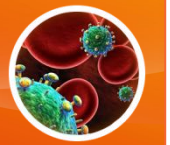
Scientific career pathways

Expert advisory networks

HIV / Infectious Diseases

Infectious disease burden continues to grow and present public health challenges

HIV



- 36.9m living with HIV worldwide; 1.2m deaths & 2m new infections annually[1]
- Resistance, adherence and addressing long-term toxicities remain areas of significant unmet medical need
- The ultimate goal is remission and cure

HBV

- Globally, 240m people have Chronic Hepatitis B[1]
- More than 780k people die each year
- HBV evades immune system, with limited options for durable remission

HCV

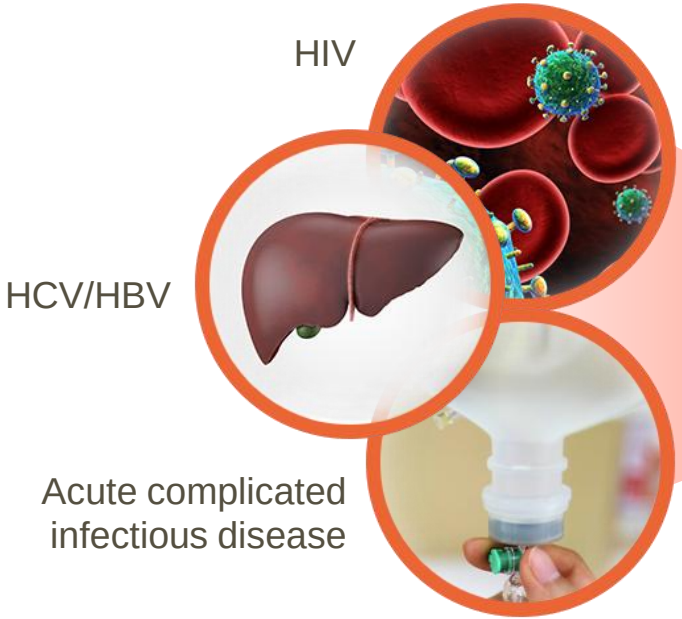
- Globally, 130-150m people have Chronic Hepatitis C[1]
- 350-500k people die each year
- Need for a cure completed in a single visit

Acute complicated infectious diseases

- Globally, ~3.5m annual deaths due to lower respiratory tract infections[2]
- Increasing antimicrobial drug resistance (MDR)
- Hospitalised infections & complications have direct costs >$35bn annually in US[3]
- Pathophysiology & tissue damage suggest aberrant host immune responses as key driver

[1] WHO 2015; [2] WHO 2014; [3] J Med Econ 2013

Infectious Diseases strategy: from innovative treatment regimens to the pursuit of cure



GSK Pipeline

- Innovative Treatment Regimens
- Long-acting Treatment
- Prevention
- Remission & Cure

Dolutegravir set to be at the heart of future treatment regimens

Dolutegravir profile

Efficacy

- Rapid and sustained viral load drop

Barrier to Resistance

- No resistance mutations selected in first line failures (one patient had E157Q/P mutation without decreased susceptibility to dolutegravir)
- Limited resistance mutation evolution in experienced patients on failure
- Distinct resistance profile compared to other INIs (RAL, EVG)

Favorable PK Profile

- Booster free
- No food requirement for adequate exposure

Well tolerated

DTG/3TC: Planned launch H1 2019

2-drug STR for HIV treatment in naïve and suppressed patients, QD
Simplification - Potential benefit on tolerability and drug burden
No food requirements

DTG/RPV: Planned launch H1 2018

2-drug STR for HIV treatment in suppressed patients, QD
Simplification - Potential benefit on tolerability and drug burden
(ViiV Healthcare - Janssen sponsored)

Triumeq™ (abacavir/dolutegravir/lamivudine): Launched **2014**

3-drug STR for HIV treatment, QD
Only currently available DTG containing Single Tablet Regimen (STR)

Tivicay™ (dolutegravir): Launched **2013**

For HIV treatment in combination with other ART, QD

Approved Investigational

ViiV Healthcare is a specialist joint venture solely dedicated to HIV, owned by GSK, Pfizer and Shionogi

PADDLE (Pilot Antiretroviral Design with Dolutegravir and LamivudinE): Investigator sponsored study design

- Investigator sponsored study
- 2 tablet treatment
- ARV naive patients
- 2 cohort study
- Open label single arm

Phase IV, pilot, open-label, single arm exploratory trial

1st cohort (n= 10)

DTG 50 mg QD
LMV 300 mg QD

2nd cohort (n= 10)

DTG 50 mg QD
LMV 300 mg QD

Patient #	Base line viral load	Week 8	Week 24
1	10.909	< 50	< 50
2	10.233	< 50	< 50
3	151.569	< 50	< 50
4	148.370	< 50	< 50
5	20.544	< 50	< 50
6	14.499	< 50	< 50
7	18.597	< 50	< 50
8	24.368	< 50	< 50
9	10.832	< 50	< 50
10	7.978	< 50	< 50
11	273.676	< 50	< 50
12	64.103	< 50	< 50
13	33.829	< 50	< 50
14	15.151	< 50	< 50
15	23.500	< 50	< 50
16	3.910	< 50	< 50
17	25.828	< 50	< 50
18	73.069	< 50	< 50
19	106.320	< 50	< 50
20	7.368	< 50	< 50

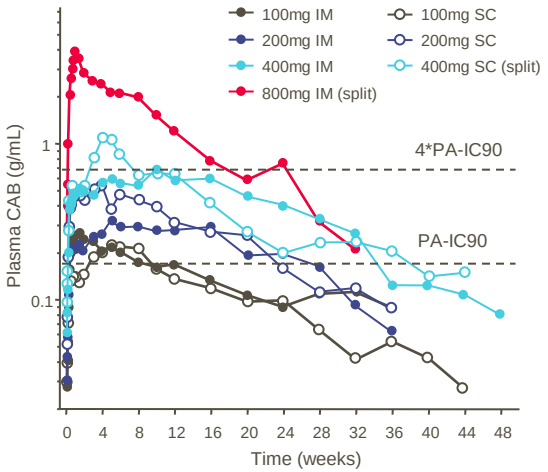
From week 8 onwards all patients VL was undetectable (pVL < 50 copies/mL)

Adapted from Cahn *et al*, EACS 2015, LBPS4/1

Cabotegravir: Long-acting antiretroviral

Long-acting

Mean concentration/time profile following single injection[1]



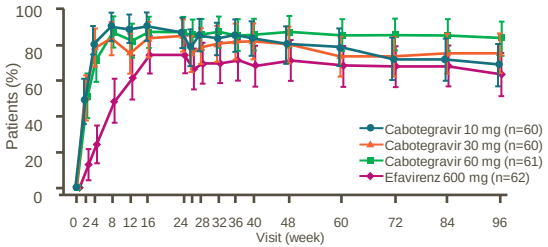
[1]Spreen *et al*, JAIDS 2014;67(5):481-486

HIV Treatment

THE LANCET Infectious Diseases

LATTE Week 96 Results[2]

Cabotegravir plus rilpivirine, once a day, after induction with cabotegravir plus nucleoside reverse transcriptase inhibitors in antiretroviral-naive adults with HIV-1 infection (LATTE): a randomised, phase 2b, dose-ranging trial

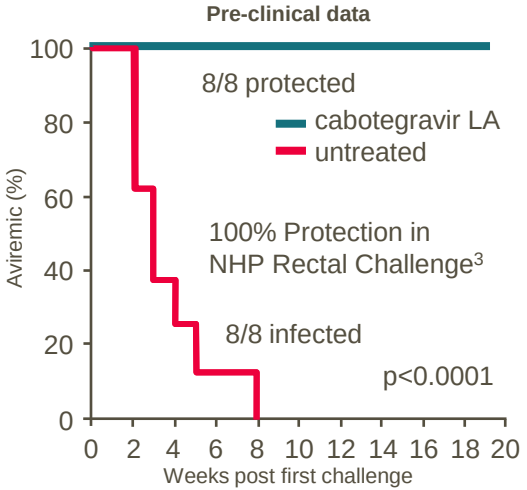


Proportion of patients with HIV-1 RNA concentration of less than 50 copies per mL by visit in the intention to-treat exposed population
Error bars indicate 95% CI

[2]Margolis *et al*, Lancet Inf Dis 2015;15(10):1145-1155

HIV Prevention

Sciencexpress



[3]Andrews *et al*, Science 2014;343(6175):1151-4

Cabotegravir long-acting clinical studies

Potential for better adherence

HIV TREATMENT

CAB LA + RPV LA

Planned launch: 2019/2020

4Q2015 LATTE 2 results

Key Phase III-enabling data: combination CAB LA + RPV LA as maintenance therapy (ViiV Healthcare - Janssen sponsored)

Mid-2016 HIV Treatment Phase III start

CAB LA + RPV LA switch studies (transition from oral therapy to long-acting)

HIV PREVENTION

CAB LA monotherapy

Planned launch: 2020+

Mid-2016 PrEP Phase III start (men)

CAB LA monotherapy vs. TDF/FTC (Truvada) in at-risk men who have sex with men/transgender women
(Collaboration with third party being considered)

End-2016 PrEP Phase III start (women)

CAB LA monotherapy vs comparator in at-risk women
(Collaboration with third party being considered)

LATTE 2 - cabotegravir LA + rilpivirine LA for treatment of HIV

Headline data – path to Phase III

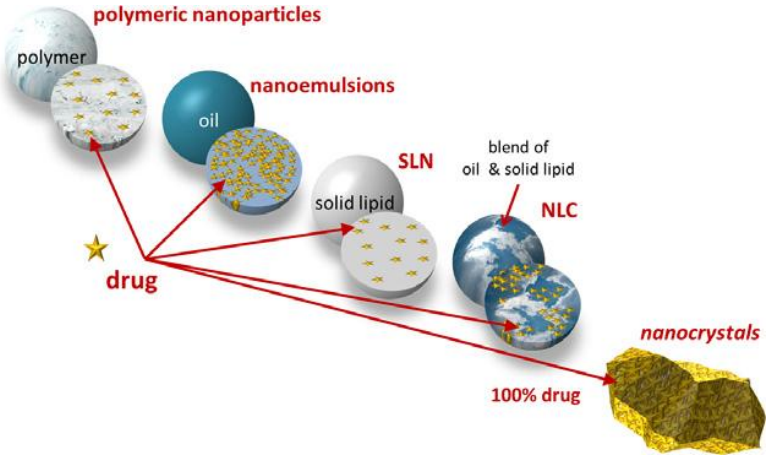
- Phase IIb trial examining long-acting (LA) cabotegravir (CAB) in combination with LA rilpivirine (RPV). 309 treatment naïve subjects initially treated with QD oral CAB 30mg + 2 NRTIs
- Following virologic suppression 286 subjects qualified for entry into maintenance phase and were randomised 2:2:1 onto: 4 week injections with CAB LA + RPV LA (Q4W); 8 week injections with CAB LA + RPV LA (Q8W) or continuation of oral CAB + NRTIs
- Through 32 weeks on 2-drug maintenance therapy with CAB LA and RPV LA, 95% (Q8W) and 94% (Q4W) of subjects were virologic successes (VL<50) compared to 91% of subjects continuing three drug oral CAB + NRTIs
- Adverse events (AEs) leading to withdrawal were 5% (n=6) for Q4W, 2% (n=2) for Q8W, and 2% (n=1) for oral CAB + NRTIs. The most common AE was injection site pain (93% of injection recipients)
- Detailed analyses just starting

Next wave cabotegravir long-acting combinations

Opportunities with broadly neutralising antibodies

- Cabotegravir long-acting
- Every 2 or 3 months

Nano-formulation



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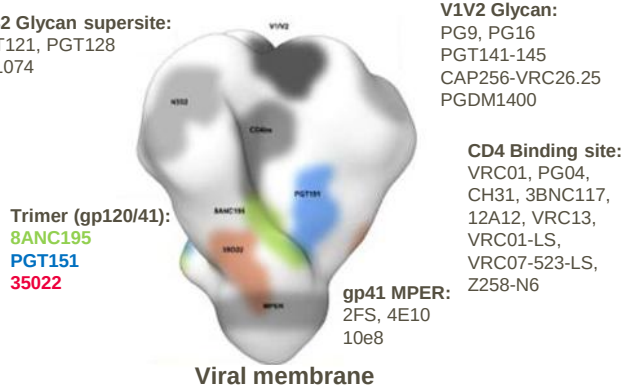
- Broadly neutralising antibodies (bnAbs)
- GSK and the National Institute of Allergy and Infectious Diseases/National Institutes of Health collaboration to be announced later this week

Potential targets for neutralisation

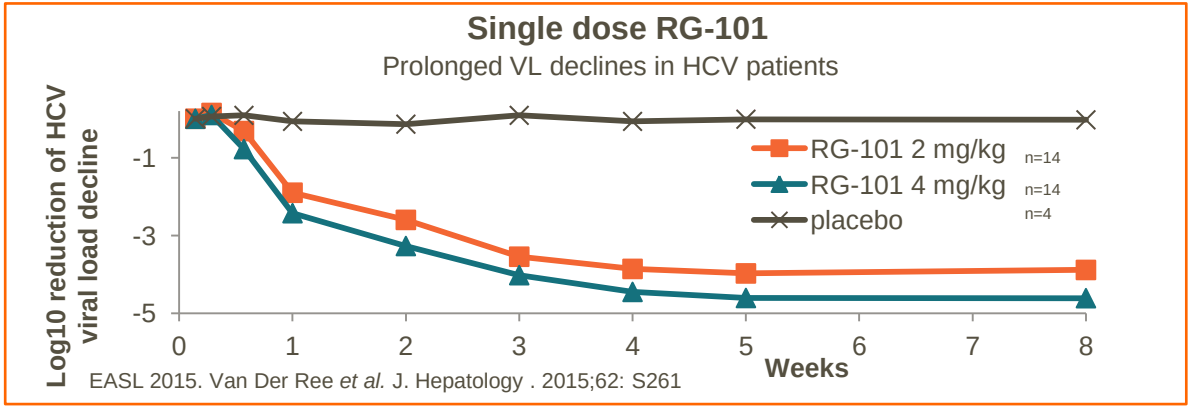


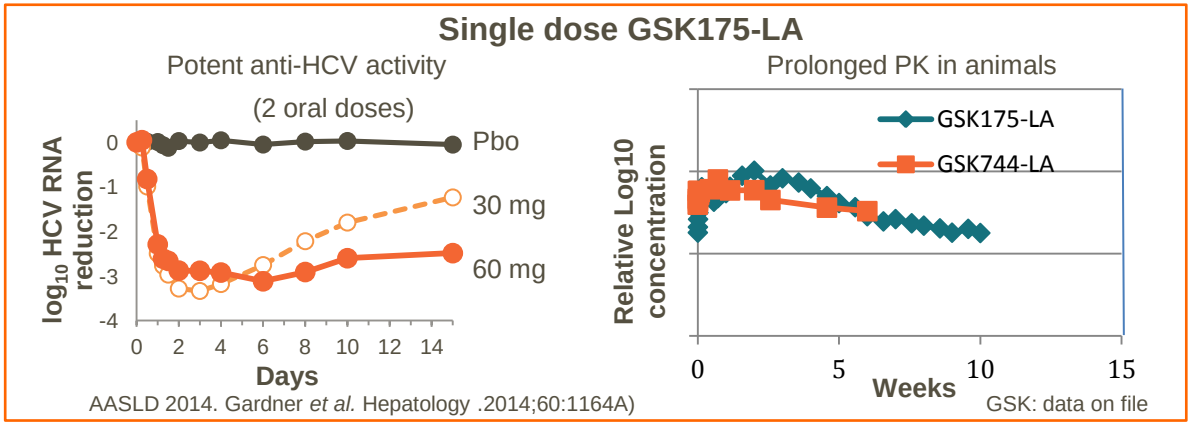
Huang *et al*. Nature 2014;515(7525):138-42

A pilot clinical combination study of VRC01 and cabotegravir is planned for 2016 start

GSK & Regulus combination offers potential for a single administration treatment for HCV

- RG101 lowers viral load
- GSK2878175 lowers viral load
- Both molecules have potential for prolonged PK/PD activity
- Prolonged pan-genotype and anti-HCV activity
- Potential single administration option
- Clinical combination study starts 2016

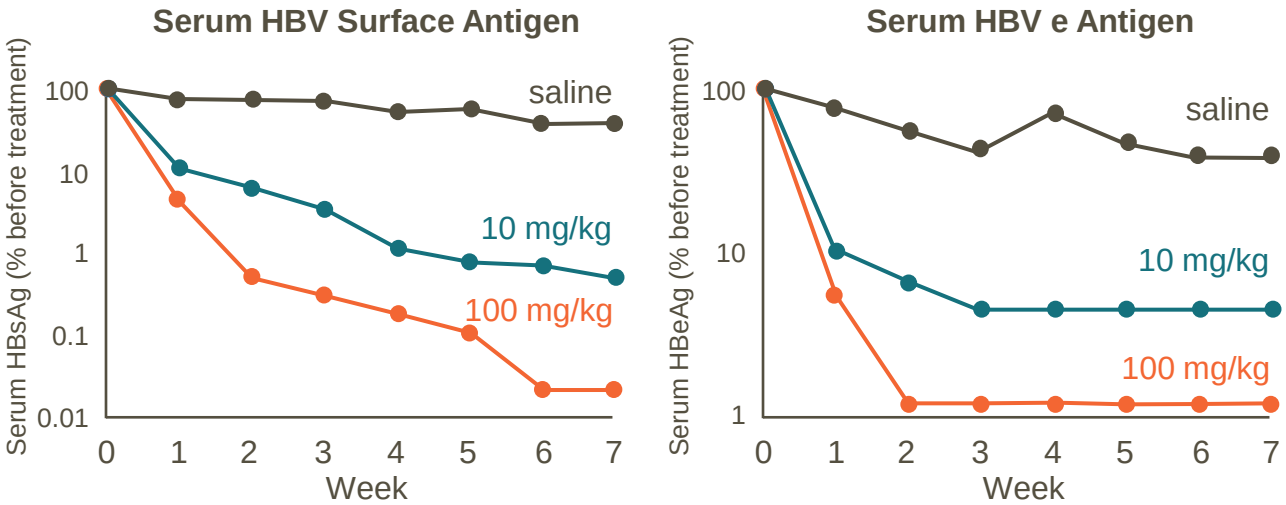




GSK & Isis collaboration targeting next generation of HBV medicines: functional cure

- Antisense approach taken to knock down immune suppressive antigens
- Entered collaboration with Isis Pharmaceuticals in 2010
  - GSK contributed target, Isis provided platform & discovery
- Lead compound GSK3228836
  - Phase II start planned 2016

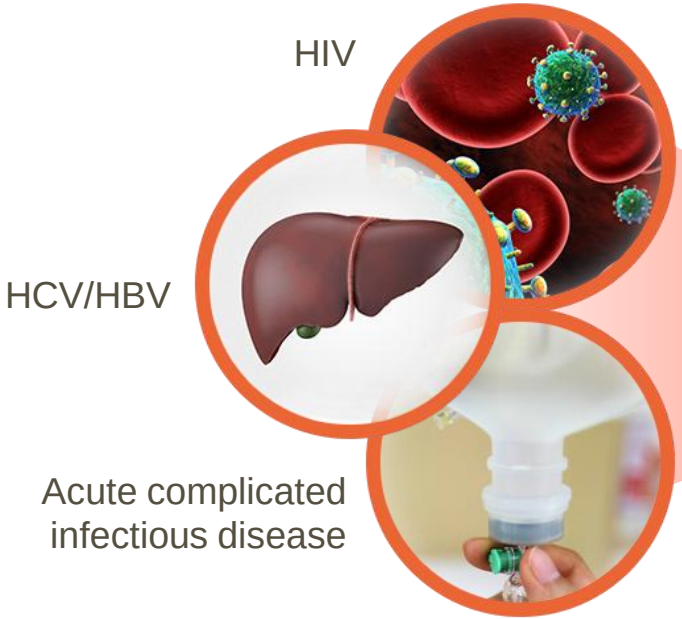
Reduction of HBV antigen by anti-HBV ASO in mice



GSK, data on file.

Note: GSK3228836 subject to exercise of option by GSK

Infectious Diseases strategy: from innovative treatment regimens to the pursuit of cure



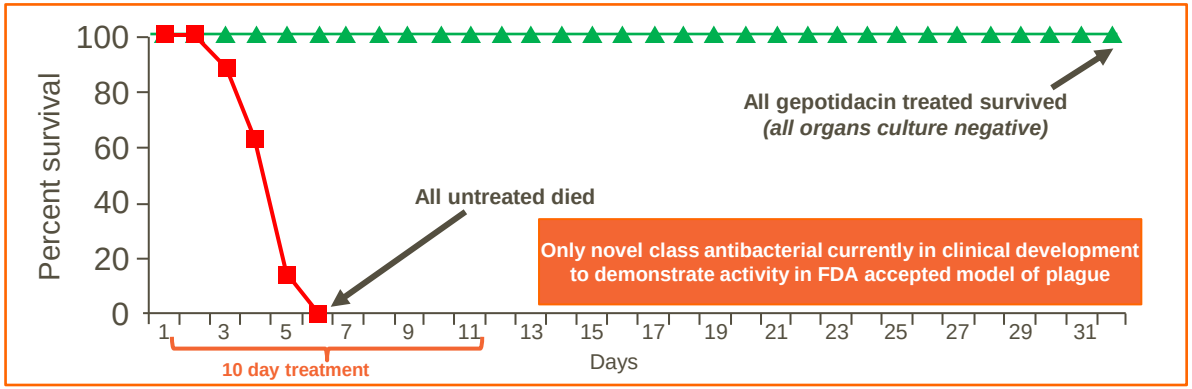
GSK Pipeline

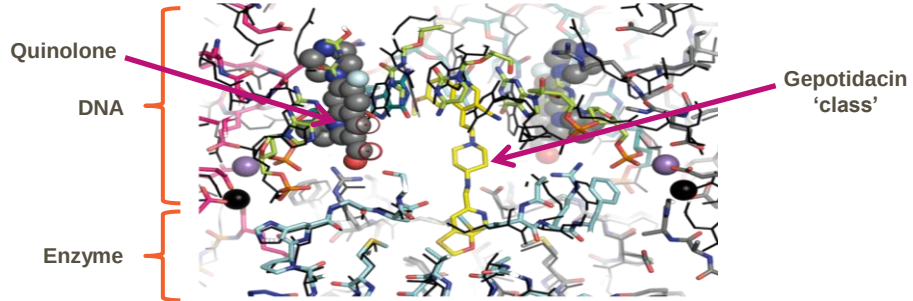
- Innovative Treatment Regimens
- Long-acting Treatment
- Prevention
- Remission & Cure

First in a new class of antibacterials: gepotidacin (GSK2140944) – a topoisomerase inhibitor

- Novel mechanism with bactericidal activity against MDR pathogens
- Promising safety & efficacy profiles in Phase II studies
- Effective against key resistant strains:
  - MDR MRSA, MDR E.*coli* & Drug resistant N.*gonorrhoeae*
- Potential to address multiple conventional & bio-threat indications
- Progressed via successful partnerships with BARDA & DTRA

Planned Filing: 2019 for resistant infections. Discussions with FDA on plague indication.





Gepotidacin binds to a novel site on gryase

Nature Struc Mol Biol, 2010,17;465

MDR: multi-drug resistant; DTRA: Defense Threat Reduction Agency (US DoD); BARDA: Biomedical Advanced Research & Development Authority (US HHS)

Infectious Diseases strategy: from innovative regimens to treatment and the pursuit of cure

- dolutegravir based regimens
- cabotegravir LA
- cabotegravir LA + rilpivirine LA
- Next generation agents and combinations

- HCV
- HBV

- gepotidacin
- tafenoquine
- i.v. danirixin

GSK Pipeline

Innovative Treatment Regimens

HIV, HCV, HBV

Long-acting Treatment

HIV, HCV, HBV

Prevention

HIV

Remission & Cure

HIV, HCV, HBV (Qura)

Respiratory

Respiratory diseases: still significant unmet need

Asthma

- Globally 242m people have asthma (32% increase since 1990)
- Gold-standard options delivered for mild/moderate asthma
- Major unmet medical need in severe asthma
  - **5-10% of asthma patients**
  - **60% of cost burden**
- Immune modulation offers potential for better disease control and even remission

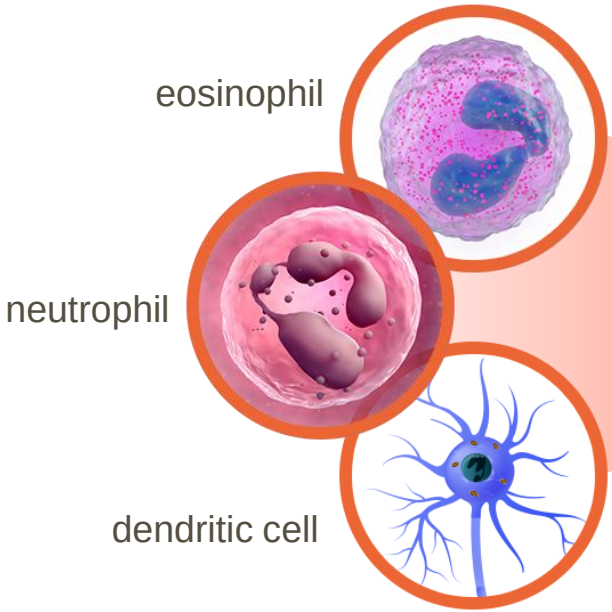
COPD

- 329m people worldwide have COPD
- 3rd leading cause of death by 2030
- Longitudinal studies (e.g. ECLIPSE) helping to identify prognostic biomarkers (e.g. fibrinogen)
- Targeting underlying drivers of disease progression is key

Lung Fibrosis & Acute Lung Injury

- Each affects ~5m patients worldwide
- Idiopathic Pulmonary Fibrosis (IPF): median survival of just 2-5 years, 2 IPF products approved
- Urgent need to improve symptoms and delay disease progression
- Acute Lung Injury (ALI): hospital mortality rates of up to 50%
- Need to identify better clinical path for drug development

Asthma R&D strategy: from secondary prevention to primary disease modification



GSK Pipeline

- Targeted Biologicals
- Extended Duration Biologicals
- Once Daily Inhaled
- Remission-inducing

Nucala™* (mepolizumab) demonstrates significant reduction in exacerbations

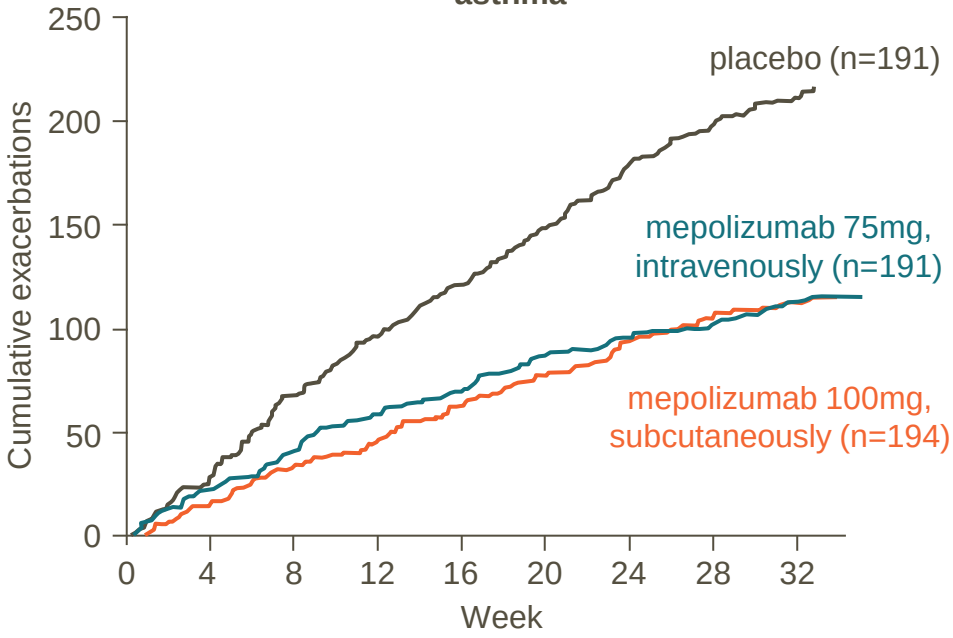
Nucala (subcutaneous anti-IL-5 mAb):

- Straightforward patient selection & biomarker
- 53% reduction in exacerbations
- 61% reduction in ER visits/ hospitalisations
- Improvement in health status by 7 points (SGRQ)
- Significant reduction in daily oral corticosteroid dose while maintaining control seen in trials
- Dosing every 4 weeks, no weight adjustment required
- Well tolerated

Indication:	Severe refractory eosinophilic asthma
Positive CHMP:	24 Sep 2015
PDUFA :	4 Nov 2015

*The name Nucala is not approved for use by the FDA or EMA.

mepolizumab (s.c. or i.v.) reduced the number of asthma exacerbations in patients with severe eosinophilic asthma



Adapted from MENSA study, Ortega *et al*. NEJM 2014; 371:1198-207

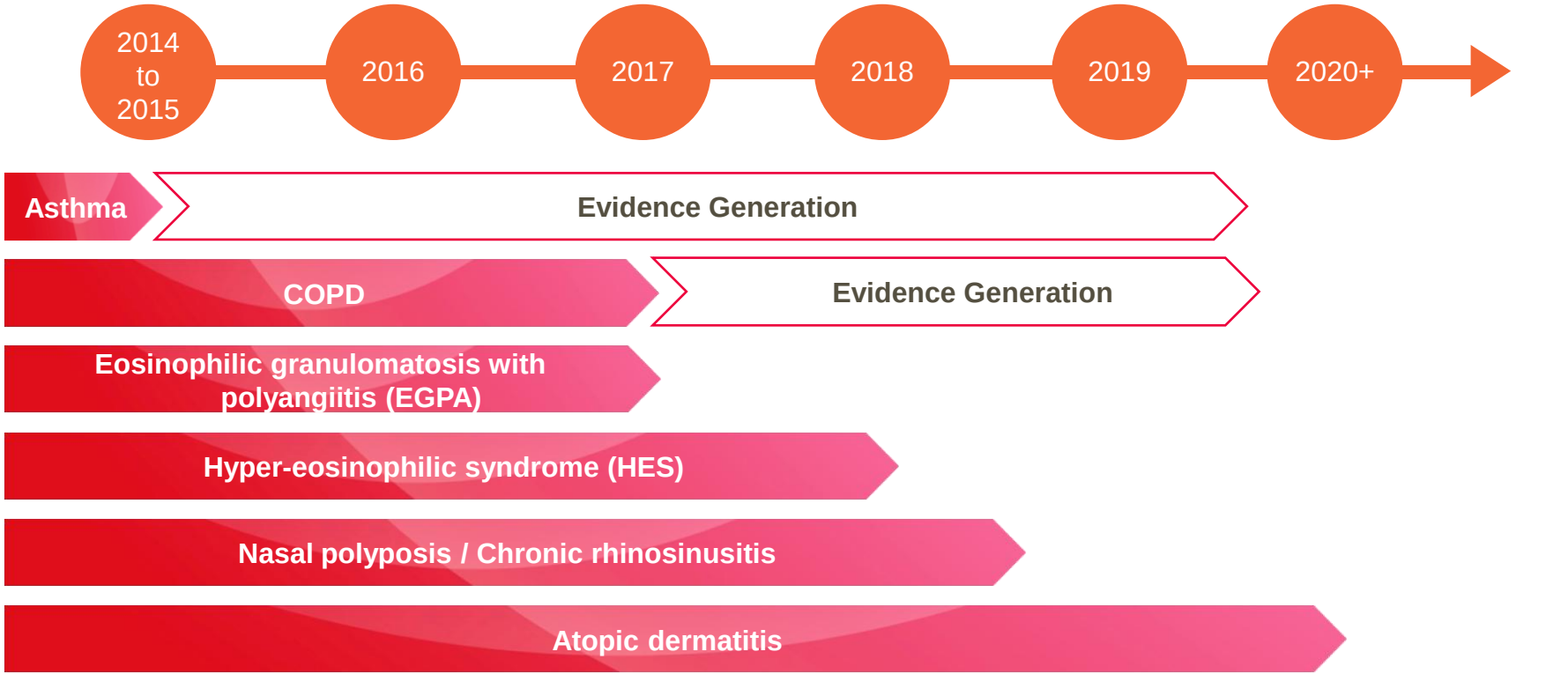
Nucala will be first in class with a strong profile

	Nucala	XOLAIR *Novartis/ Genentech*	reslizumab *Teva*	benralizumab *AstraZeneca*	lebrikizumab *Roche*	tralokinumab *AstraZeneca*	dupilumab *Sanofi/ Regeneron*
Phase	Submitted	Launched	Submitted	Ph III ongoing	Ph III ongoing	Ph III ongoing	Ph III ongoing
Earliest launch assumption*	Q4 2015	Launched	Q4 2015/ Q1 2016	2017	2017	2019	2019
Mechanism	Anti-IL-5	Anti-IgE	Anti-IL-5	Anti-IL-5R	Anti-IL-13	Anti-IL-13	Anti-IL-4Rα
Delivery mechanism	SC	SC	IV	SC	SC	SC	SC
Efficacy data Ph III	✓	✓	✓	Phase III ongoing			
Safety data Ph III	✓	✓	✓				

*Based on published filing date plus average review times

Nucala* has potential in other indications

Anticipated file timelines



*The name Nucala is not approved for use by the FDA or EMA and may not be approved for additional indications.

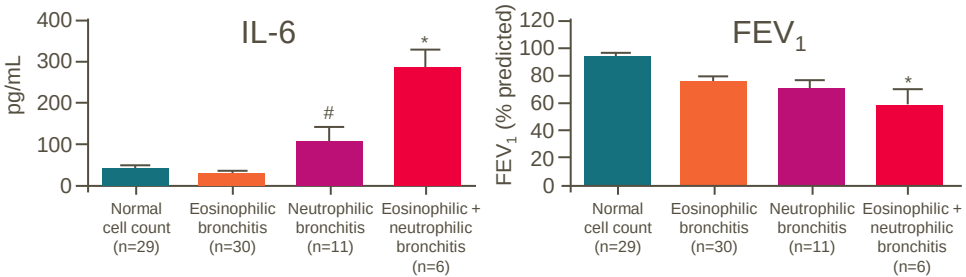
Two novel biologicals

Targeted approaches for uncontrolled asthma patients

sirukumab* (IL-6 mAb): Non-Th2 asthma

- Targets severe disease ineligible for Th2/eosinophilic directed mAbs (40% of severe asthma patients)
- IL-6: key inflammatory driver and genetic association of this pathway in asthma
- Expected to improve symptoms and exacerbations
- Phase II study start in 2016

Elevated IL-6 associated with eosinophilic-neutrophilic inflammation and decreased pulmonary function (FEV_1) in asthma patients



*p < 0.05 vs neutrophilic bronchitis and eosinophilic bronchitis groups
#p < 0.05 vs eosinophilic bronchitis group

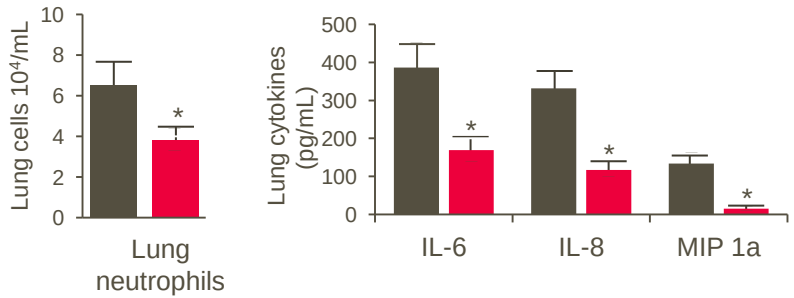
Chu, Allergy Asthma & Clinical Immunology.2015;11:14

* sirukumab is part of a GSK Janssen Biologics (Ireland) collaboration

TSLP dAb: Inhaled biologic

- Thymic Stromal Lymphopoietin (TSLP): key cytokine in epithelial immune response in asthma
- Inhaled domain antibody (dAb) directly targets site of action and reduces systemic exposure to improve risk:benefit profile
- Clinical proof of concept demonstrated for anti-TSLP approach
- Phase I start in 2016

Target engagement after inhaled delivery of dAb: *exemplar*
Inhaled TNFR1 dAb reduced endotoxin (LPS) induced inflammation in healthy volunteers



* p<0.05 t=test
n=18 subjects per group

placebo inhaled TNFR1 dAb (26mg)

Data on file (study TFR116236)

Nucala is at forefront of a diverse asthma biologic pipeline

	Nucala *Anti-IL-5*	**sirukumab** *Anti-IL-6*	*Long acting* *Anti-IL-5 (NBE)*	*Anti-TSLP dAb*	*Anti-IL-5/13*
Modality	mAb	mAb	Extended pharmacology mAb	Inhaled dAb in Ellipta	Bispecific dAb-mAb extended pharmacology
Delivery mechanism	SC	SC	SC	Inhaled	SC
Expected file	2014	2021-25	2021-25	2021-25	2021-25
Status	Filed	Phase II start 2016	Phase I/II start 2017	Phase I start 2016	Preclinical
Asthma segment	Severe eosinophilic	Severe without elevated eosinophils	Moderate-severe eosinophilic	Moderate-severe eosinophilic and neutrophilic	Moderate-severe eosinophilic
Reason to believe	Clinical data and strong mechanism rationale	IL-6 is key driver of non-eosinophilic inflammation	Extended pharmacology allows six monthly dosing	Key cytokine in epithelial immune response; Inhaled - directly targets site of action	Additive efficacy of two complimentary mechanisms, in six monthly dosing

GSK2245035 intranasal TLR7 agonist

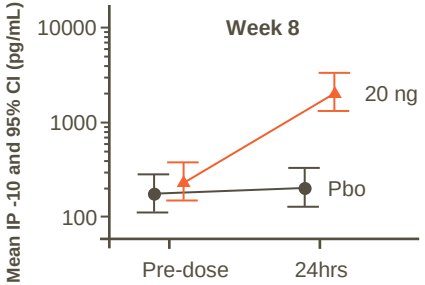
Demonstrates prolonged suppression of allergic response

- Activates immune pathways that suppress exaggerated Th2 response in asthma
- Allergen-independent immune modulation
- Clinical data demonstrate target engagement (IP-10) with no tachyphylaxis
- Protection from nasal allergen challenge up to 3 weeks after last dose
- Weekly treatment may induce remission from asthma
- Phase II asthma study 2016

Status:	Phase IIa
Indication:	Asthma remission
Planned Filing:	2021-2025

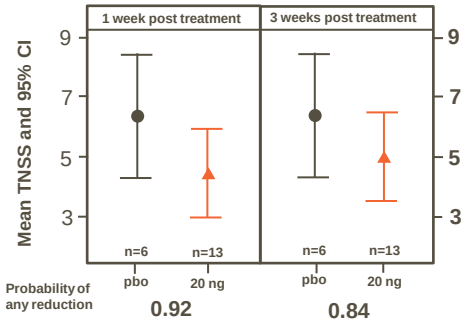
Weekly dosing with intranasal GSK2245035 for 8 weeks in allergic rhinitis patients

Target engagement



Increase in IP-10 levels 24 hours after last dose of 8 weekly treatments

Protection from allergen challenge

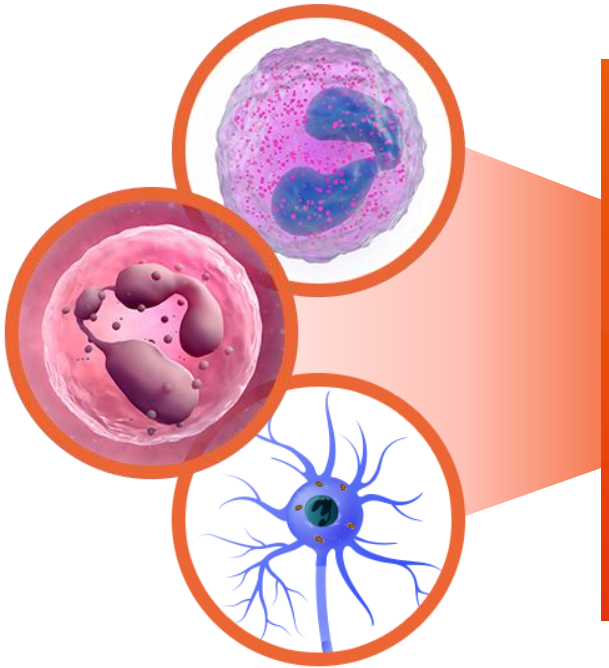


Total nasal symptom score (TNSS) reduced after 8 weekly treatments and maintained 3 weeks after last dose

GSK, data on file (study TL7116958)

Asthma R&D strategy:

From secondary prevention to primary disease modification



GSK Pipeline

Targeted Biologicals

- Nucala
- sirukumab
- Anti-TSLP dAb
- Anti-IL-5/13

Extended Duration Biologicals

- Long-acting anti-IL-5
- Anti-IL-5/13

Once Daily Inhaled

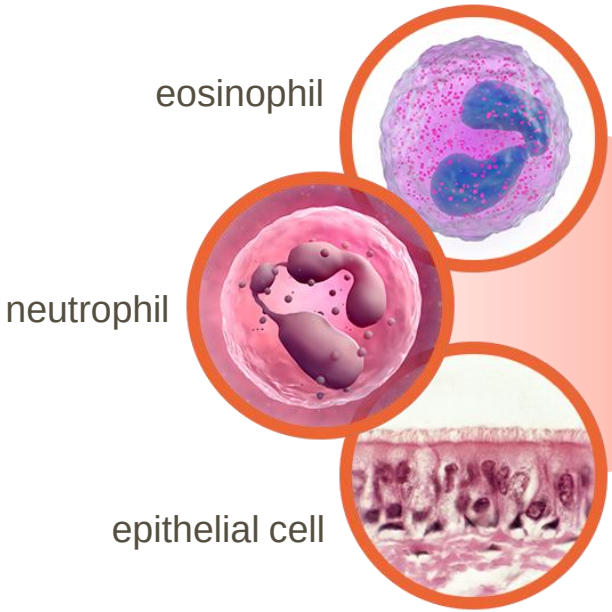
- Relvar/Breo Ellipta™
- Arnuity Ellipta™
- Incruse Ellipta™
- Anti-TSLP dAb

Remission-inducing

- TLR7 agonist

COPD R&D strategy:

Targeting the fundamental drivers of disease



GSK Pipeline

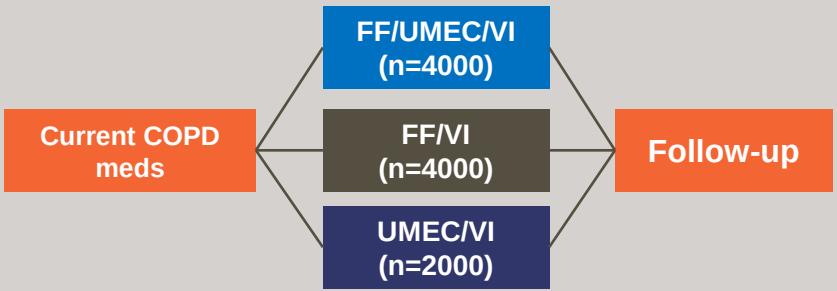
- Targeted Biologicals
- Infection Driven Exacerbations
- Once Daily Inhaled
- Preserve Lung Function

Closed Triple: once daily triple therapy in established Ellipta inhaler

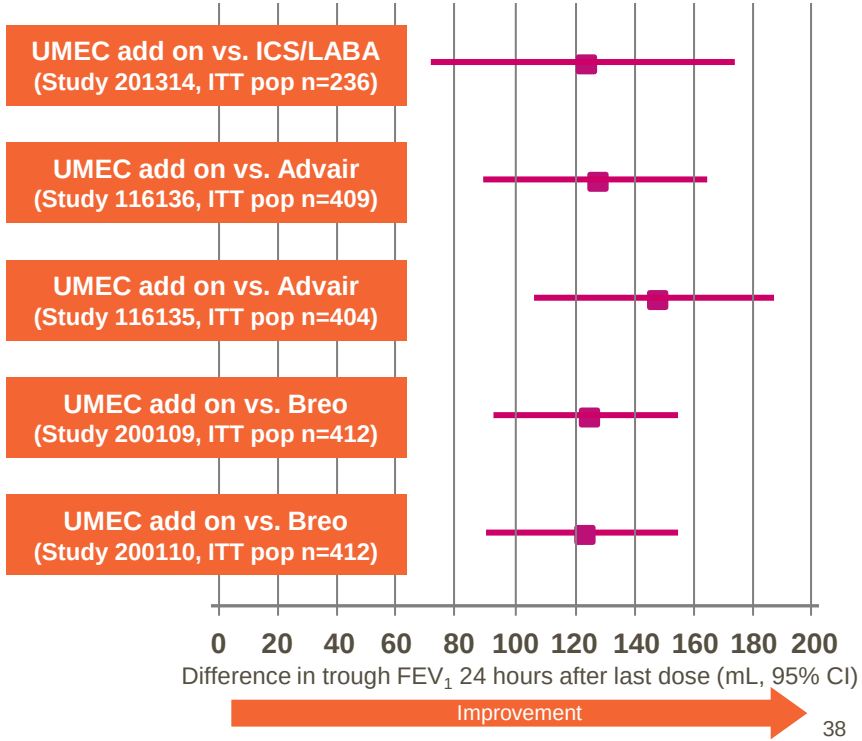
- Collaboration with Theravance
- Open triple filed with FDA
- Phase IIIa lung function study fully recruited (FULFIL)
- EU Closed Triple filing: end 2016 (lung function)
- US Closed Triple filing: H1 2018 (exacerbations)
- Triple therapy already part of some clinical practice[1]

[1]Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2015

Eosinophil signature being evaluated prospectively in IMPACT study



Consistent improvement in lung function with UMEC plus ICS/LABA vs. ICS/LABA

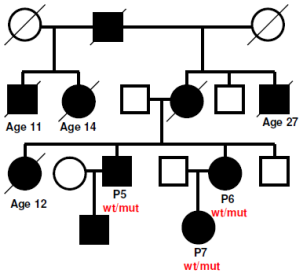


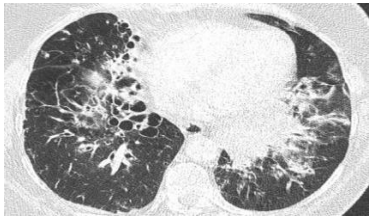
GSK2269557, inhaled PI3Kδ inhibitor targets neutrophil-mediated lung damage in COPD

- PI3Kδ over-activation causes human rare disease activated PI3Kδ syndrome (APDS)
- APDS patients display severe recurrent COPD-like bacterial infections
- Inhaled delivery offers potential efficacy/safety advantage and opportunity for combination therapy
- Target engagement demonstrated in healthy smokers (PIP3)
- GSK2269557 on top of standard of care in COPD shows decreased markers of inflammation
- Currently testing in exacerbating COPD patients and Phase IIb studies to start 2016/17

Status:	Phase IIa
Indication:	COPD exacerbation
Planned Filing:	2021-2025

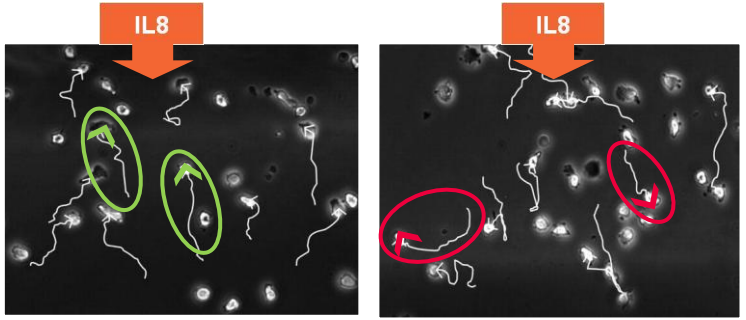
Activating mutations in PI3Kδ in APDS drive lung infections





Angulo *et al*. Science 2013; 342: 866

Directionality of neutrophil migration is aberrant in COPD patients and corrected by PI3Kδ inhibition - *in vitro*



Healthy control **COPD**

Sapey *et al*. AJRCCM 2011;183:1176

Danirixin (GSK1325756): an oral CXCR2 antagonist

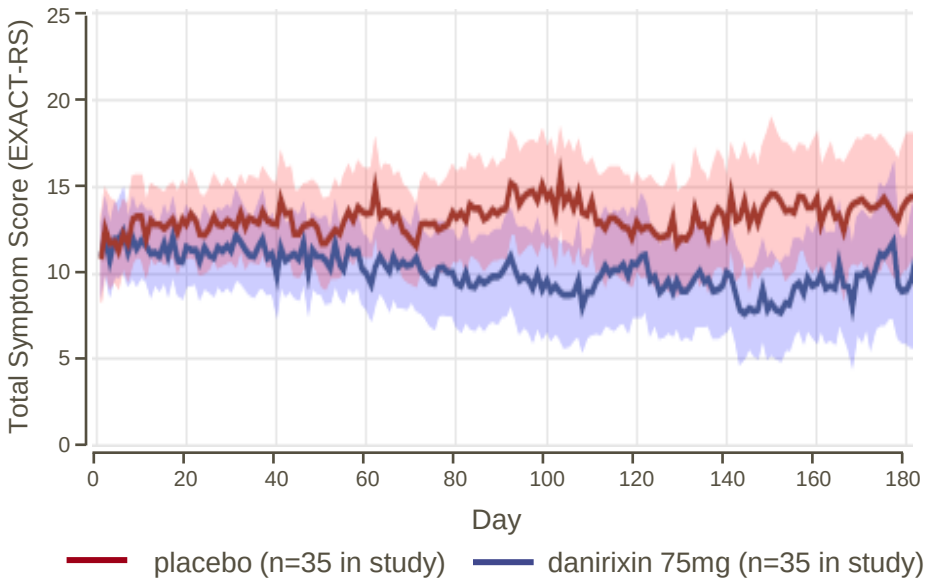
Demonstrates potential to reduce lung damage in COPD

- Blocks chemokine receptor on neutrophils and other cell types (CXCR2)
- Target engagement demonstrated with danirixin (neutrophil activation biomarker, CD11b)
- Competitor compounds produced clinical effects, but with reduction in blood neutrophils[1]
- In the clinic, danirixin has efficacy at a dose not associated with reduced blood neutrophils
- COPD Phase IIb start 2016
- Influenza infection Phase IIa study ongoing

[1]Am J Respir Crit Care Med 2015;191:1001–1011

Status:	Phase IIa
Indication:	Symptomatic COPD
Planned Filing:	2021-2025

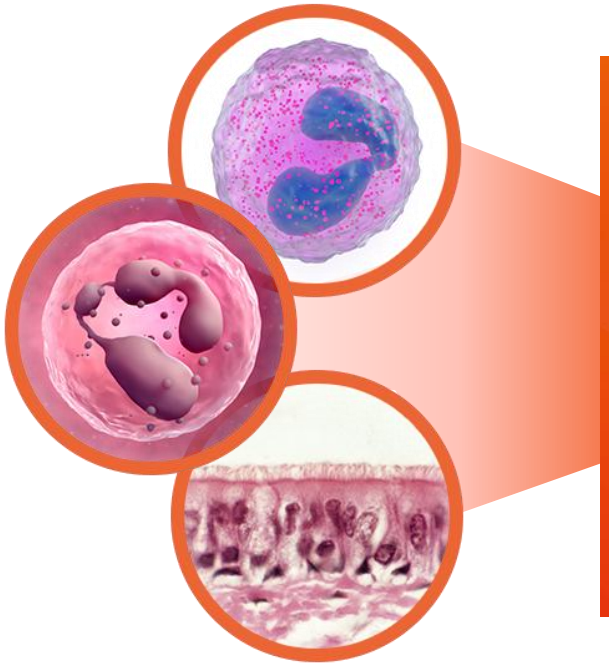
Real-time data demonstrate improvement of symptoms with danirixin in symptomatic COPD (frequent exacerbators)



GSK, data on file (study 200163)

COPD R&D strategy: pipeline

Targeting the fundamental drivers of disease



GSK Pipeline

Targeted Biologicals

- Nucala

Infection Driven Exacerbations

- PI3Kδ
- danirixin

Once Daily Inhaled

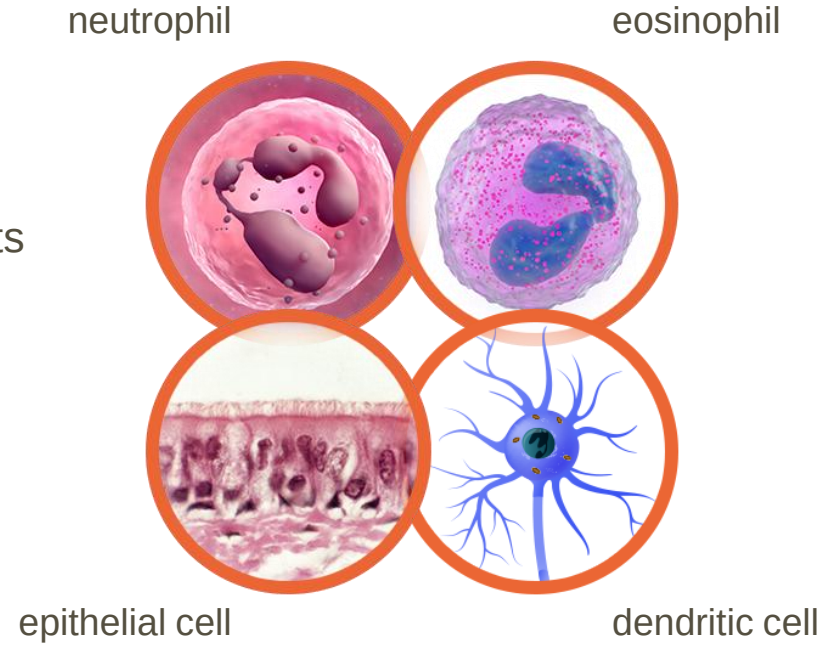
- Anoro™ Ellipta
- Relvar/Breo Ellipta
- Incruse Ellipta
- Closed Triple (Ellipta device)
- GSK961081 +FF
- PI3Kδ

Preserve Lung Function

- PI3Kδ
- danirixin

Drivers of our long-term leadership in asthma and COPD

- Excellence in inhaler / delivery technologies
- Targeted biological know-how
- Deep understanding of novel respiratory targets
- Understanding of patient phenotypes
- Expertise in trial design and delivery



Respiratory R&D beyond Asthma and COPD

Taking our respiratory know-how into new diseases

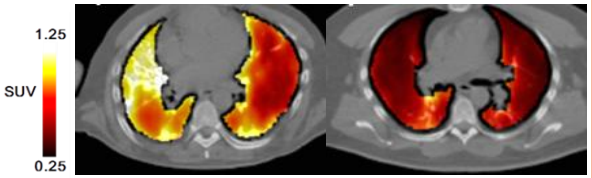
Platform for clinical development of IPF (GSK3008348)

- αvβ6 expression in IPF lung biopsies predicts mortality
- Small molecule inhaled αvb6 inhibitor (deposition of Tc - labelled salbutamol in lungs of IPF patients supports inhaled approach)
- Displacement of αvb6 PET ligand allows dose ranging in patients

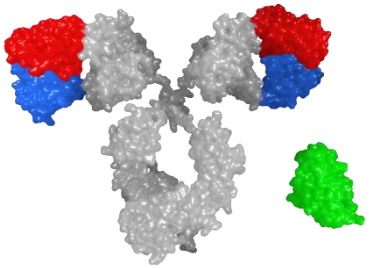
An inhaled dAb platform for acute lung injury (GSK2862277)

- High sTNFR1 levels associated with high mortality
- dAb blocks TNFR1 signalling without impacting beneficial TNFR2 signalling
- Inhaled TNFR1 dAb reduced endotoxin (LPS) induced inflammation in healthy volunteers
- Now in Phase II study

αvβ6 PET ligand binds to fibrotic regions in IPF lungs



αvβ6 PET ligand FDIH



mAb (grey, blue, red) vs. dAb (green)

PHI and Oxygen Sensing

Daprodustat[1] (GSK1278863) low dose PHI for treatment of anaemia of CKD: New Phase IIb data

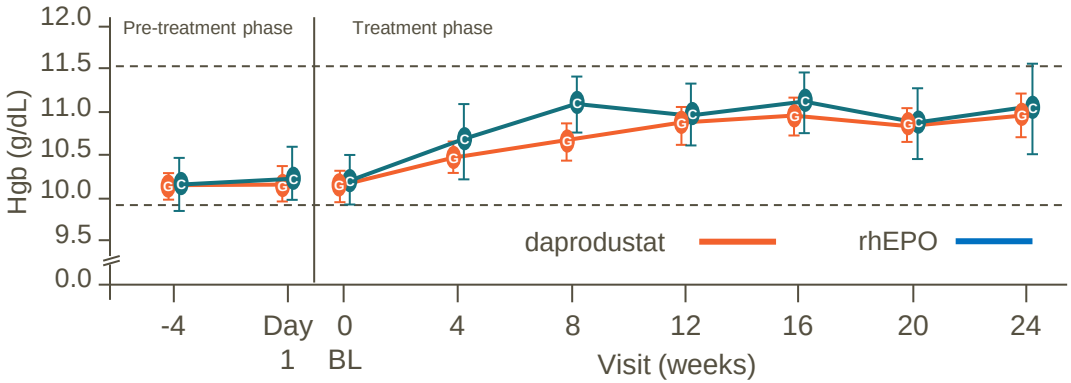
- Standard of care (rhEPO) limited by increased CV risk and IV/SQ administration
- PHI oral tablet to replace injectable rhEPO: low dose, convenient titration, potential for improved CV safety

Phase II summary (IIa and new IIb)

- Phase IIa data recently published[2]
- Raises Hgb in dialysis and non-dialysis subjects, either naïve to or switching from rhEPO
- Low dose (most subjects ≤10mg); Simple titration regimen
- Durable effect (up to 6 months in Phase IIb)
- Minimal elevation in EPO levels; No BP increase
- Safety profile consistent with CKD
- Phase III start 2016

Status:	Phase II
Indication:	Treatment of anaemia of CKD in subjects on dialysis and not yet on dialysis
Planned Filing:	2019 Japan, 2021 US/ROW

daprodustat Phase IIb[3]:
Pre-dialysis subjects naive to rhEPO; target Hgb 10.0-11.5 g/dL (n=96)



[1] USAN, INN approval pending
[2] J Am Soc Nephrol Oct 22, 2015 (epub)
[3] GSK, data on file (Study PHI113737)

Daprodustat: success factors for development

- Low dose
- No inhibition of collagen-4-hydroxylase
- Single Phase III CV outcomes studies for non-dialysis and dialysis

Key success factors	
Large experience in CKD subjects	659 (up to 6 months)
Active comparator for CV safety assessment	Yes (rhEPO)
Low dose	≤ 10mg QD in most subjects
Flexible dose regimen: Non-Dialysis Dialysis	QD QD / TIW
Phase III designed for clear assessment of CV risk	Single CV outcome trials for ND and HD
Inhibition of collagen-4-hydroxylase (cardiac tox risk)	No
Concern for hepatotoxicity (e.g. exclusion of acetaminophen in phase III trials)	No

Daprodustat

Indication expansion to maximise value of HIF-activating mechanism

Diabetic Foot Ulcer

- Preclinical data demonstrate benefit of HIF induction in diabetic skin
- Topical daprodustat formulation in ongoing Phase Ib study
  - No systemic exposure and no Hgb elevation
  - Efficacy data on wound healing in 2016

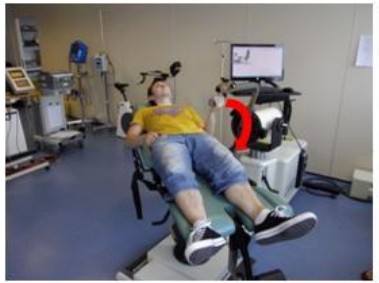
Muscle Injury

- Novel muscle repair activity discovered in pre-clinical injury model
- Phase I: Reduction in muscle injury in healthy volunteers

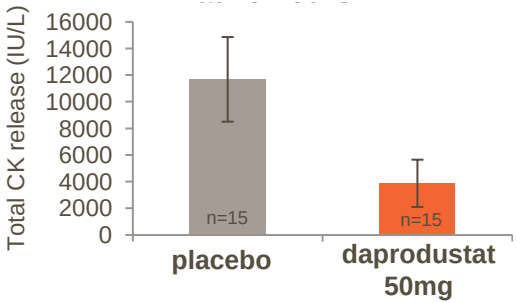
Future potential expansion into other anaemia indications

- Myelodysplastic Syndrome (MDS)
- Peri-surgical anaemia (ortho, GI, CV)

Muscle injury from repetitive arm motion in healthy volunteers



daprodustat reduces total CPK release over 72 hours



GSK, data on file (Study PHI20084)

Introducing our experts

GSK's leading scientists in infectious disease, respiratory medicine and CV

Zhi Hong

Senior Vice President,
Head Infectious Diseases
TAU

John Pottage

Senior Vice President,
Chief Scientific and Medical
Officer for ViiV Healthcare

Dave Allen

Senior Vice President,
Head Respiratory TAU

Edith Hessel

Vice President, Head
Refractory Respiratory
Inflammation DPU

Steve Pascoe

Vice President,
Head Unit Physician
Respiratory

John Lepore

Senior Vice President,
Head Metabolic Pathways
and Cardiovascular

Ruchira Glaser

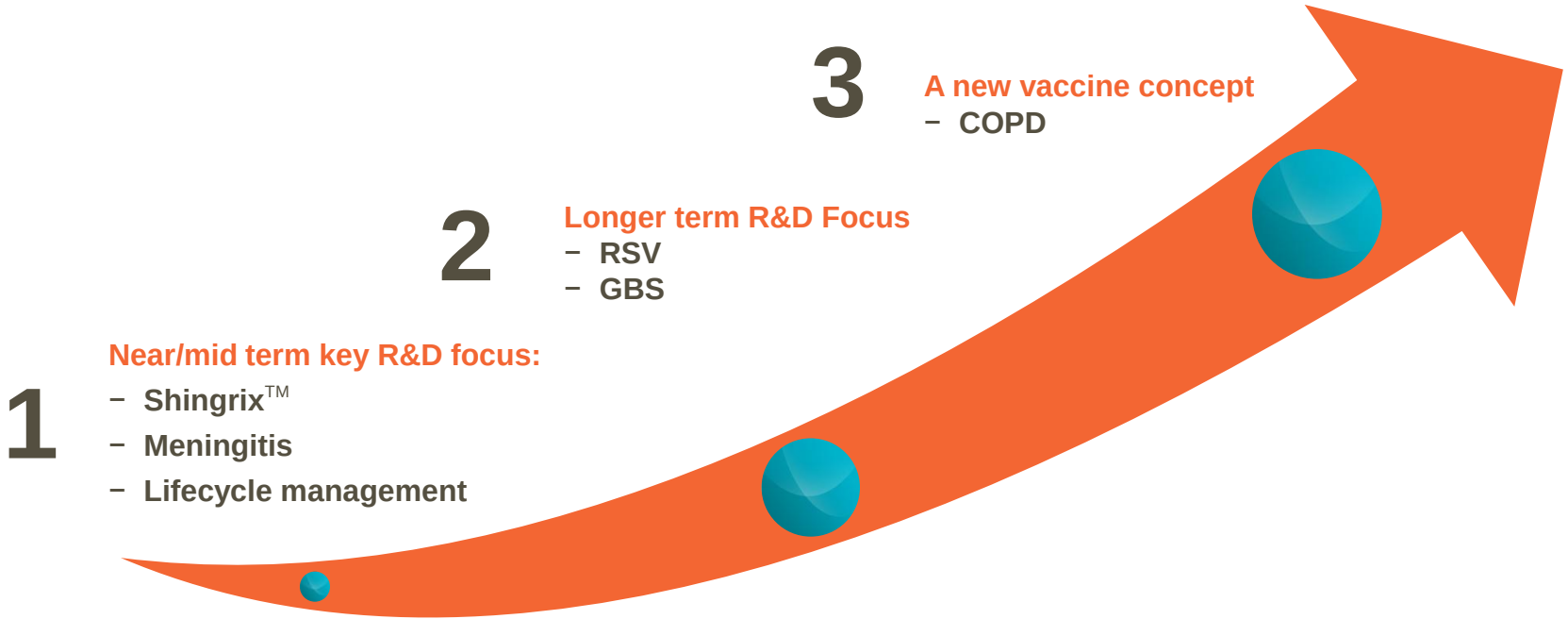
Clinical Development Director,
Metabolic Pathways and
Cardiovascular

Q&A

Moncef Slaoui

Chairman of Vaccines

R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms



1

Near/mid term key R&D focus:

- Shingrix™
- Meningitis
- Lifecycle management

2

Longer term R&D Focus

- RSV
- GBS

3

A new vaccine concept

- COPD

RSV=Respiratory Syncytial Virus; GBS=Group B Streptococcus; COPD=Chronic Obstructive Pulmonary Disease

Shingrix™

Shingrix™ is not approved for use by the FDA or EMA

Existing zoster vaccine

One dose, live attenuated vaccine

Efficacy: 51% against shingles in ages 60+
- **Inverse correlation between age at vaccination and protection**
- **Limited persistence of protection**

Indication for ages 50+
US ACIP recommendation for ages 60+

Contraindicated in immunocompromised individuals

Estimated to have <25% coverage in US*

2014 reported sales of $868m (>$600m in US)

*CDC: MMWR, February 2015; http://www.cdc.gov/Mmwr/preview/mmwrhtml/mm6404a6.htm; Zostavax™ US PI
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on US PI.

Shingrix candidate vaccine developed to differentiate

Two doses, sub-unit (non-live) vaccine, novel adjuvant

Efficacy: 91% - 97% against shingles
- **High efficacy across identified age groups**
- **Persistence over time**

Targeting indication and recommendation in ages 50+

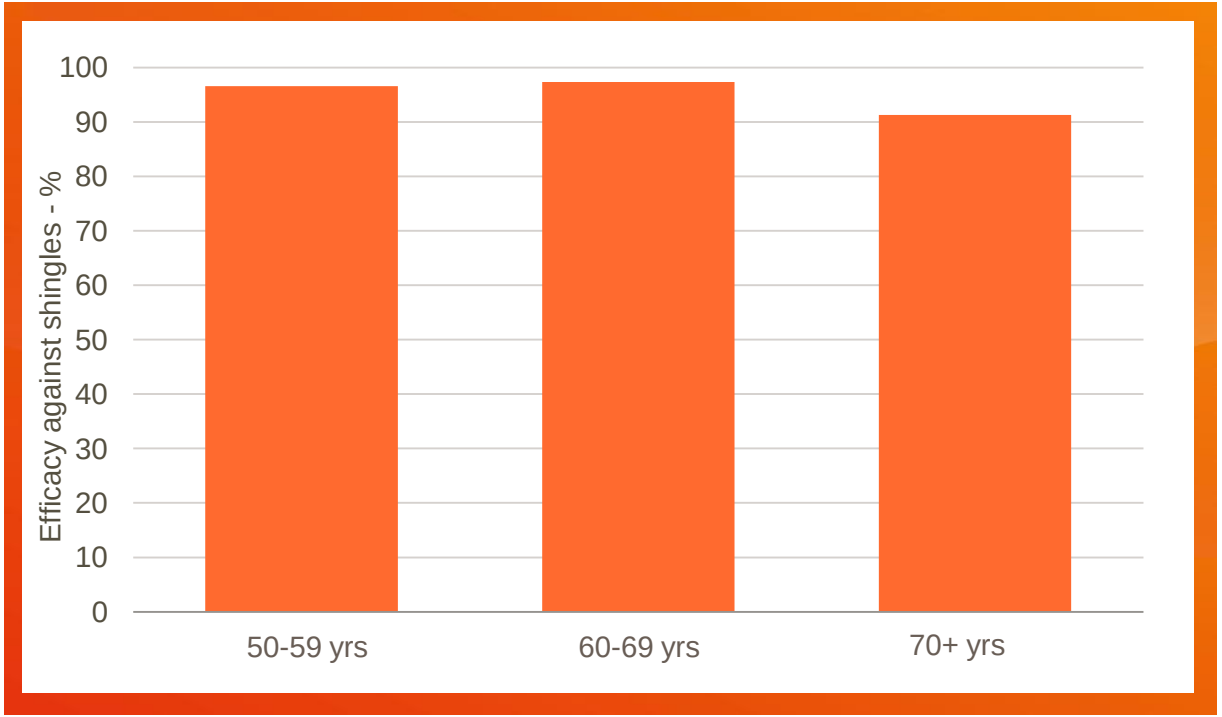
Data on immunocompromised individuals in 2017

Expect US, EU, Japan filings in 2H 2016

Expected to contribute ~1/3 of 2020 sales growth targets for GSK vaccines

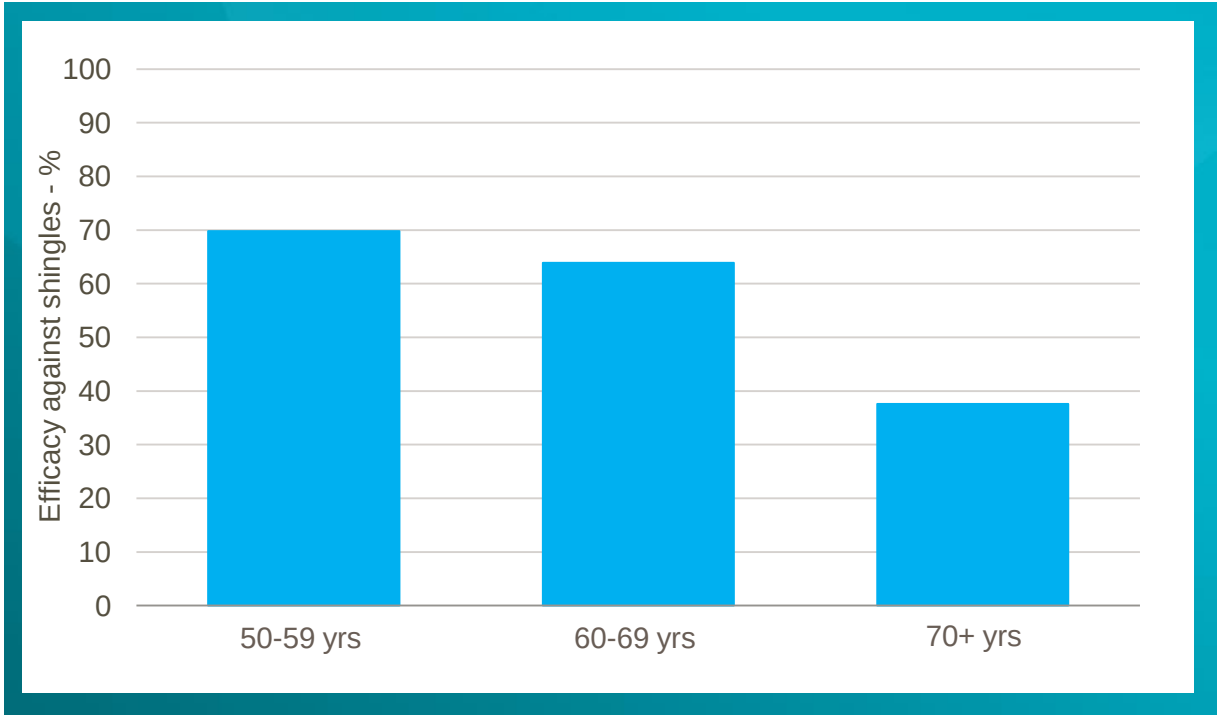
Lal *et al*. N Engl J Med 2015; ZOE-50 and ZOE-70 pooled analysis – unpublished data
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on ph III clinical trials.

Shingrix - Efficacy against shingles



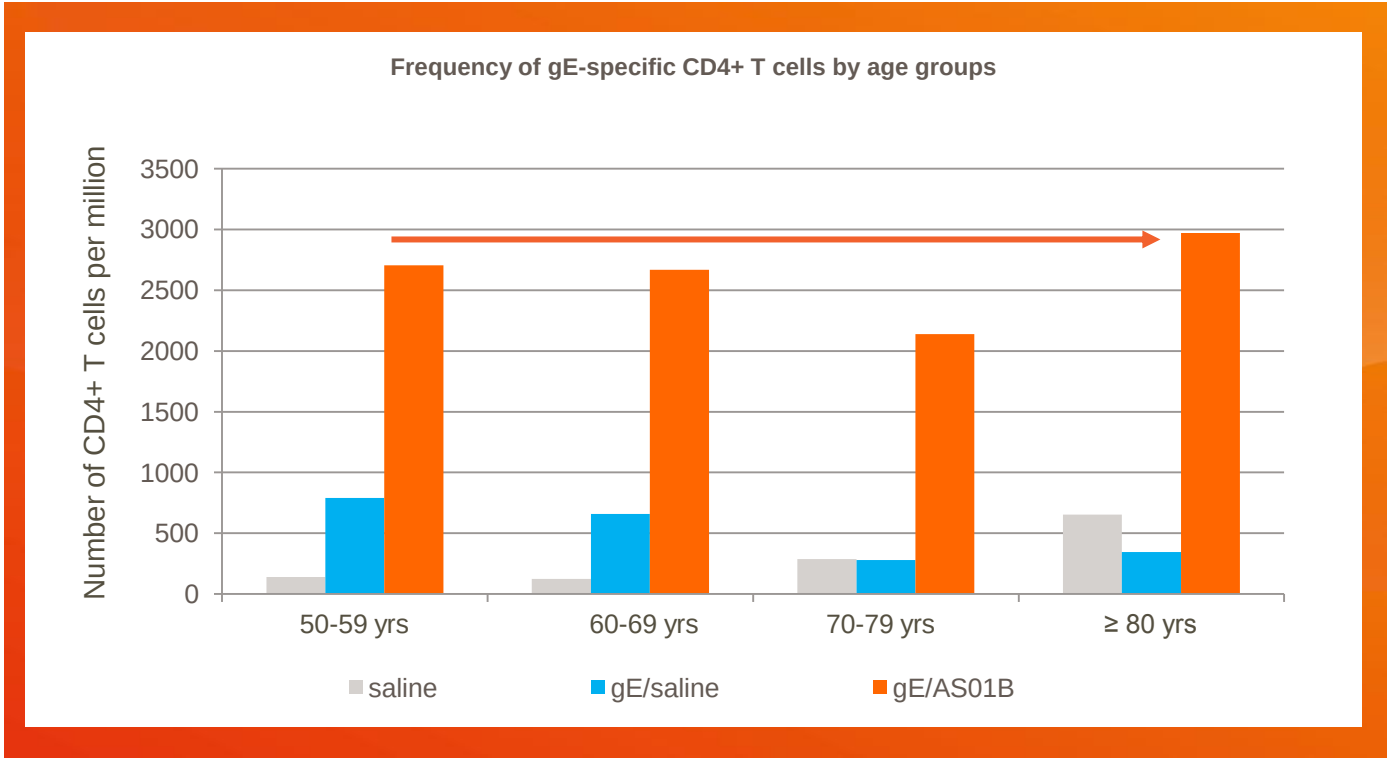
Lal *et al*. N Engl J Med 2015; ZOE-50 and ZOE-70 pooled analysis – unpublished data
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on ph III clinical trials.

Existing vaccine - Efficacy against shingles



Oxman *et al*. N Engl J Med 2005; 352: 2271–84;
Schmader *et al*. Clinical Infectious Diseases 2012;54(7):922–8;
Zostavax™ US PI
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on US PI.

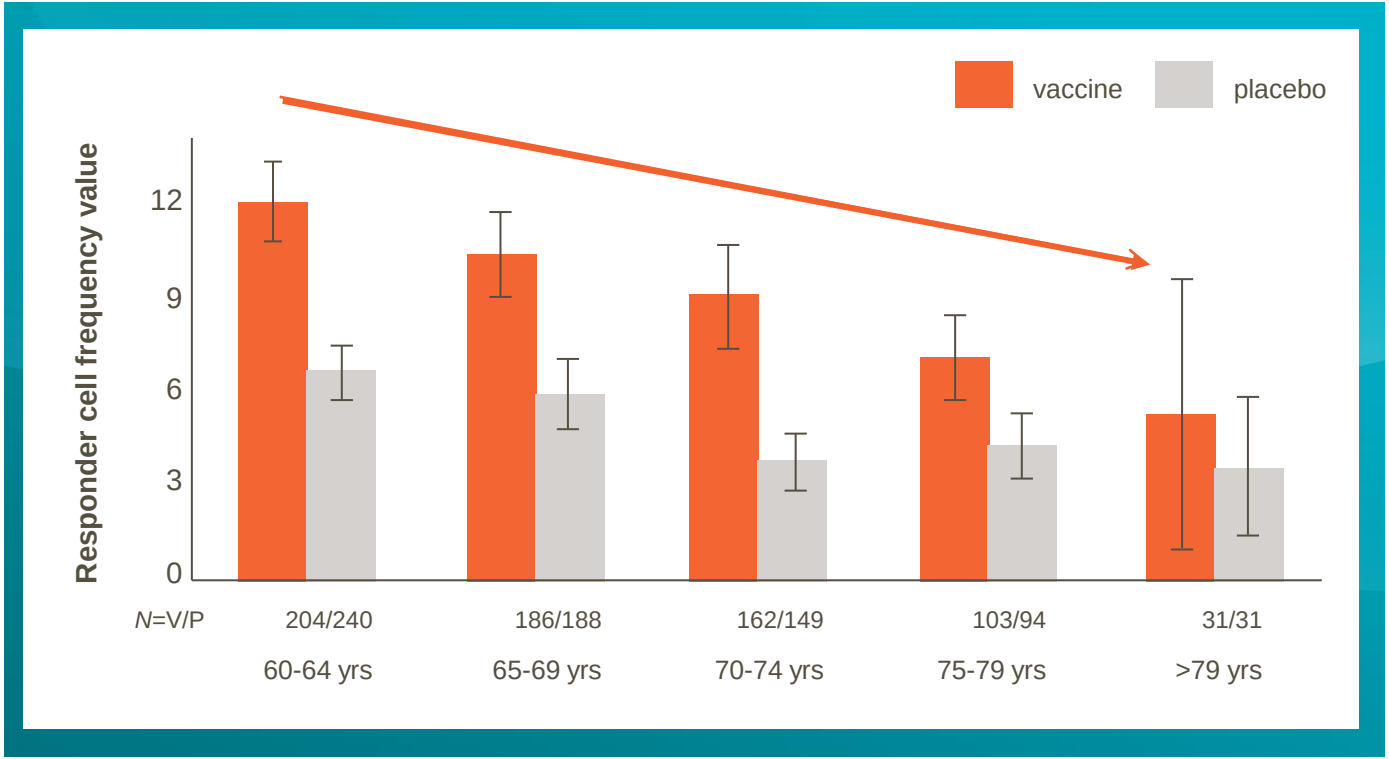
Shingrix - Immune response across age segments



Chlibek *et al*. J Infect Dis 2013; 208:1953-61

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on clinical trials.

Existing vaccine - Immune response across age segments

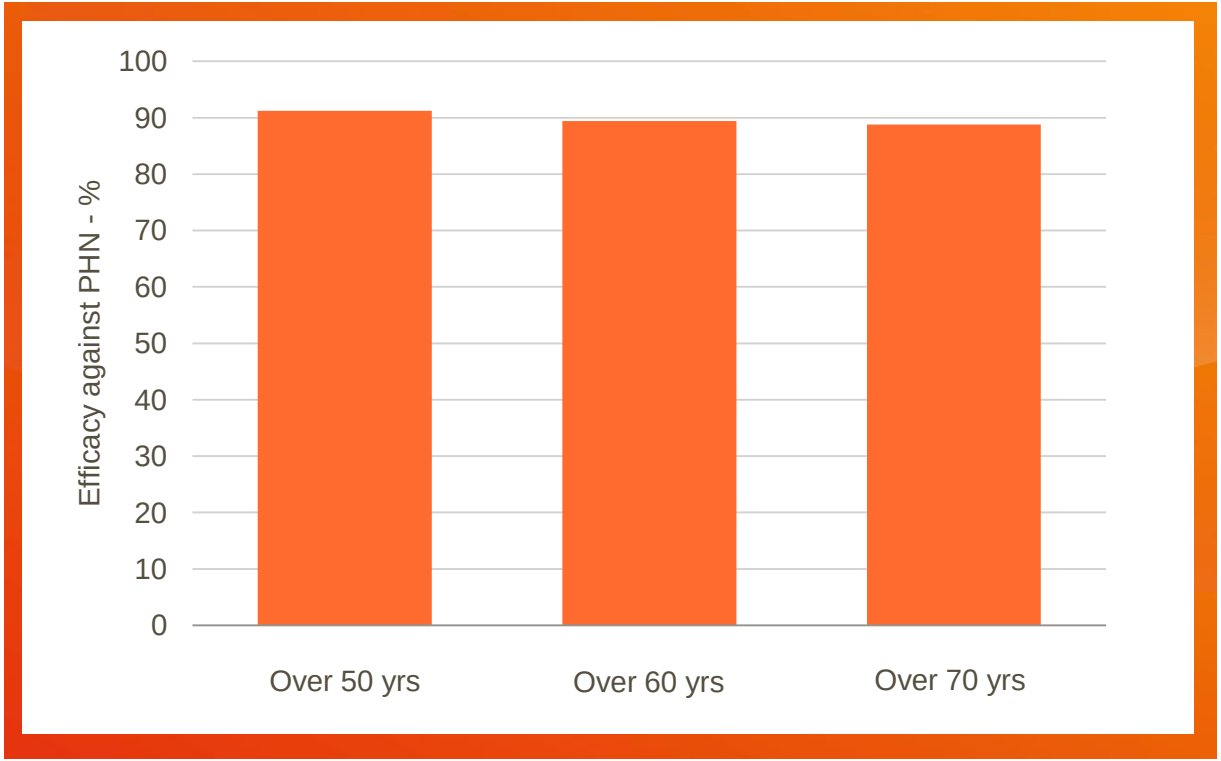


Levin *et al*. J Infect Dis 2008; 197:825–35

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Shingrix - Efficacy against PHN

PHN: post herpetic neuralgia, a severe complication of zoster

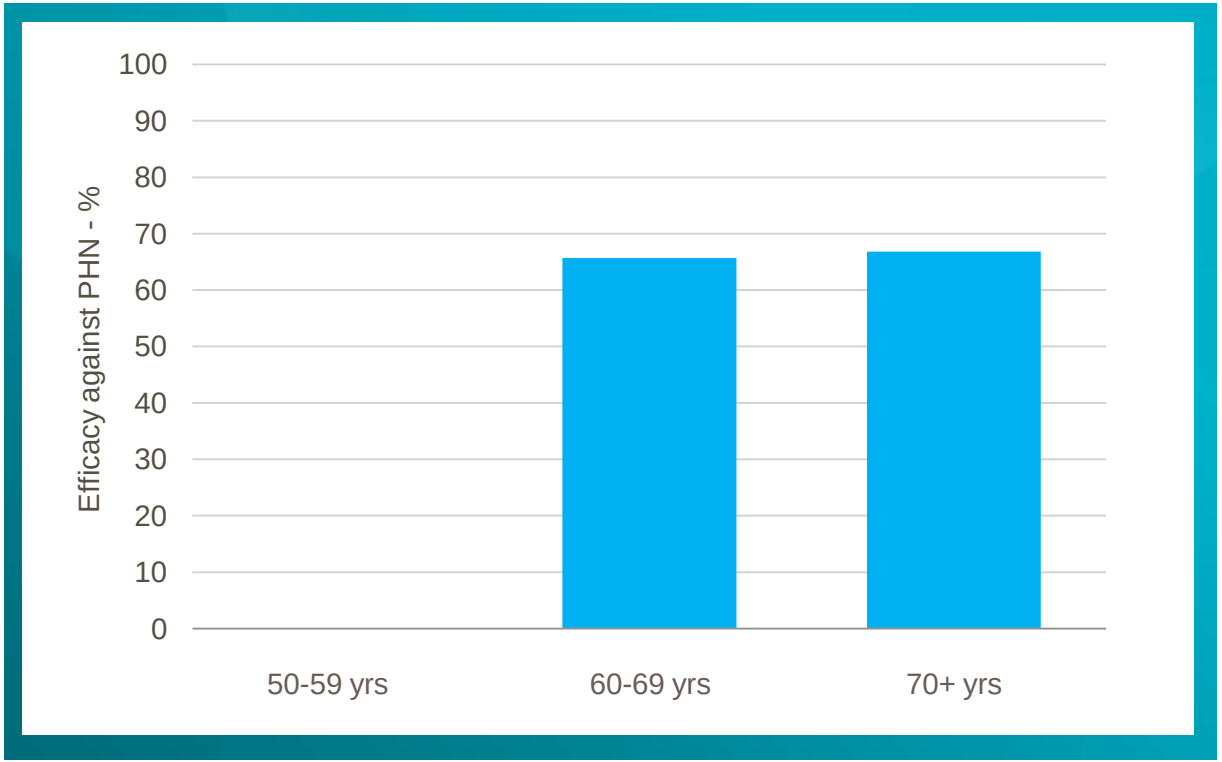


ZOE-50 and ZOE-70 pooled analysis – unpublished data

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on ph III clinical trials.

Existing vaccine - Efficacy against PHN

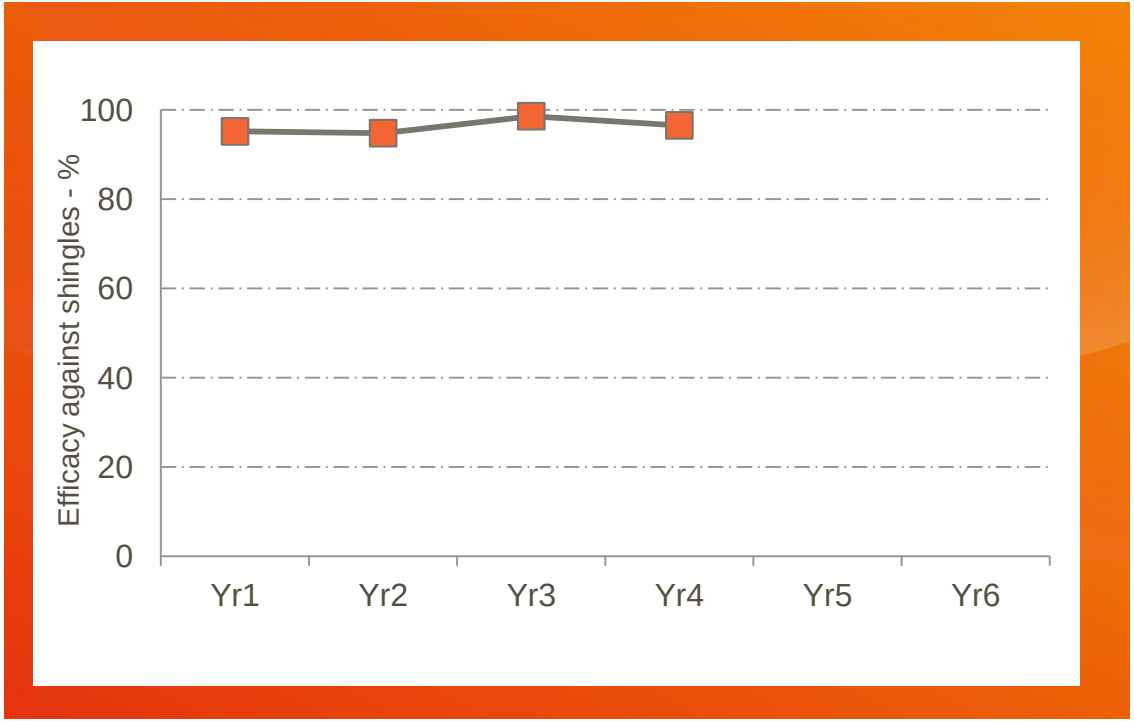
PHN: post herpetic neuralgia, a severe complication of zoster



Zostavax US PI; Oxman *et al*. N Engl J Med 2005

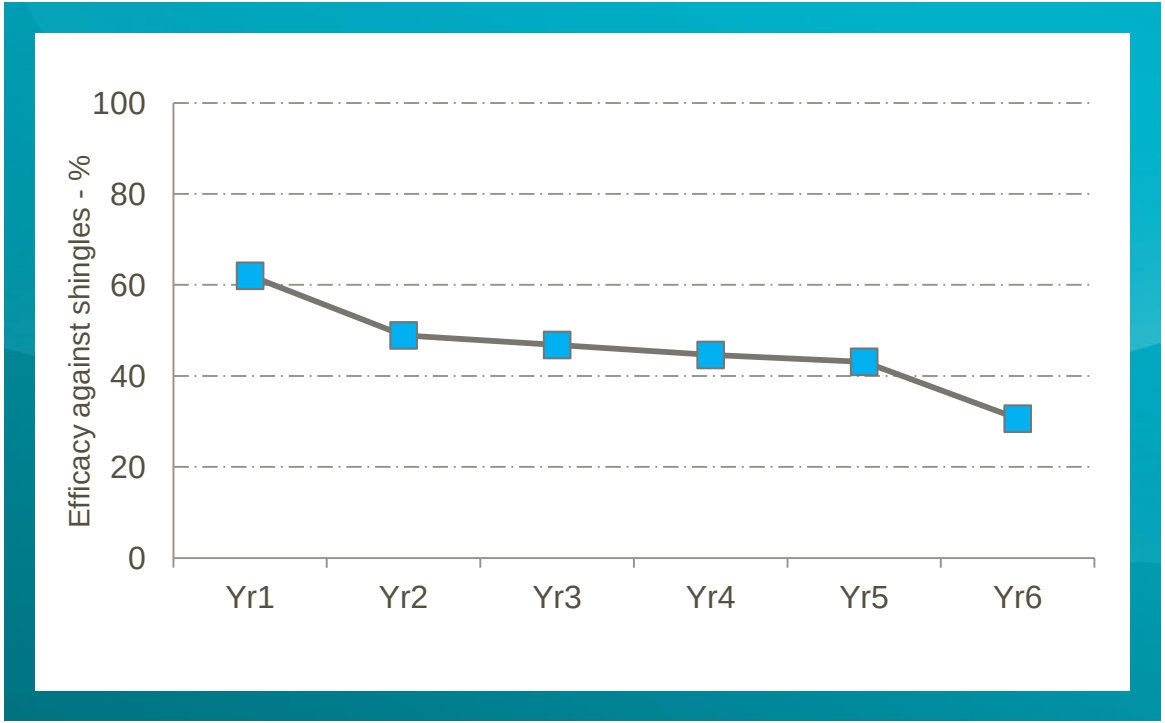
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Shingrix - Duration of protection against shingles



ZOE-50 statistical report – unpublished data
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on ph III clinical trials.

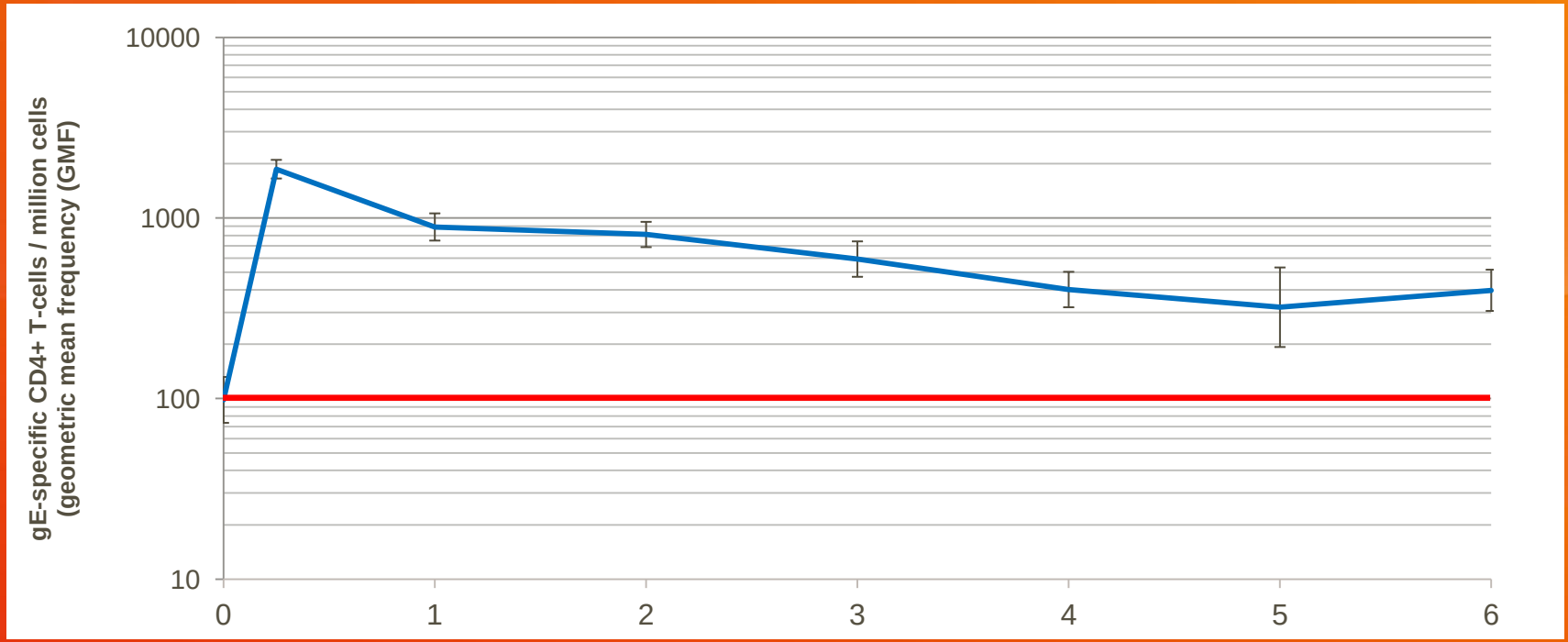
Existing vaccine - Duration of protection against shingles



Morrison *et al*. Clin Infect Dis 2015; 60: 900-909
Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Zostavax data based on published data.

Immune response persistency is a good predictor of duration of efficacy

Shingrix immune response



Chlibek *et al*. Vaccine 2015 doi:10.1016/j.vaccine.2015.09.073

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on clinical trials.

Shingrix: a potentially significant advance in vaccination to prevent shingles

High overall vaccine efficacy across identified age groups, including oldest persons

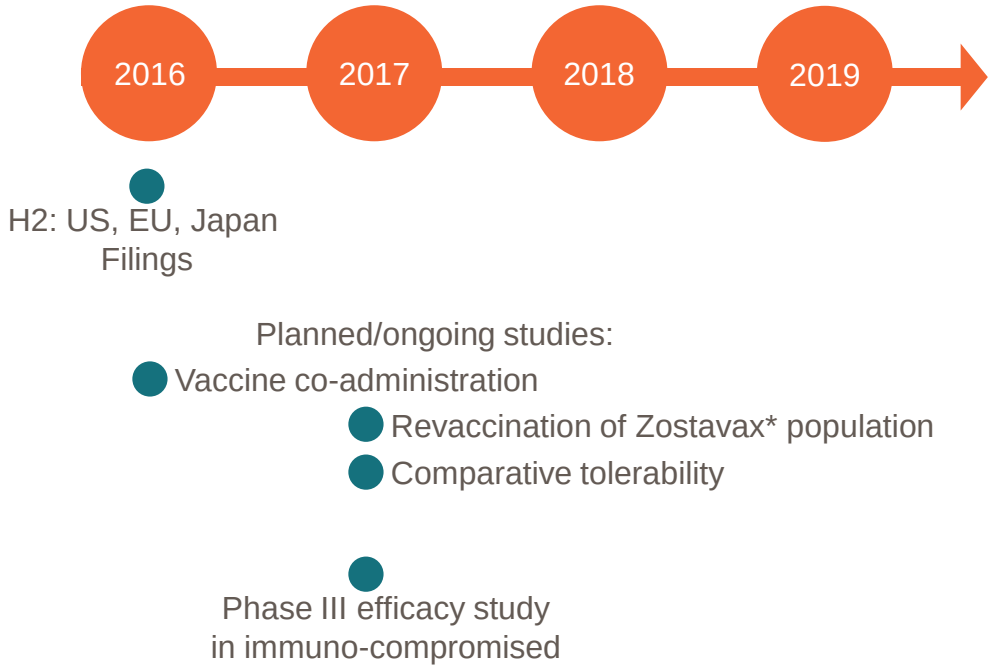
Persistence of vaccine efficacy up to 4 years across all ages

Six-year persistence of immune response, modeled to persist above baseline for at least 15 years (based on 6 year data)

Clinically acceptable reactogenicity

AS01 adjuvant = new platform for elderly vaccines

Annual capacity of ~25-30m doses by 2020



*Zostavax is a trademark of Merck & Co

Not based on head to head data; Shingrix™ and Zostavax™ have not been tested head to head. Shingrix data based on clinical trials.

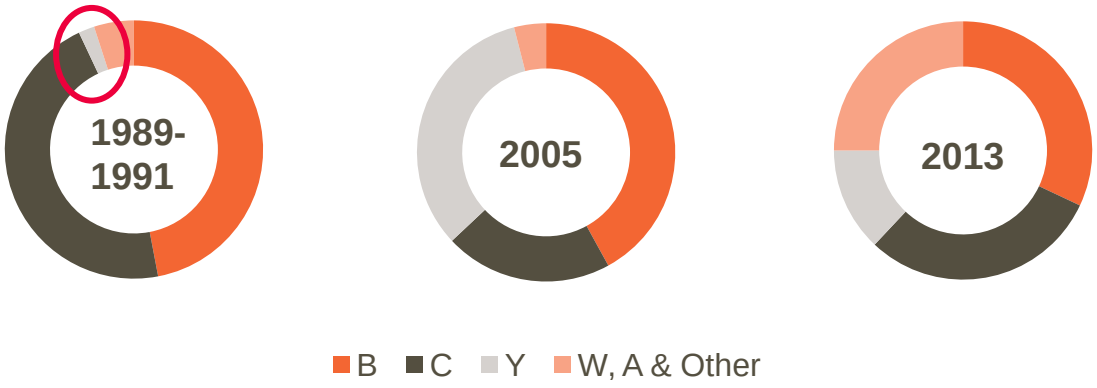
Meningococcal Meningitis

Meningococcal disease: evolving and unpredictable epidemiology – requires combination vaccine

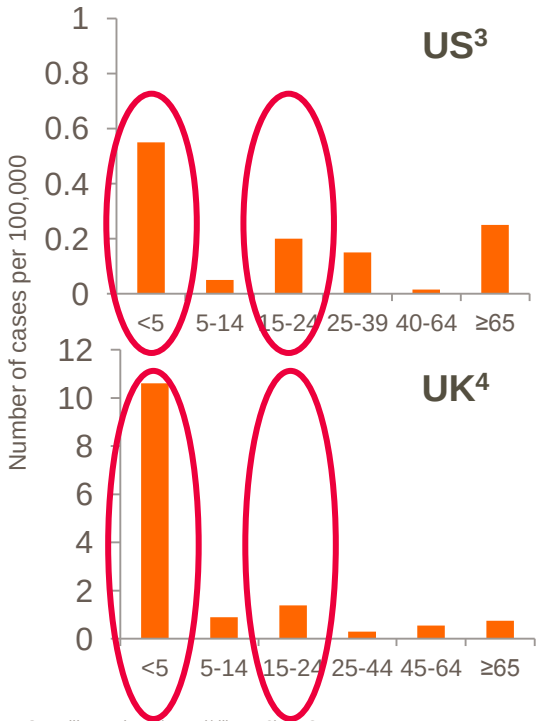
~139 million annual global birth cohort [1]

~4m US, ~5m EU, ~130m ROW

Changes in serogroup distribution in US over time[2]



Disease incidence by age (2012)



Sources: 1) CDC http://goo.gl/RykLaI; Eurostat http://goo.gl/3wp9pp; UNICEF http://goo.gl/DD8pXp 2) Jackson & Wenger MMWR 1993 http://goo.gl/fsbbBz; Active Bacterial Core Surveillance: http://goo.gl/riji5X 3) CDC http://goo.gl/PPtAEj; US Census Bureau https://goo.gl/liNpPU 4) UK.gov https://goo.gl/NxThrj Office for National Statistics http://goo.gl/GJLRpX

Most advanced meningitis vaccines portfolio, including candidate pentavalent

Menveo™

- MenACWY tetravalent vaccine
- Approved in US and EU (2010)
- ACIP recommendation for adolescents
- Approved in 64 countries
- 2015 sales (Mar – Sept): £135m

Bexsero™

- MenB vaccine
- Approved in US in 2015 (adolescents) and EU (2 months old and above)
- ACIP category B (permissive) recommendation
- Approved in 38 countries
- 2015 sales (Mar – Sept): £78m

MenABCWY

- Candidate pentavalent combination vaccine for adolescent in US
- Most advanced in development
- Phase III start in 2017
- US filing expected in 2020

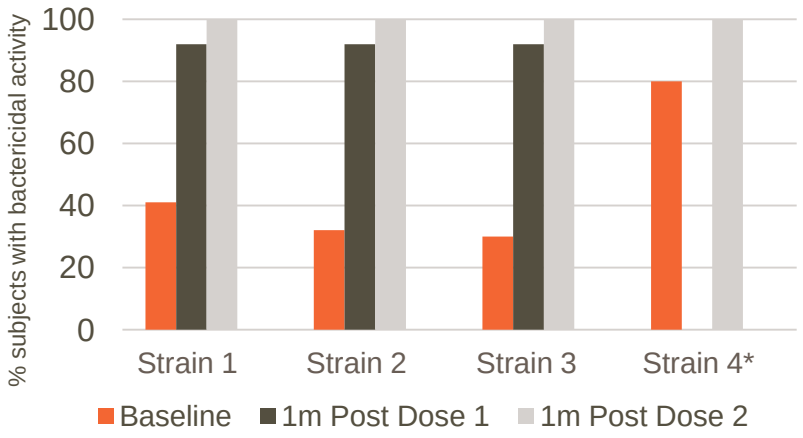
Meningitis portfolio expected to contribute ~1/3 of 2020 sales growth targets for GSK vaccines

Bexsero: multi-component antigen composition adds value, differentiation

Bexsero

– 4 antigens composition

– 2 dose regimen



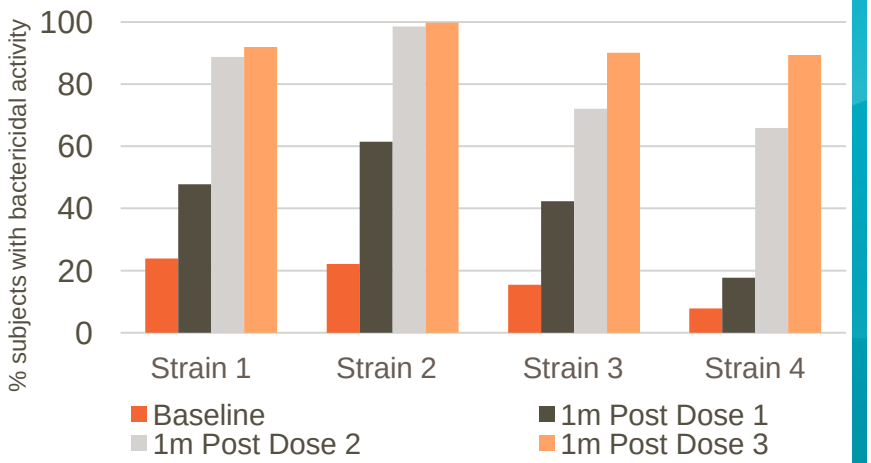
Sources: Santolaya *et al*. Hum Vac & Imm 2013 http://goo.gl/8oWB4P; * Strain 4 GSK data on file. Post hoc assays on a subset

Competing vaccine for MenB

Competing vaccine

– 1 antigen composition with 2 variants

– 3 dose regimen



ClinTrial.gov, study NCT01299480 https://goo.gl/Eqbmph

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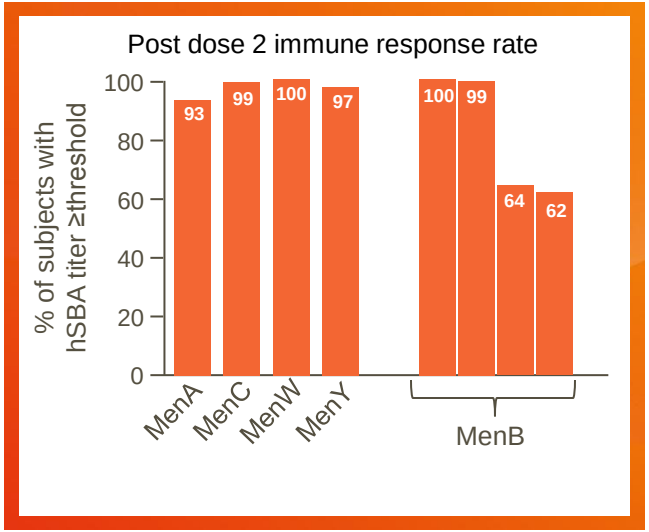
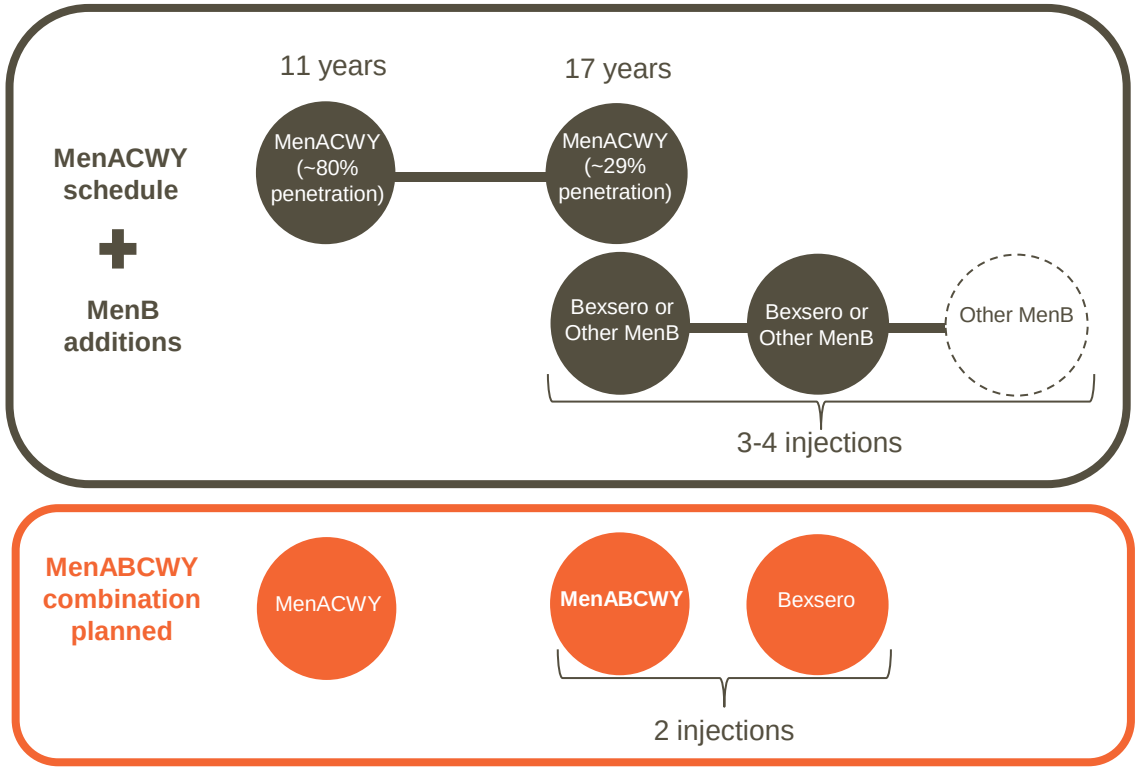
MenABCWY Phase III starts in 2017

- US focused development
- 1 dose adolescent booster
- Phase III programme start in 2017
- Filing expected 2020 for adolescents previously immunised for MenACWY





Saez-Llorens X *et al*. Hum Vacc Imm 2015 http://goo.gl/PXXRs6; GSK data on file. CDC MMWR: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6429a3.htm#tab1

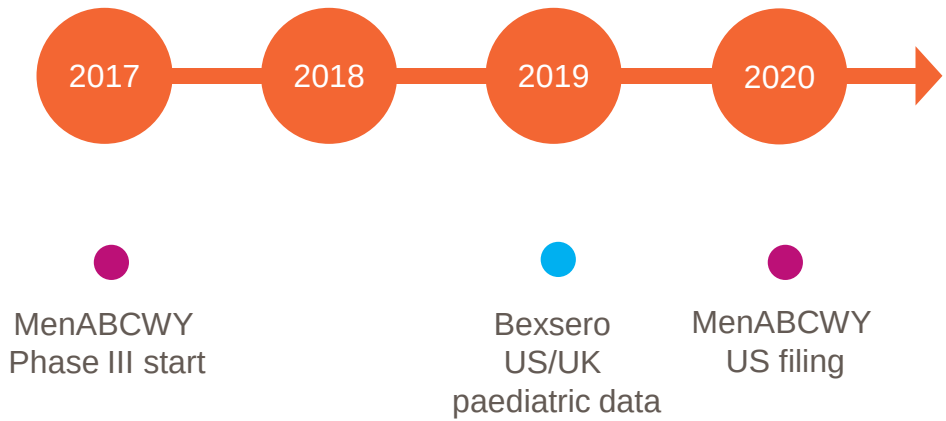
Meningitis portfolio presents significant opportunity

GSK has most advanced and comprehensive portfolio for meningitis vaccines

Bexsero demonstrated significant public health benefit, could drive further UMV recommendations

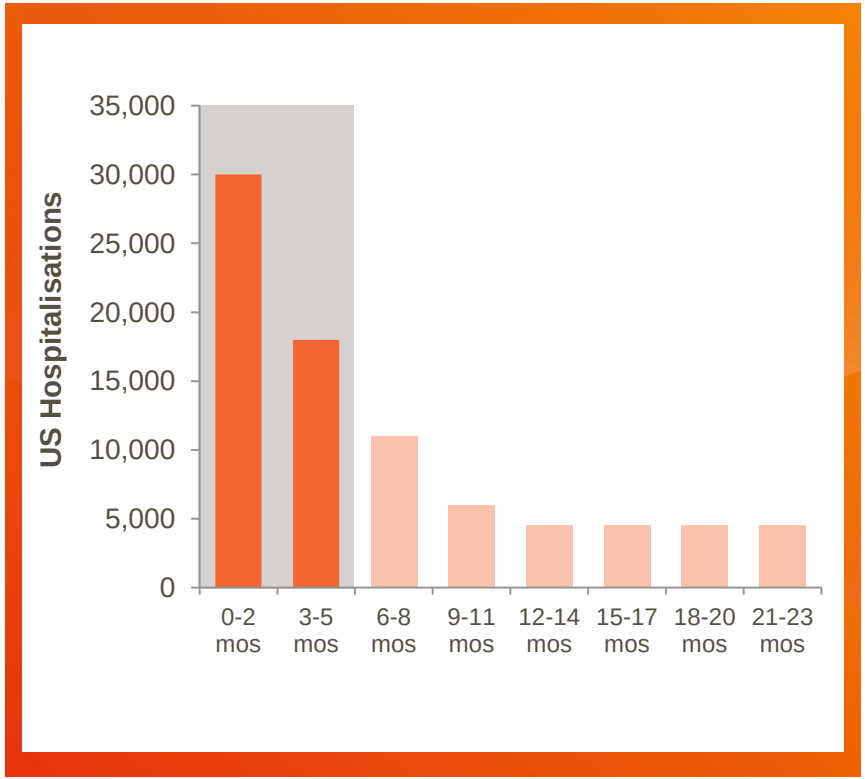
Combination approach is optimal option for prevention

Bexsero capacity ~25m doses in 2018



Respiratory Syncytial Virus (RSV)

Period of most severe RSV cases for young infants occurs from birth to 12 months



Paramore, Pharmacoeconomics 22:274-285, 2004

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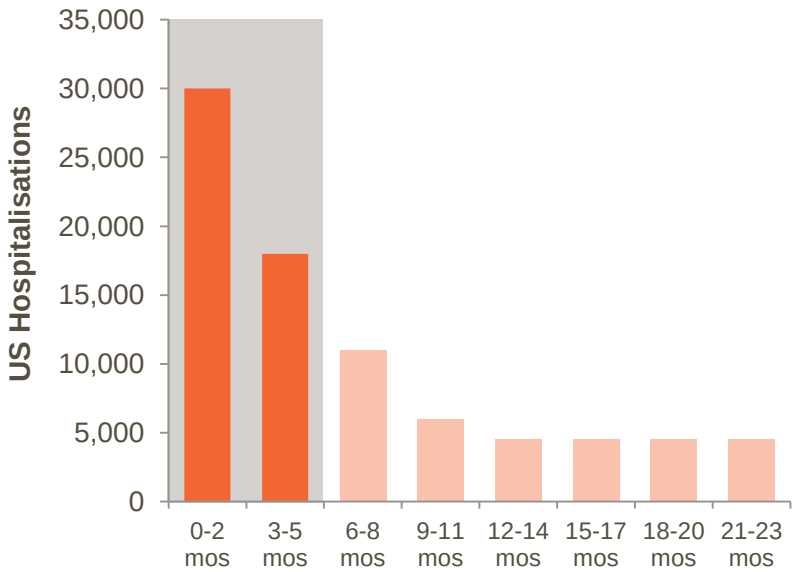
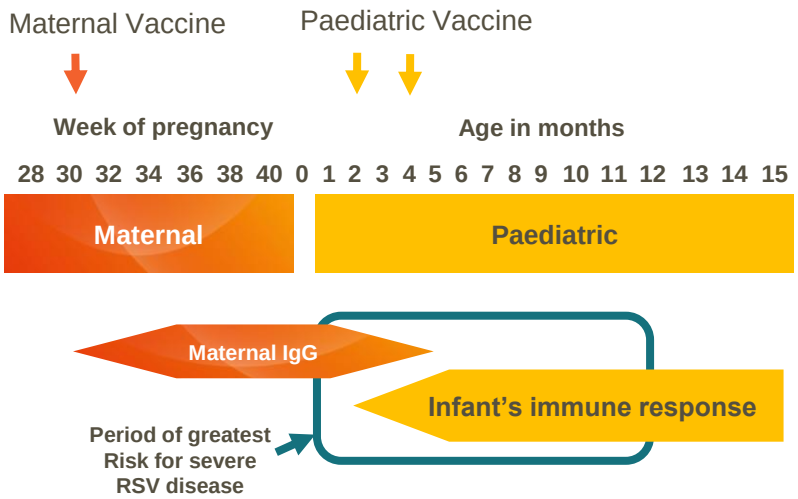




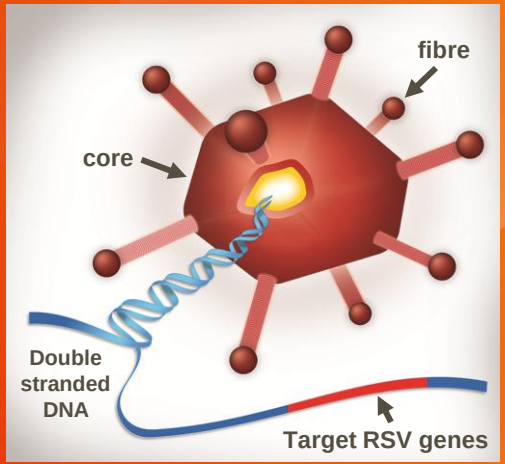
Paramore, Pharmacoeconomics 22:274-285, 2004

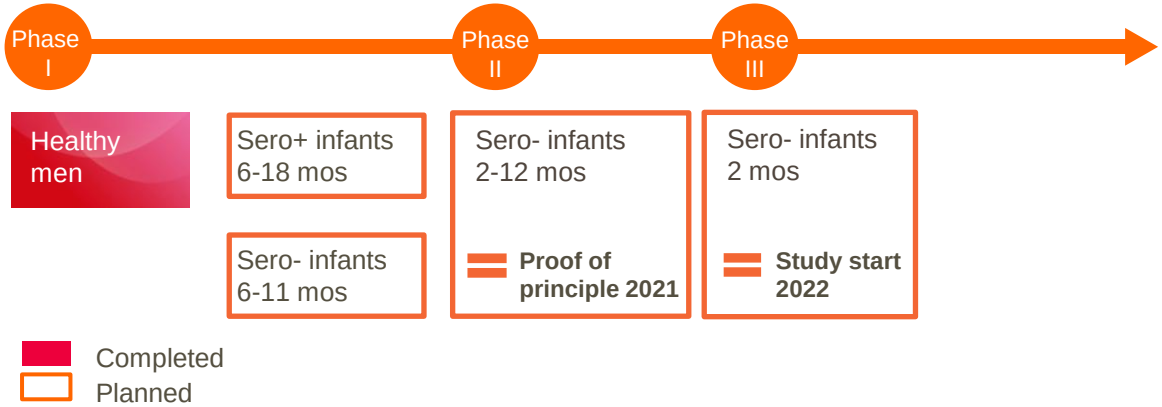
Candidate paediatric RSV vaccine, a novel approach

Genetically engineered recombinant CHAd155

Same vector used in ebola vaccine

Non-alum composition

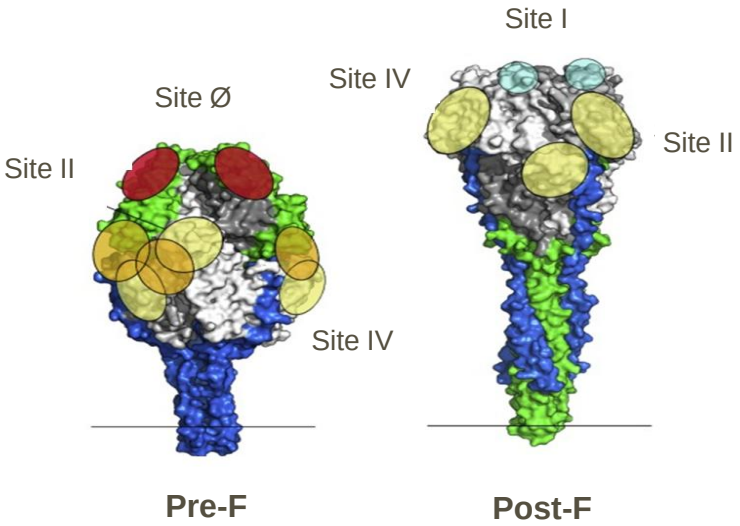




Novel candidate RSV maternal vaccine approach

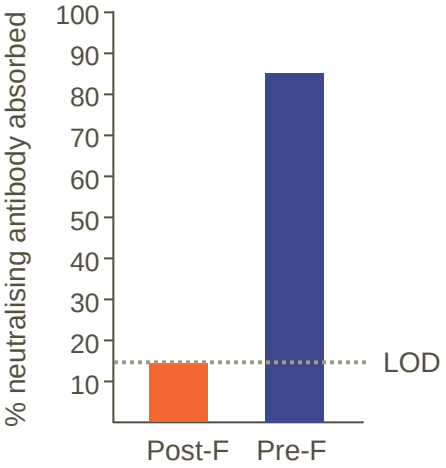
For RSV F protein, the correct antigen structure is critical

Pre-F absorbs out neutralising RSV antibodies more than 10x better than Post-F and induces potent antibody responses in humans



Graham B et al., Current Opinion in Immunology 35; 30-38, 2015

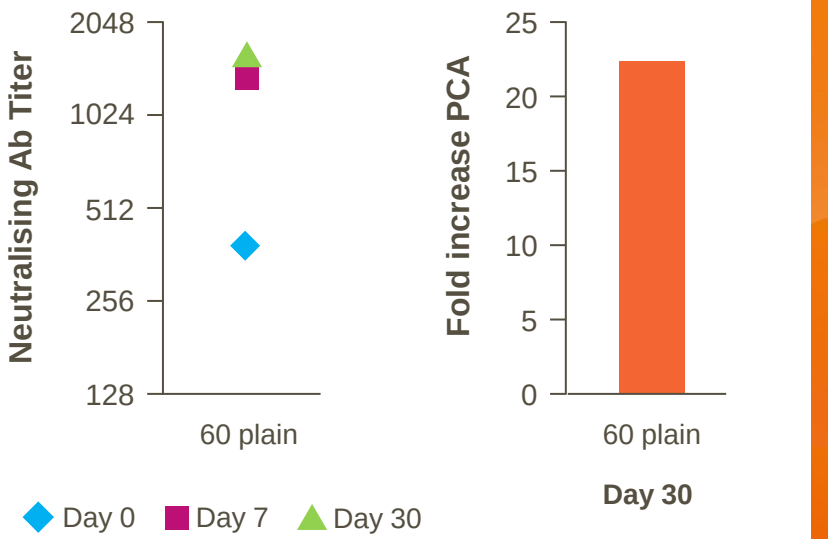
Absorbtion with Pre-F but not Post-F depletes neutralising IgG from convalescent serum



GSK preclinical data, unpublished

Stabilised Pre-F generated high titers by Day 7 and potent boost of PCA without adjuvant

GSK Pre-F

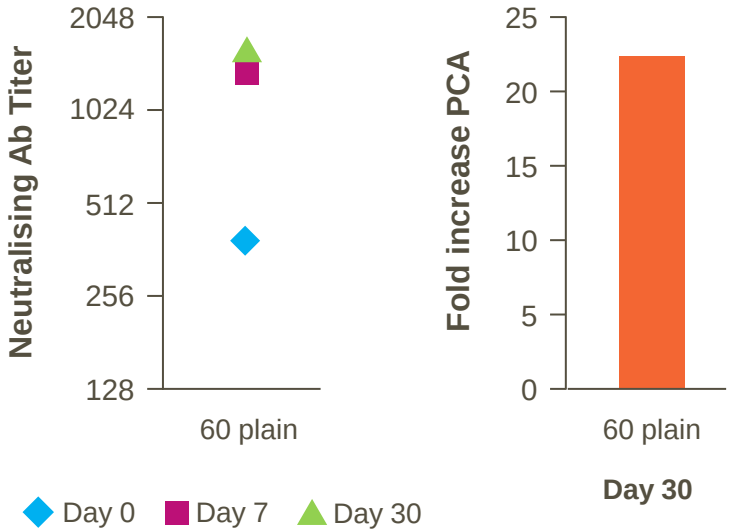


>20 fold PCA increase after single dose without adjuvant

GSK internal data, unpublished

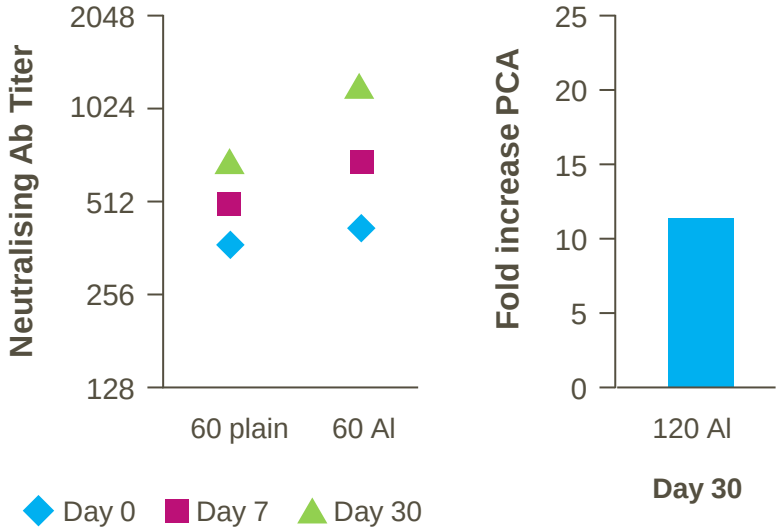
Stabilised Pre-F generated high titers by Day 7 and potent boost of PCA without adjuvant

GSK Pre-F



>20 fold PCA increase after single dose without adjuvant

Post-F

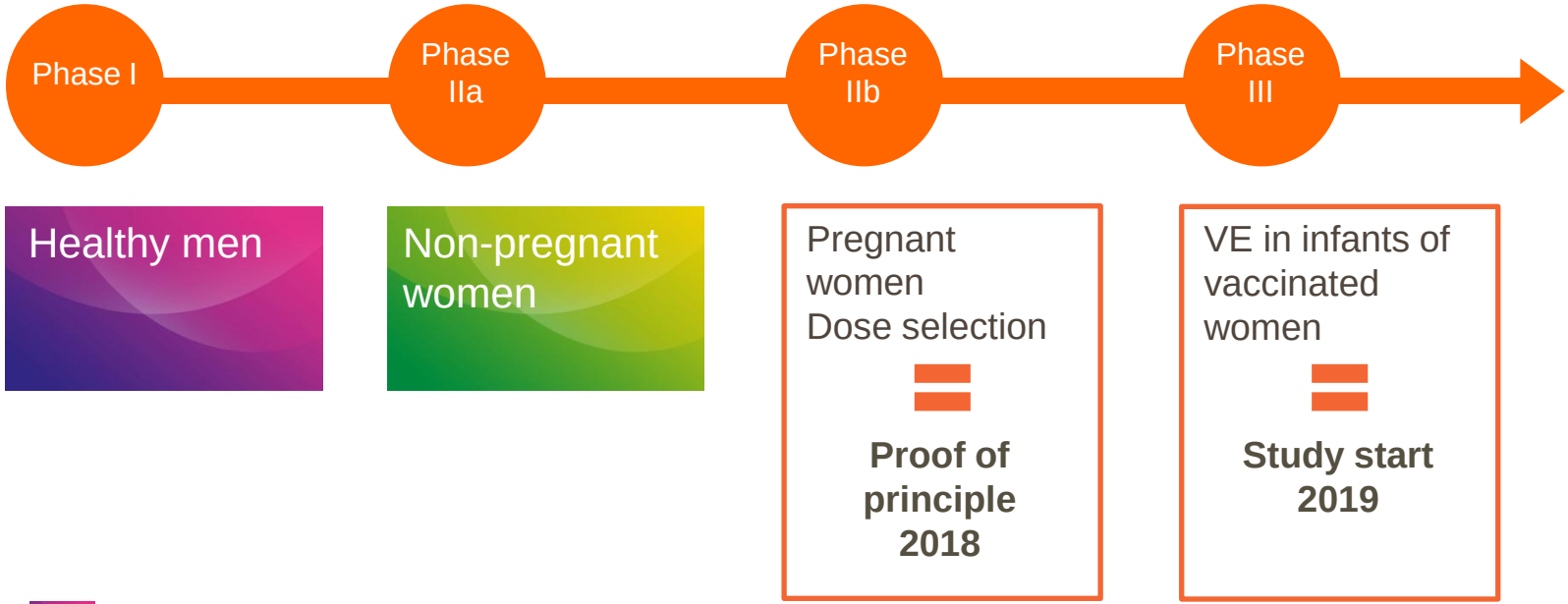


>10 fold PCA increase requires 120 ug + adjuvant

GSK internal data, unpublished

Glenn GM, J Infect Dis. 2015 Aug 10. pii: jiv406. [Epub ahead of print] (data on 60 ug with/without alum)
Presentation by Novavax at World Vaccine Congress April 2015 (data on 120 ug/alum dose PCA)

Novel candidate RSV maternal vaccine approach



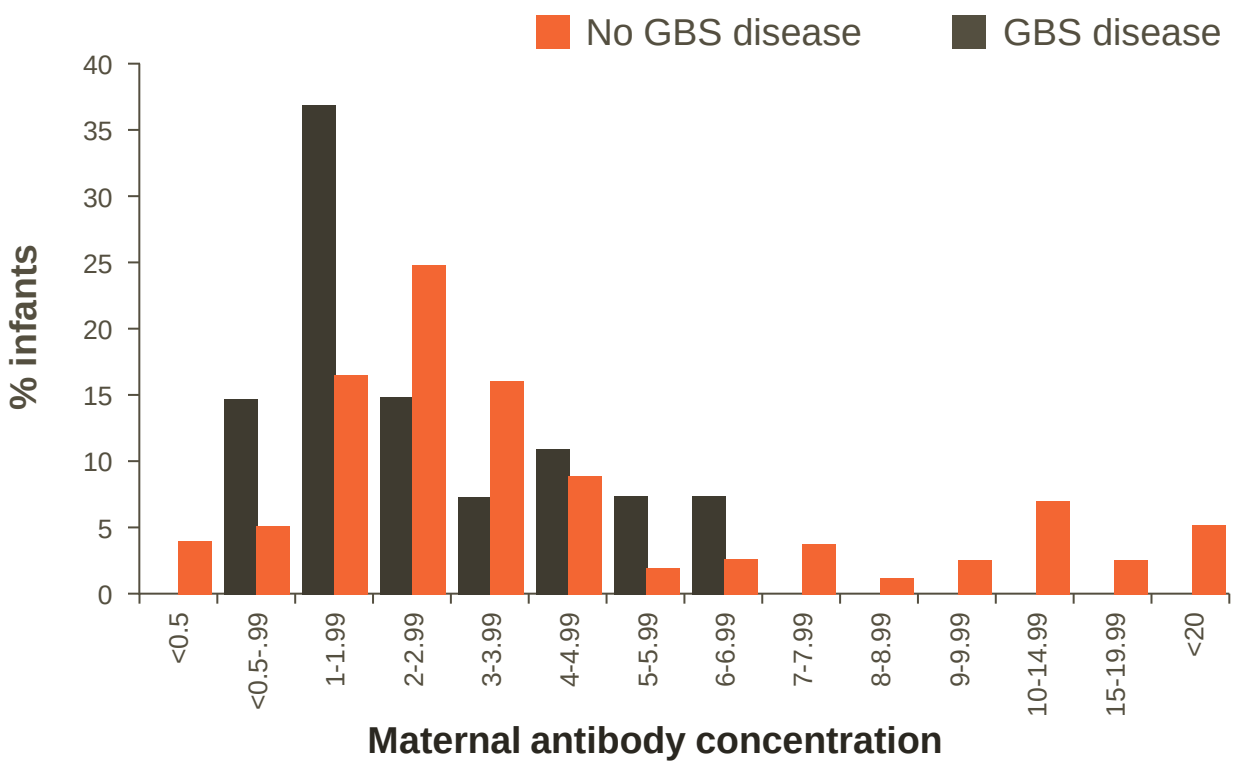
Group B Streptococcus (GBS)

Maternal immunisation for GBS

The leading cause of pneumonia, meningitis and sepsis in neonates

1 in 2500 of babies develop GBS disease despite antibiotic prophylaxis of colonised mothers

No vaccine is available



Gibbs, Obstet Gynecol, 104;1062-1075, 2004

Lin FY *et al*. J Infect Dis. 2004;190:928-934

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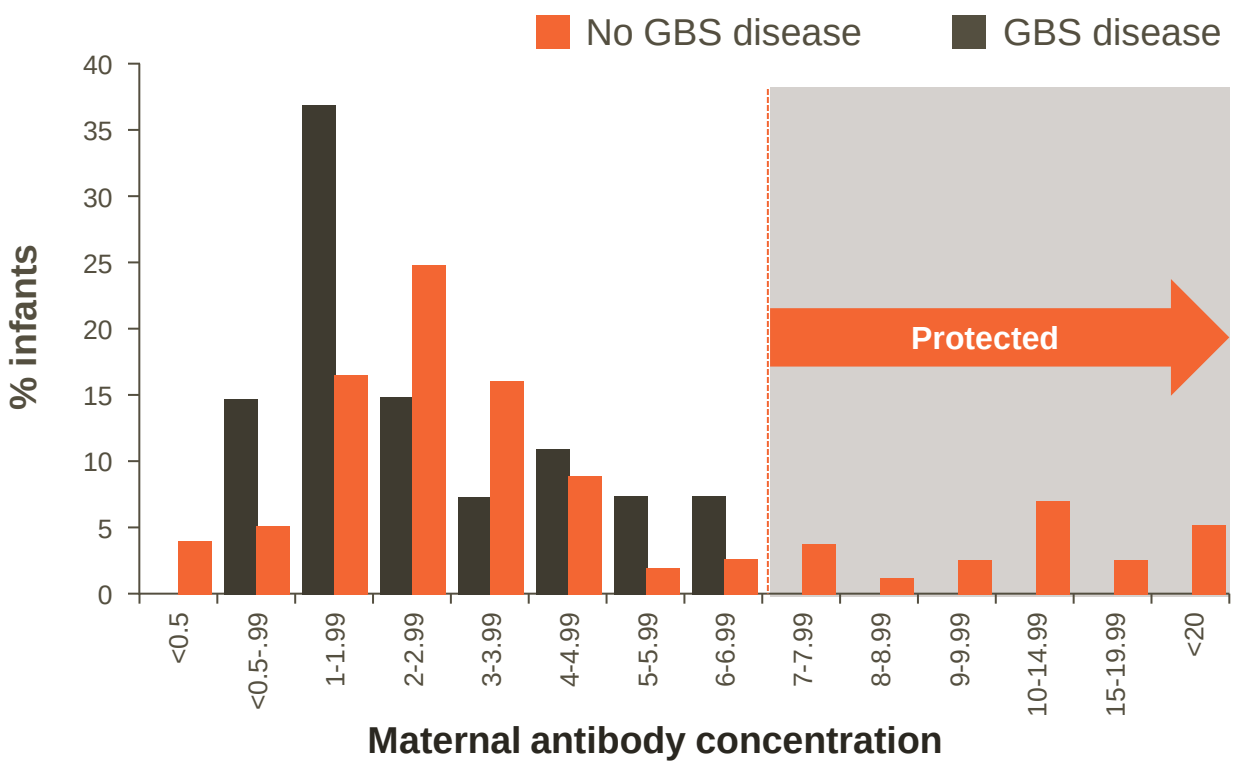


Gibbs, Obstet Gynecol, 104;1062-1075, 2004

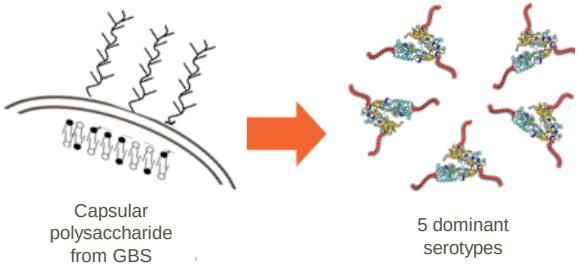
Lin FY *et al*. J Infect Dis. 2004;190:928-934

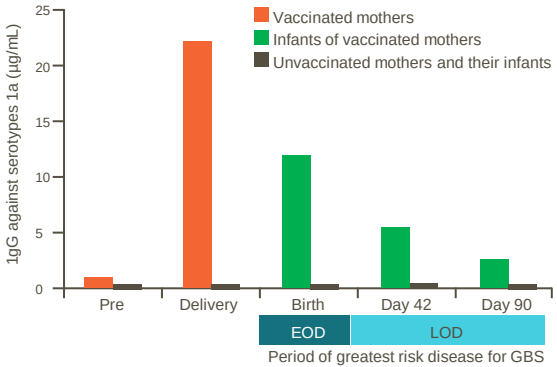
GBS maternal immunisation expanded programme

Based on Capsular polysaccharide (CPS) from 5 dominant GBS serotypes conjugated to a protein carrier

Designed to help protect against >95% of globally prevalent serotypes

Phase II trivalent vaccine antibody data shows response at period of greatest risk



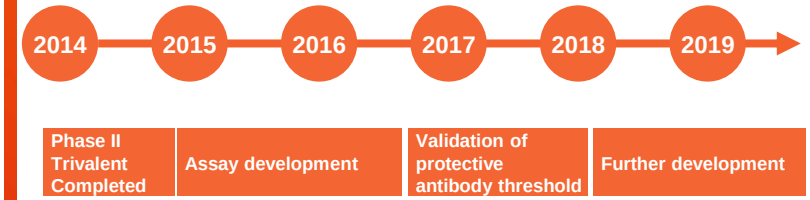


Large Phase II trivalent completed

Decision to expand composition to pentavalent

Validate correlate of protection with FDA

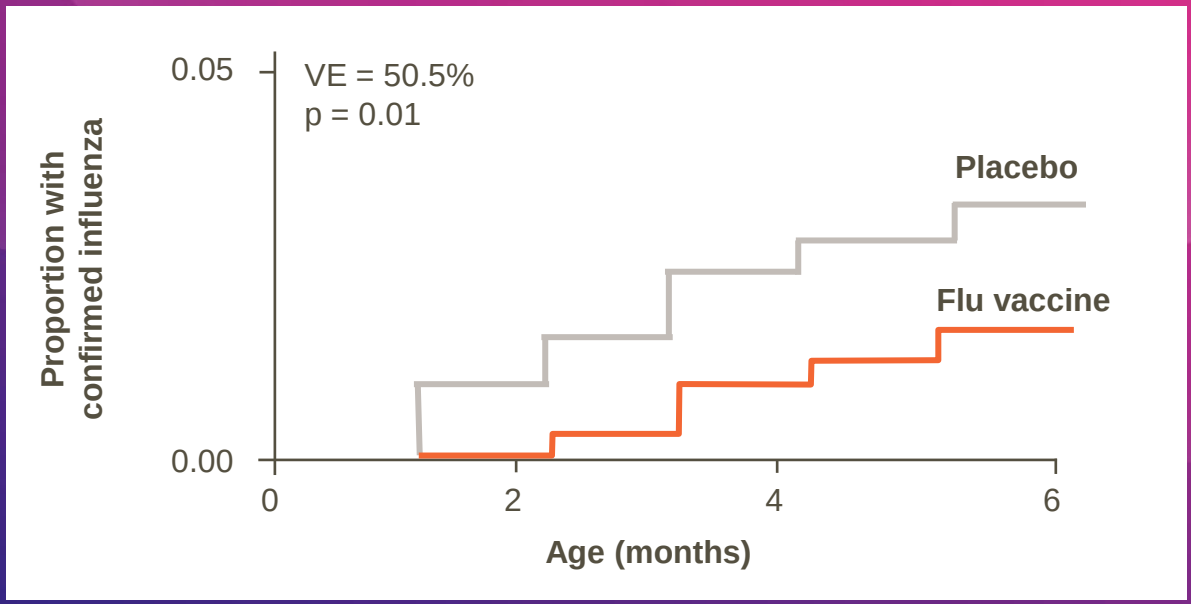
Clinical development plan to be agreed with FDA



Le Doare, Vaccine 31(4) D7, 2013 ; GSK clinical data, unpublished

Maternal immunisation validated strategy to prevent diseases that afflict very young infants

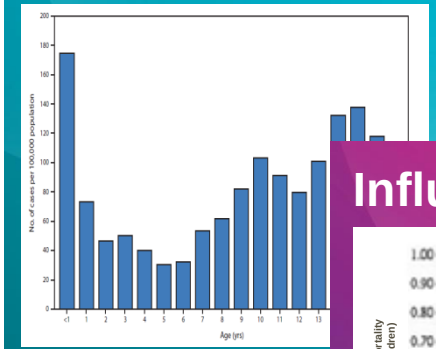
Infants protected by maternal flu vaccination



Source: N Engl J Med. 2014 Sep 4;371(10):918-31

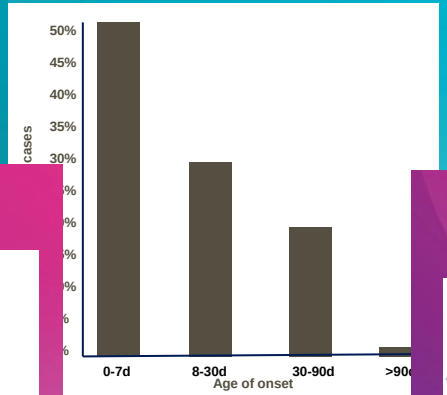
GSK potential maternal immunisation vaccine portfolio

Pertussis



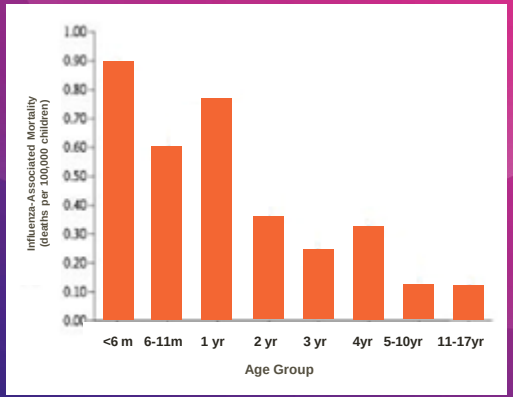
Winter K, MMWR 63:1122-1140,2014

GBS



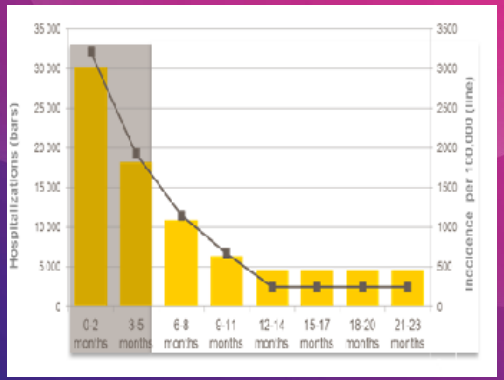
Melin, Clin Microbiol Inf, 17;1294-1303, 2011

Influenza



Bhat N Engl J Med.353:2559-67, 2005

RSV



Paramore, Pharmacoeconomics 22:274-285, 2004

A new vaccine concept

Testing hypothesis for a COPD vaccine

Epi studies show association between lung infections & COPD exacerbations[1,2]

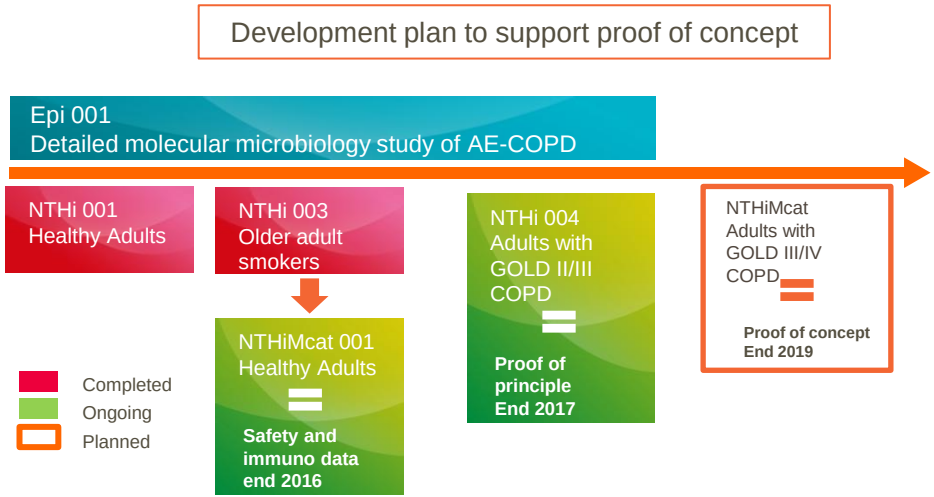
NTHi and Mcat: 2 lung pathogens potentially associated with 30-50% of COPD exacerbations[1,2]

75% effective vaccine could eliminate 20-35% of exacerbations

3 antigen vaccine covering NTHi using AS01 adjuvant in Phase II POC trial

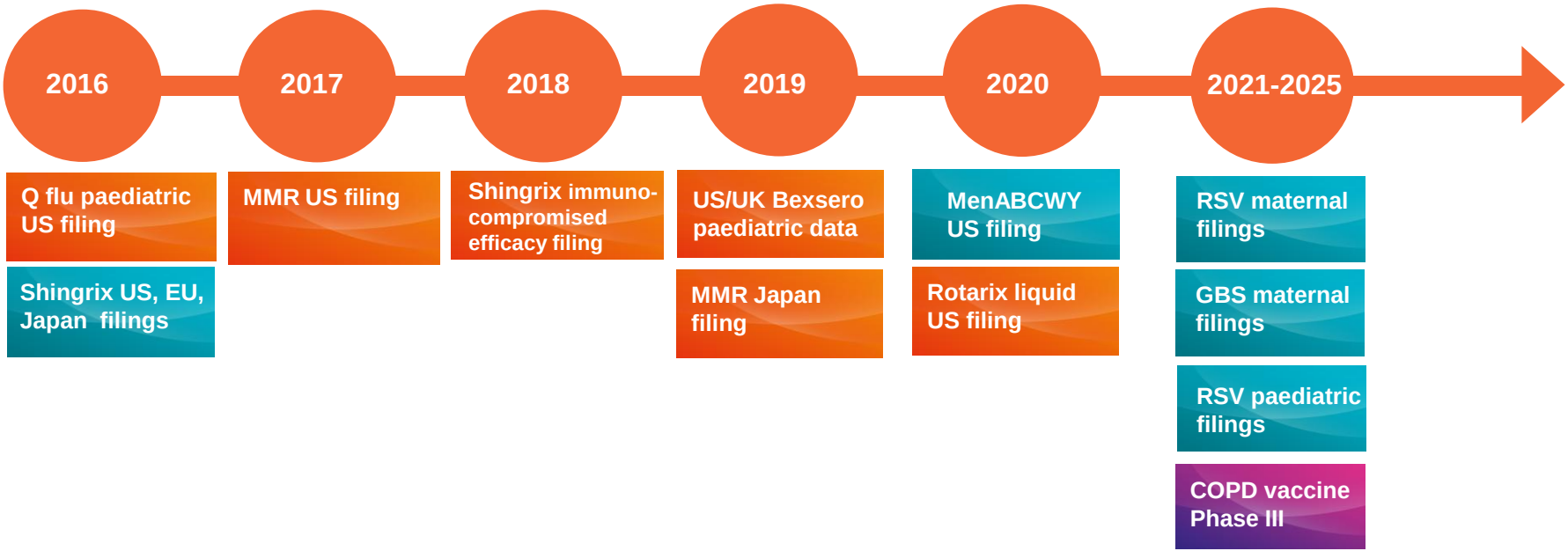
Key POC data in COPD patients = 2017

Phase III to be defined based on POC data

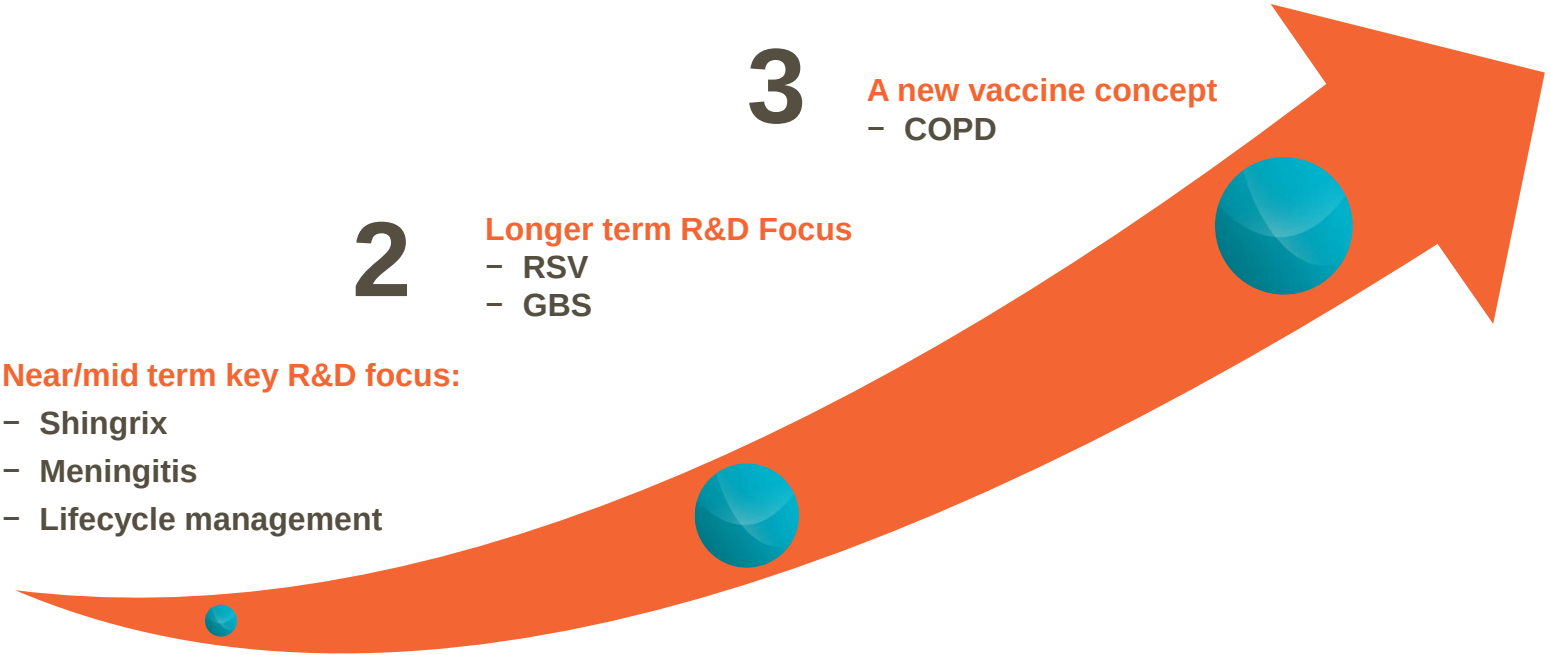


1GSK unpublished data EpiHip001. 2Sethi *et al*. N Engl J Med. 2002 Aug 15;347(7):465-71.

Data and planned filings support positive growth outlook



R&D programmes to deliver near-term growth with significant future opportunities and novel immunisation platforms



1

Near/mid term key R&D focus:

- Shingrix
- Meningitis
- Lifecycle management

2

Longer term R&D Focus

- RSV
- GBS

3

A new vaccine concept

- COPD

Introducing the Vaccines panel

GSK's leading scientists in vaccines

Alain Brecx

Vice President
Vaccine Development Lead - Zoster

Emmanuel Hanon

Senior Vice President,
Head of Vaccines R&D

Giovanni Della Cioppa

Vice President,
Head of Siena R&D Centre

Rip Ballou

Vice President
Head of Rockville R&D Centre

Q&A

Immuno-Inflammation

Immuno-Inflammation areas of focus

Immune modulation to alter disease course, induce and sustain remission

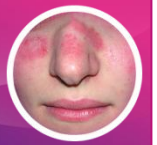
Rheumatoid Arthritis (RA)

- Circa 5.3m RA patients in G7 countries[1]
- Aging demographics a major driver of market growth
- Highly debilitating; associated with higher mortality & progression to other serious conditions
- Significant medical needs for remission-inducing therapies & for patients resistant to current standard of care

Osteoarthritis (OA)

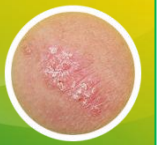
- Circa 72m OA patients in G7 countries; largest proportion of musculoskeletal diseases[2,3]
- Aging demographics a major driver of market growth
- Major opportunity for a disease-modifying therapy
- Immune modulation offers opportunity to move from only alleviating symptoms of "wear and tear"

Systemic Lupus Erythematosis (SLE)



- Prevalence: 40 -100 out of 100,000 [4]; 9/10 sufferers are women in their 20s & 30s[4]
- Chronic disease with poor QoL, involving musculoskeletal, haematological, cutaneous & renal systems
- Mortality rate 3x higher than the general population, and 10x higher in under 40[5]
- Benlysta IV - 1st drug approved for SLE in 50 years (2011)

Other immune-mediated diseases

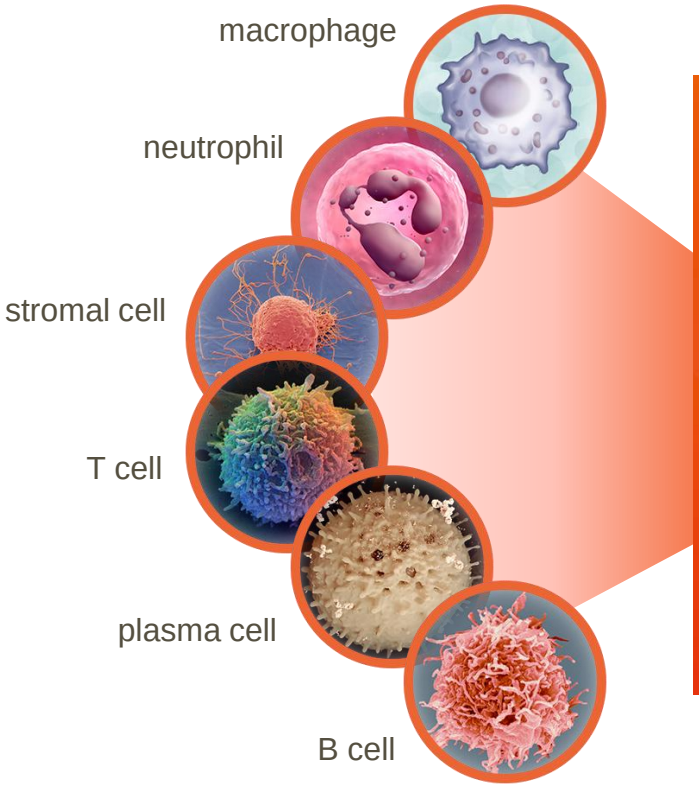


- Mechanisms are relevant for mainstream diseases e.g psoriasis, Crohn's disease & ulcerative colitis
- Opportunities exist to treat less common disease e.g. primary Sjögren's syndrome, systemic sclerosis & myasthenia gravis

[1] Decision Base Rheumatoid Arthritis 2015 ; [2] World Health Organisation 2010; [3] Decision Resources OA Pain 2012; [4] Danchenko N *et al*. Epidemiology of SLE: a comparison of worldwide disease burden. Lupus 2006; 15:308–318 [5] Bernatsky S, Boivin JF, Joseph L, *et al*. Mortality in systemic lupus erythematosus. Arthritis Rheum 2006; 54:2550–2557.; * Decision resources 2013 estimate

Immuno-Inflammation R&D strategy:

From symptomatic benefit to sustainable remission



GSK Pipeline

Targeted Biologicals

Targeted Small Molecules

Targeting Resistant Disease

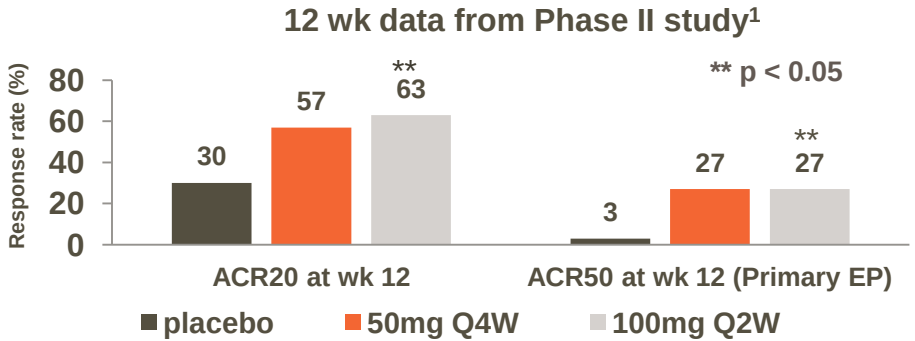
Early Intervention & Remission Induction

sirukumab: rheumatoid arthritis

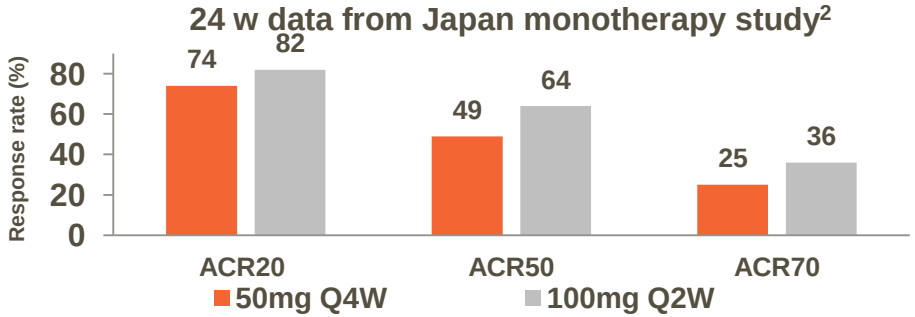
The anti-IL-6 class is the fastest growing of the biologicals in RA

- Collaboration with Janssen Biologics (Ireland)
- Low frequency sc dosing potential (monthly)
- Targets the cytokine
- Efficacy demonstrated in Phase II; consistent safety profile across doses
- >3000 patients in studies to date
- Phase III interim read-out, full read out expected by year end 2015
- Indication expansion: Phase III in Giant Cell Arteritis started screening. Phase II in asthma start in 2016

Status:	RA: Phase III
Indications:	RA (lead), GCA, asthma
Planned Filing:	RA 2016



[1]adapted from Smolen et al 2014 Ann Rheum Dis 73 (9)

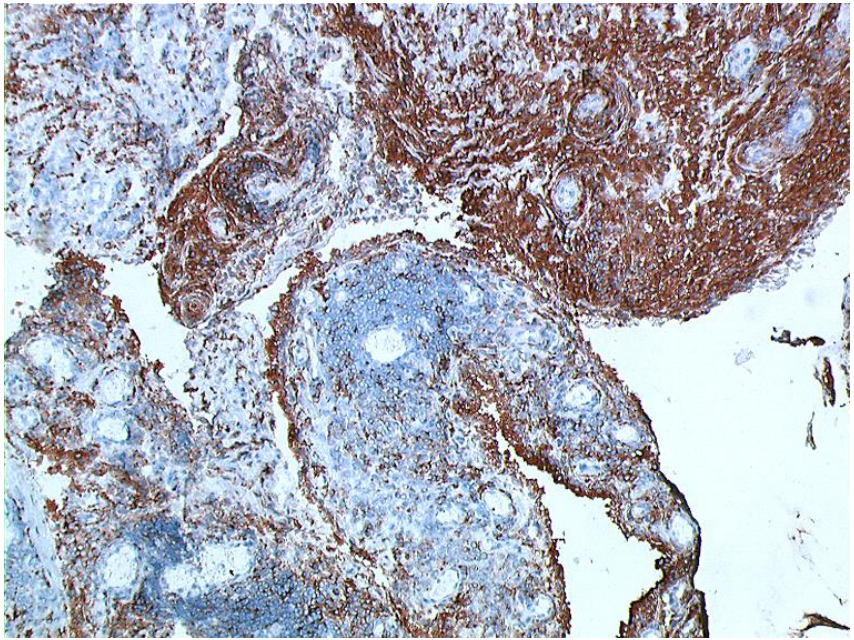


[2] ACR 2015 abstract #1672

Clinical improvement in RA is consistently associated with decreased macrophage infiltration

- Activated macrophages are abundantly expressed in early RA synovial tissue, representing the predominant cell type
- Reduction in macrophage infiltration correlates with improvement in disease activity scores[1,2]
- Macrophage is a primary cause of tissue destruction and affects many other cell types
- GM-CSF is important in every step of macrophage production and infiltration in the tissues

GM-CSF plays a key role in activation of macrophages at the site of injury or inflammation



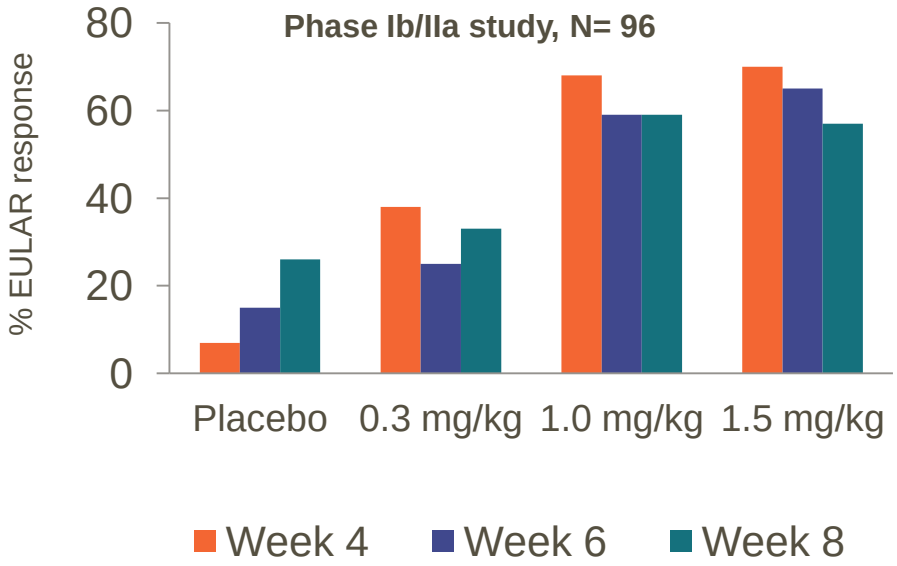
[1] Boumans MJ, *et al*. Arthritis Rheum. 2011;63:3187-94.
[2] Bresnihan B, *et al*. J Rheumatol 2009;36:1800-2.

GSK3196165 – aGM-CSF, targets key effector cells in RA

Aiming to induce remission in early rheumatoid arthritis

- In-licensed from MorphoSys AG
- Good magnitude of effect with fast onset of action and long duration post treatment
- Effect size appears similar or greater than anti-TNF
- Targeting the macrophage in early RA
- Potential for early use to induce remission
- BAROQUE (RA Phase IIb) ongoing. Initial clinical read-out 2016

% EULAR good/moderate response at 4 weeks: Rapid onset of action



Behrens, *et al*. Ann Rheum Dis. 2015;74:1058-64

Status:	Phase IIb
Indication:	Rheumatoid Arthritis
Planned Filing:	2021-2025

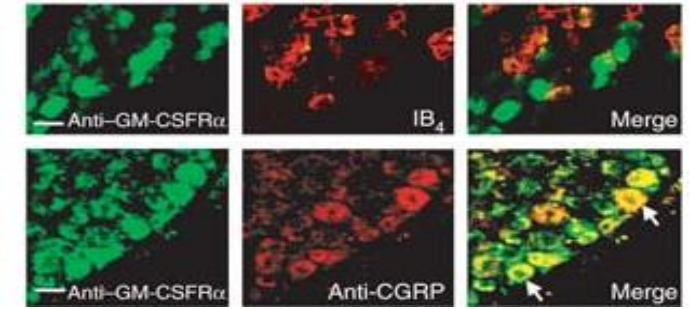
GSK3196165: Potential for disease modification & analgesic activity in hand osteoarthritis (HOA)

- The macrophage is a mediator of tissue destruction in OA
- aGM-CSF is effective in animal models of OA
- aGM-CSF rapidly reduces pain (through effect on nerves) in animal models of OA
- Hand OA presents unique clinical development path
- Phase II to start in 2016

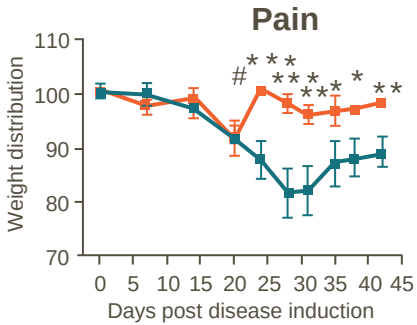
Status:	Phase II start 2016
Indication:	Hand OA
Planned Filing:	2021-2025

GSK3196165 in-licensed from MorphoSys AG

GM-CSF receptor expression on primary afferent nerve fibres in mouse tibial bone and periosteal nerves



M Schweizerhof *et al*. Nature Medicine 2009;15:802-807



* p<0.05,
** p<0.01,
*** p<0.001,
control vs. anti-GM CSF # p<0.0001, control and anti-GM-CSF vs. t=0 readings

Cook *et al*. Arthritis Res Ther. 2012;14:R199

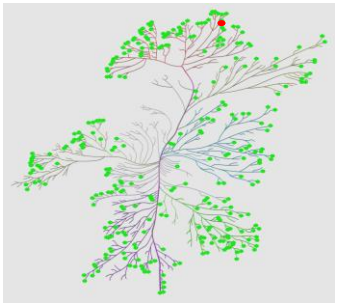
GSK2982772: RIP1 kinase inhibitor in the clinic

"a key regulator of inflammation, apoptosis and necroptosis, RIP1 is positioned at a strategic crossroads of multiple signalling nodes in the innate immune response".[1]

- New class, oral therapeutic
- World leading internal team
- Anti-TNF effect with additional protection against effects of cell death
- GSK2982772 well tolerated at all doses with robust target inhibition achieved
- Exquisite kinase selectivity
- Multiple potential indications

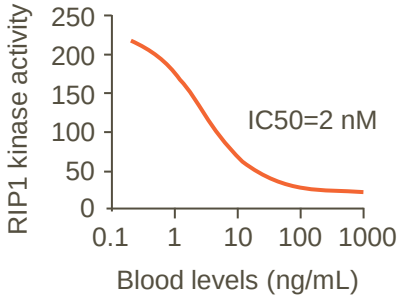
Status:	Phase I
Indications:	Rheumatoid arthritis, Psoriasis, Ulcerative Colitis
Planned Filing:	2021-2025

Kinome plot



GSK2982772 -most selective ATP competitive kinase inhibitor to advance into man

RIP1 kinase inhibition achieved in the clinic



Molecular Cell

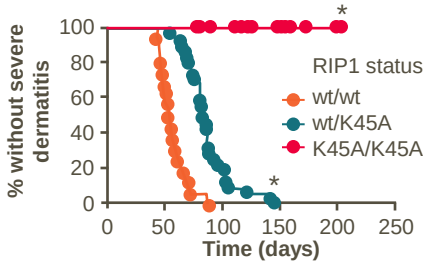
"NF-κB-Independent Role of IKKα/IKKβ in Preventing RIPK1 Kinase-Dependent Apoptotic and Necroptotic Cell Death during TNF Signaling"

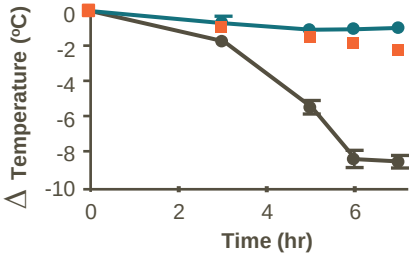
Authors: Yves Dondelinger, Sandrine Jouan-Lanhouet, Tatyana Divert, Emilie Theatre, John Bertin, Peter J. Cough, Piero Giansanti, Albert J.R. Heck, Emmanuel Dejardin, Peter Vandenabeele, Mathieu J.M. Bertrand

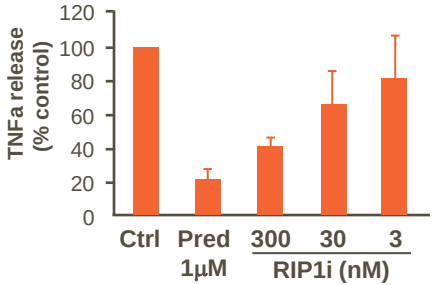
[1]Ofengeim & Yuan. Nat Rev Mol Cell Biol. 2013;14:727-36

GSK2982772: studies in three indications to start in 2016

Key target, compelling target, compelling pre-clinical data







Blocks severe skin inflammation[1]

Prevents against TNF induced shock[1]

Inhibits TNF production in human gut from Crohn's[2]

Clinical Studies

- rheumatoid arthritis
- ulcerative colitis
- psoriasis

Three Phase II clinical studies to progress in parallel mid-2016

Plans in place to rapidly deliver clinical validation in 2017

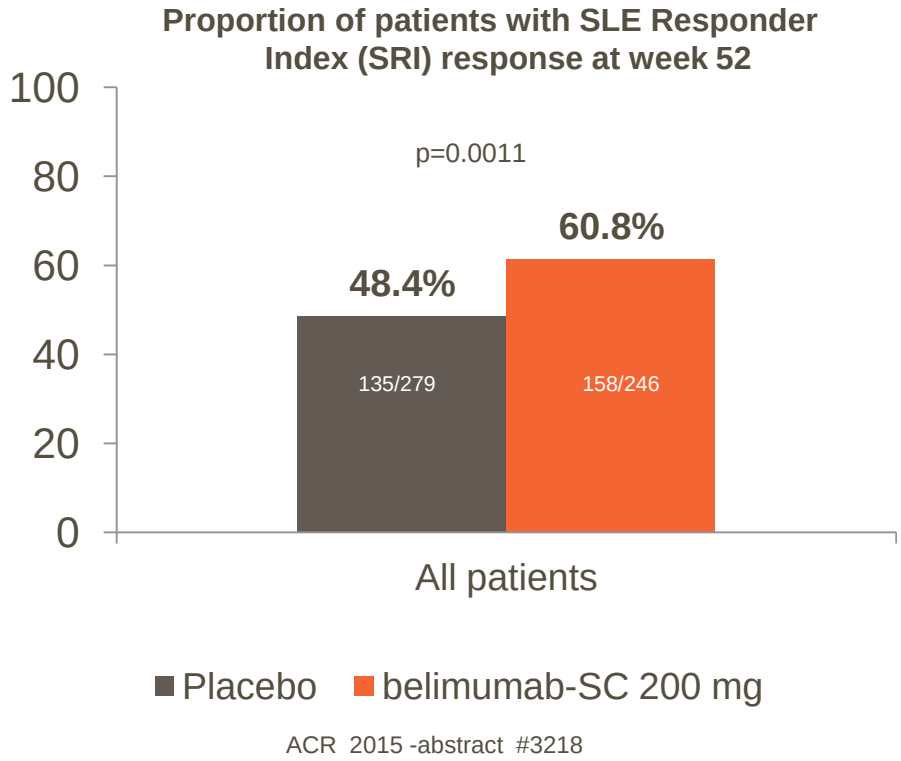
Filing: 2021 - 2025

[1]Berger *et al*. J Immunol. 2014;192:5476-80
[2]GSK, data on file.

Benlysta™ (belimumab):

3rd consecutive positive pivotal study – new data

- Benlysta – the only medicine to treat systemic lupus erythematosus (SLE) to have succeeded in Phase III. Three other medicines have failed.
- Improvement in time to first severe flare (HR 0.5 p< 0.0003) – flare is the major driver of disease progression.
- Trend for reduction in corticosteroid use seen again (p=0.07). Further evaluation ongoing.
- Subcutaneous weekly medicine.
- 9 ongoing studies, including subgroups in SLE and other indications.

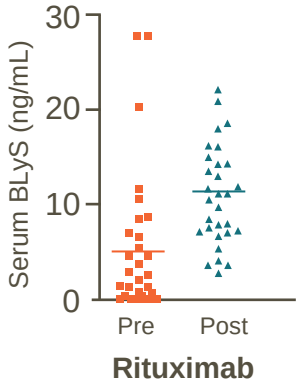


ACR 2015 -abstract #3218

Status:	IV approved 2011
Indication:	SLE
Planned Filing:	SC file Q4 2015/Q1 2016

Translating clinical experience into a new hypothesis: Phase II experimental study to start 2016

- After B-cell depletion with aCD20, BLyS levels increase
- BLyS drives persistence and re-population with auto-immune B-cells
- Benlysta suppresses BLyS
- Single patient case report suggests complete and persistent response in patient treated with aCD20 + Benlysta

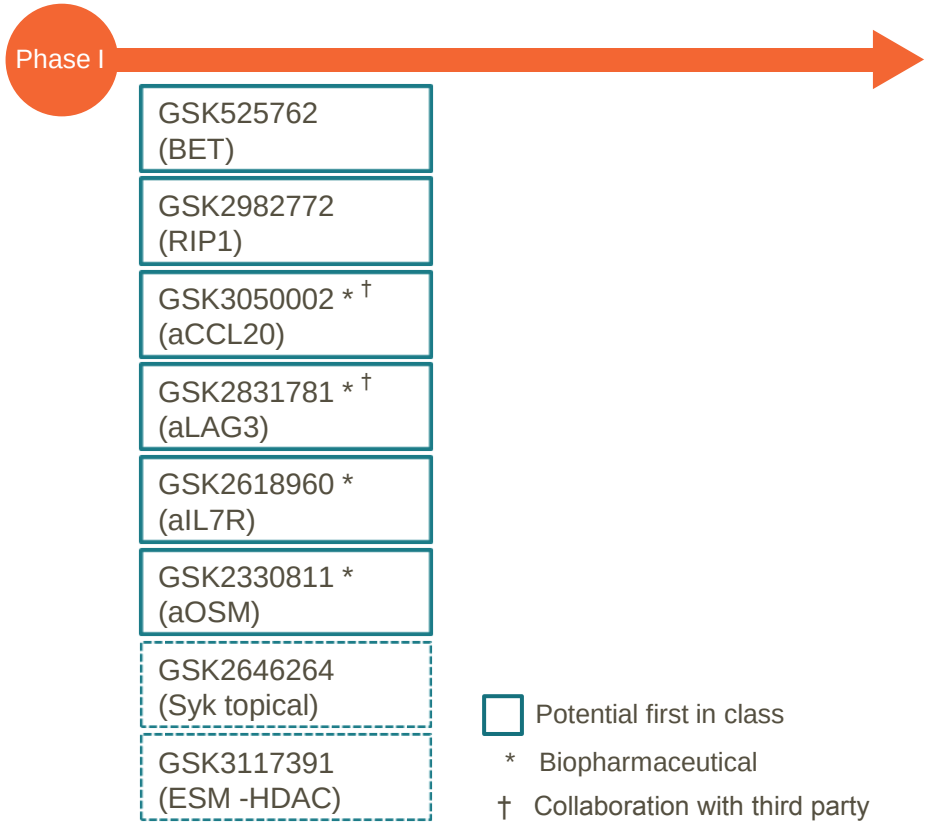


CASE REPORT

De Vita, Clin Exp Rheum. 2014;32, 490-494

- Severe, refractory Sjögren's syndrome, parotid B-cell lymphoma and cryoglobulinaemic vasculitis
- Failed several immunosuppressants, plasma exchange & surgical therapy as well as Benlysta alone and rituximab alone
- Dramatic response to combination including complete and persistent regression of lymphoma

Early Immuno-Inflammation clinical phase pipeline with multiple first in class assets



- Multiple first in class assets
- Eight key disease mechanisms
- Four biologicals
- Smart clinical development programmes to get early data read-outs

Four “first in class” antibodies in the clinic: GSK2618960

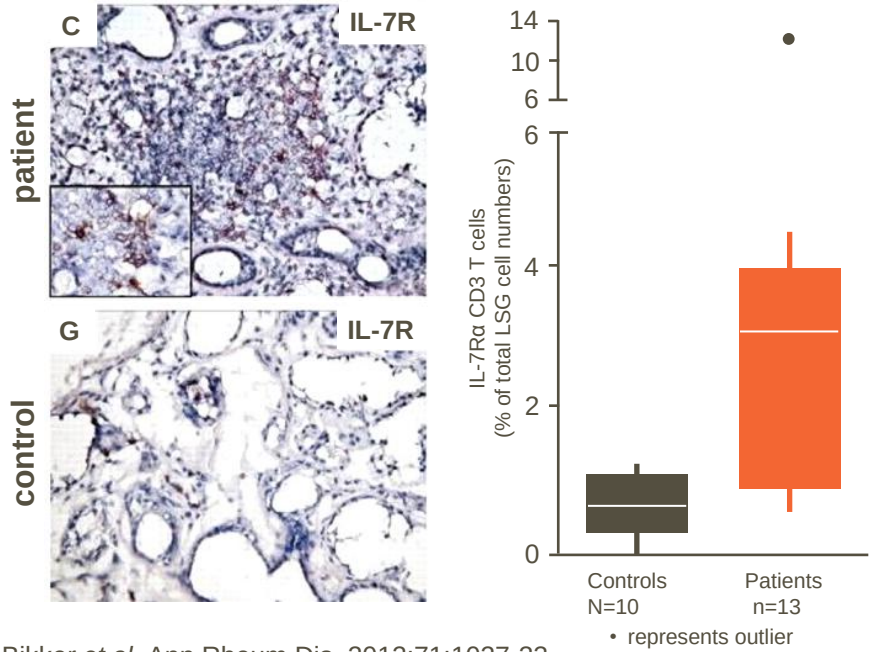
Anti-IL-7R antibody

“First in class” treatment for Sjögren’s syndrome

- IL-7R inhibition affects pathogenic T cell survival, reducing cytokine and auto-antibody production
- IL-7 promotes Sjögren’s-like syndrome in animal models[1]
- Potential for disease modification by prevention of salivary and lacrimal gland destruction
- Phase I study in healthy volunteers completed - well tolerated

Status: Phase II start 2016
Planned Filing: 2021-2025

Ectopic lymphoid tissue and increased IL-7R$^+$ cells in salivary glands of patients with Sjögren’s syndrome



Bikker *et al*. Ann Rheum Dis. 2012;71:1027-33.

1. Jin *et al*. Arthritis.Rhematol. 2013;65:2132-2142

Four “first in class” antibodies in the clinic: GSK3050002

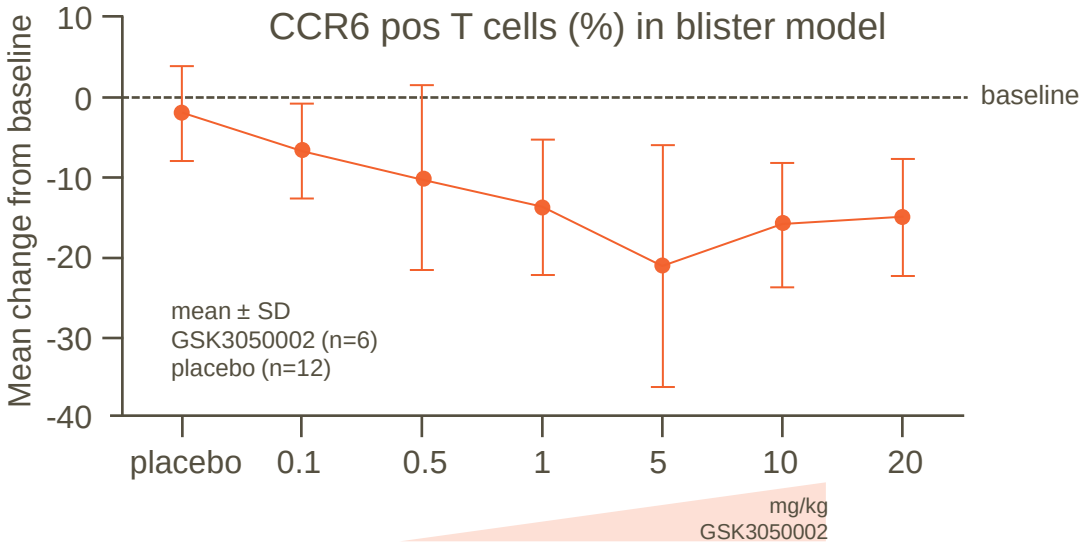
Anti-CCL20 antibody
Collaboration with Morphotek / Eisai

“First in class” treatment for psoriatic arthritis

- Unique MOA - CCL20 inhibition blocks recruitment of pathogenic immune cells - single receptor
- Potential to perturb chronic inflammation & reduce disease activity – applicability in multiple diseases
- Inhibits CCR6+ T cells migration into inflamed tissue in humans *in vivo*

Status: Phase II start 2016
Planned Filing: 2021-2025

Anti CCL20 prevents CCR6+ cells migration into inflamed blister in humans *in vivo*



GSK, data on file. GSK3050002 in experimental medicine study (200784)

- Selective inhibition (CCR6 +ve cells only)
- Dose dependency

Four “first in class” antibodies in the clinic: GSK2831781

Cell depleting anti-LAG3 antibody

Collaboration with Prima BioMed

“First in class” treatment for T-cell driven II indications

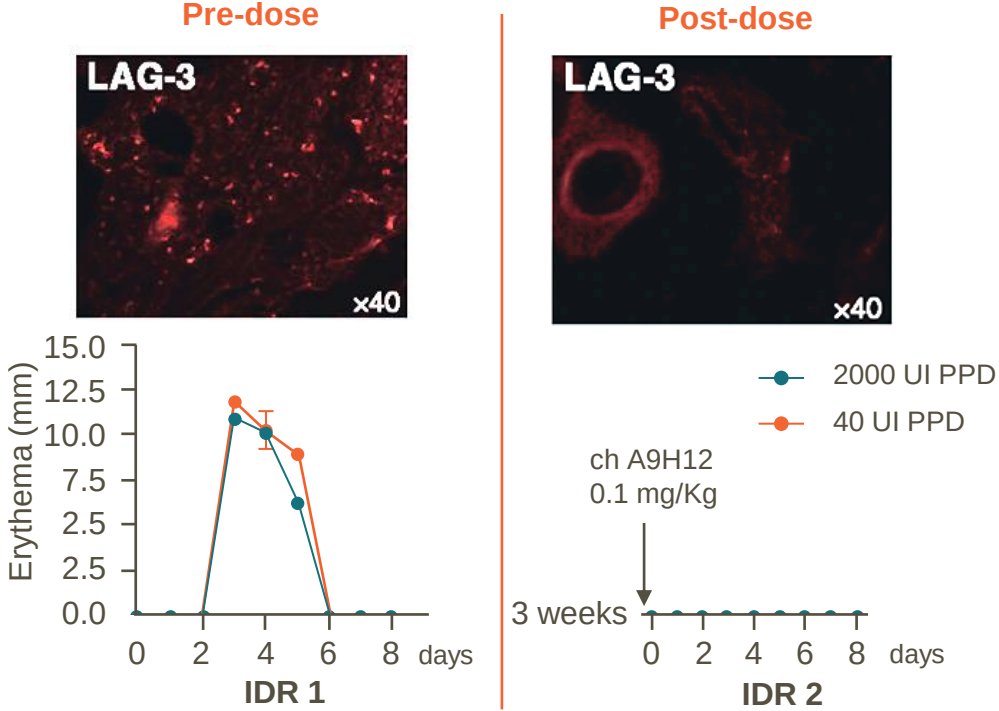
- Unique MOA – a-LAG3 depletes recently activated, “pathogenic” T cells
- Potential for long term disease remission in multiple T cell-driven indications

Status: Phase I ongoing
Planned Filing: 2021-2025

Targeted depletion of LAG-3 T-cells with an antibody (A9H12) suppresses the immune reaction to the tuberculin antigen

Depletion of LAG-3 T-cells at challenge site ...

..results in suppression in the skin reaction



Poirier *et al*. Clin Exp Immunol. 2011;164:265-74.

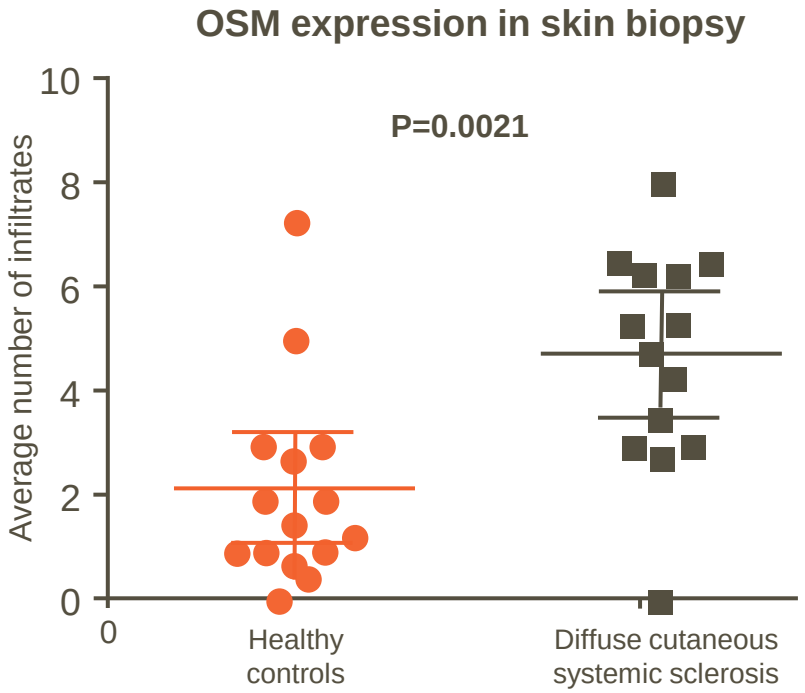
Four “first in class” antibodies in the clinic: GSK2330811

Anti-OSM antibody

“First in class” treatment for systemic sclerosis

- Systemic sclerosis patients have increased OSM serum levels and upregulated OSM and OSM-related genes in skin biopsies (data at ACR)
- Inhibition of OSM signalling is expected to reduce inflammation, vascular dysregulation and fibrosis

Status: Phase I ongoing
Planned Filing: 2021-2025



ACR 2015, abstract #1914

Four “first in class” antibodies in the clinic

All expected to progress to PhII in 2016

Anti-IL-7R antibody

“First in class” treatment for Sjögren’s syndrome

- IL-7R inhibition affects pathogenic T cell survival, reducing cytokine and auto-antibody production
- IL-7 promotes Sjögren’s syndrome in animal models
- Potential for disease modification by prevention of salivary and lacrimal gland destruction
- Phase I study in healthy volunteers completed - well tolerated

Status: Phase II start 2016
Planned Filing: 2021-2025

Anti-CCL20 antibody

Collaboration with Morphotek / Eisai

“First in class” treatment for psoriatic arthritis

- Unique MOA - CCL20 inhibition blocks recruitment of pathogenic immune cells - single receptor
- Potential to perturb chronic inflammation & reduce disease activity – applicability in multiple diseases
- Inhibits CCR6+ T cells migration into inflamed tissue in humans *in vivo*

Status: Phase II start 2016
Planned Filing: 2021-2025

Cell depleting anti-LAG3 antibody

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Status: Phase I ongoing
Planned Filing: 2021-2025

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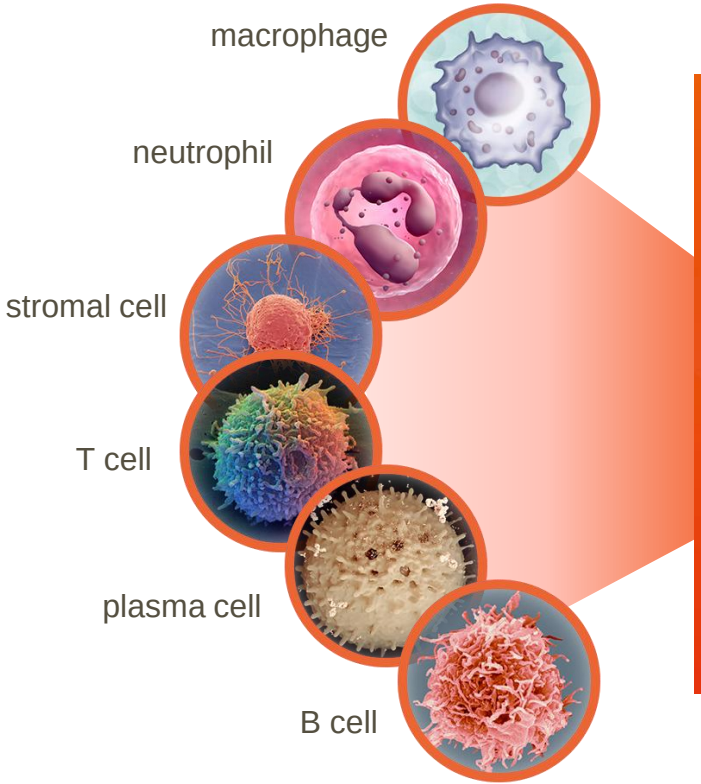
- Systemic sclerosis patients have increased OSM serum levels and upregulated OSM and OSM-related genes in skin biopsies (data at ACR)
- Inhibition of OSM signalling is expected to reduce inflammation, vascular dysregulation and fibrosis

Status: Phase I ongoing
Planned Filing: 2021-2025

Immuno-Inflammation R&D strategy:

From symptomatic benefit to sustainable remission



GSK Pipeline

Targeted Biologicals

- Benlysta
- sirukumab
- Anti-GM-CSF
- Anti-IL-7
- Anti-LAG3
- Anti-CCL20
- Anti-OSM

Targeted Small Molecules

- RIP1
- I-BET

Targeting Resistant Disease

- RIP1
- I-BET
- Anti-IL-7
- Anti-LAG3
- Anti-CCL20
- Anti-OSM

Early Intervention & Remission Induction

- Anti-GM-CSF
- RIP1
- Anti-CCL20
- Anti-LAG3

Oncology

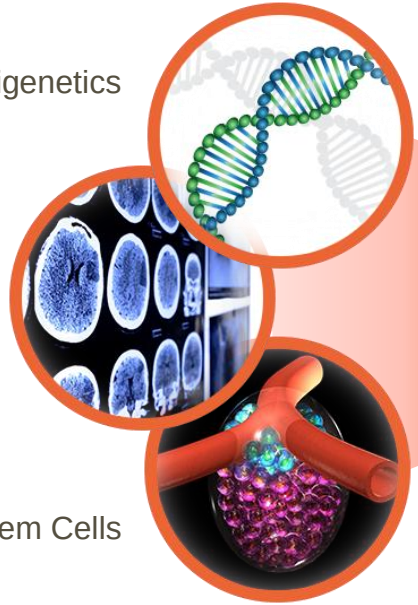
Oncology R&D strategy

Focusing on 3 areas fundamental to oncology

Cancer Epigenetics

Immuno-Oncology

Cancer Stem Cells



GSK Pipeline

Long-Term Survival & Cures

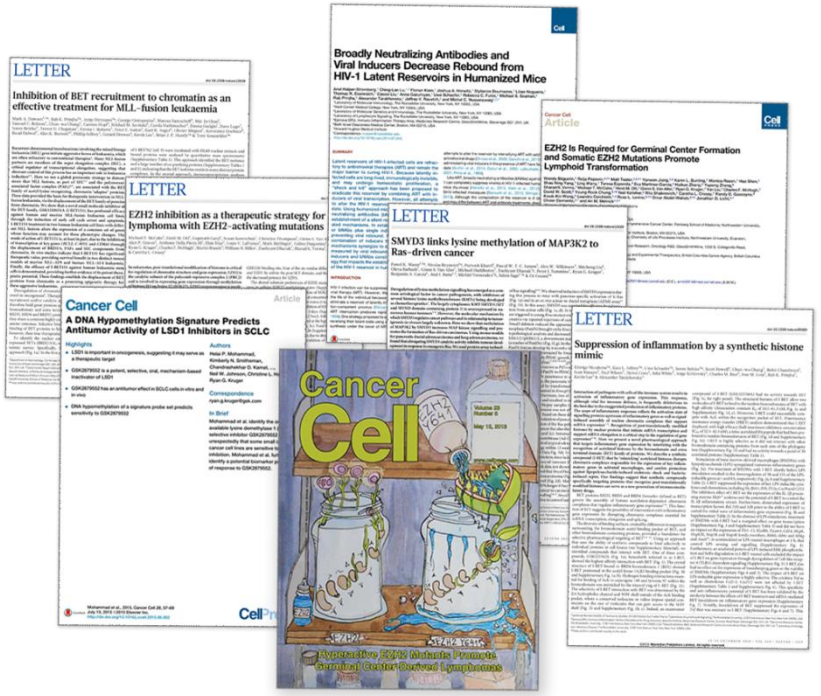
Reprogram Cancer Cells

Stimulate Anti-Tumour Immunity

First in Class Medicines & Combination Therapy

GSK Epigenetics: an early commitment with a pipeline now at the forefront of industry

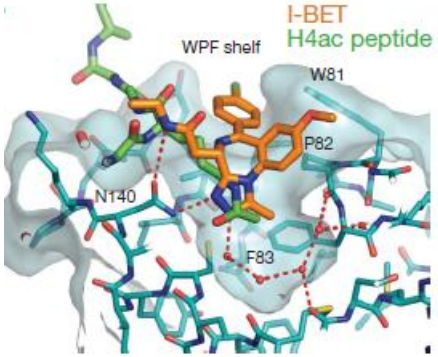
- World-leading science in epigenetics since 2008
- Team has published 9 papers in *Nature* & *Cell*
- World-leading academic collaborations
- Strategic collaborations with biotech



GSK525762: potential first in class BET inhibitor

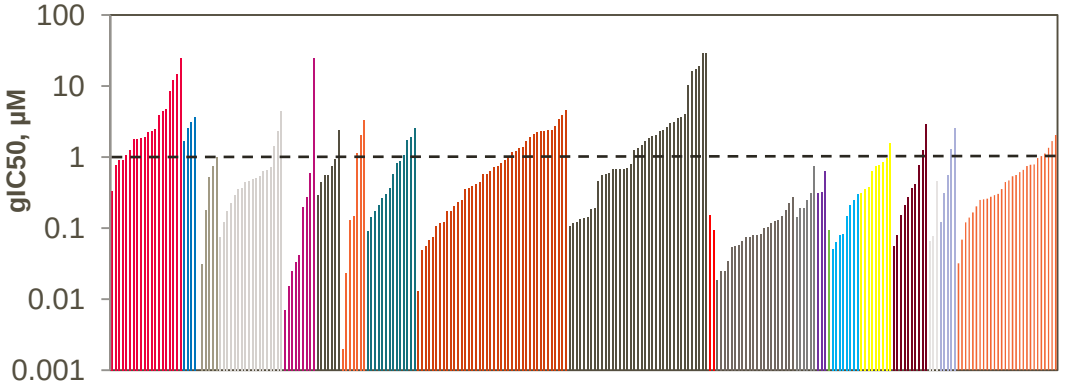
Potential for broad activity

- GSK525762 blocks binding of BET family proteins (BRD2, 3 and 4) to transcriptional mediators changing gene expression including suppressing oncogene expression
- Potential use in many potential indications
- Broad activity in preclinical cell line models
- PoC opportunity in NUT midline carcinoma (NMC)
- Rare and rapidly lethal cancer caused by chromosomal translocation involving BET target (NUT gene and either BRD3, BRD4, or NSD3 (which binds BRD4) gene)



Nature 2010;468:1119-1123

Status:	Phase I
Indications:	Solid Tumours, Heme Malignancies
Filing:	2018



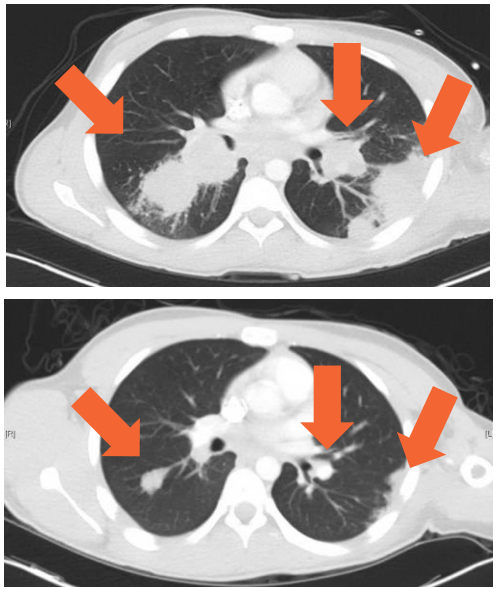
Preclinical data show activity of GSK525762 in many cancer types (gIC50 < 1 µM)

GSK525762: early evidence of potential clinical benefit

Potential new treatment for rapidly lethal cancer

- Responses observed in NUT midline carcinoma
  - 6 patients treated at 60-100 mg QD with 4 Partial Responses
- Solid tumour studies underway across multiple tumour types;
  - 36 patients enrolled across CRC, NMC, CRPC, SCLC, BC & MM
- Haematological studies underway; partial responses seen in AML
  - 20 patients enrolled cross AML, NHL & MM

GSK525762 active in NMC, a very difficult to treat cancer



Chest CT of patient with NMC treated with GSK525762: ~ 90 % reduction in tumour volume at week 16

GSK, data on file.

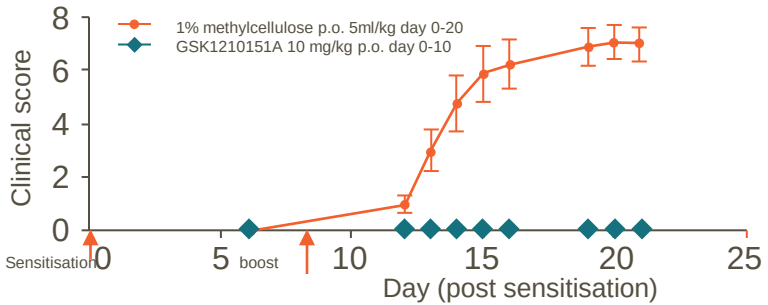
GSK525762: potential to treat and reset disease in rheumatoid arthritis: *Extensive preclinical data package for BET inhibition*

- GSK525762 interferes with stromal cells driving autonomous disease progression in RA
- Profound cytokine, chemokine and immunoglobulin inhibition in human macrophages[1] and RA patient samples and biopsies
- Modulation of macrophage[1], osteoclast[2] and Th17 cell types
- Profound inhibition of disease in multiple RA preclinical models[2]
- Rebalances gene expression in RA stromal cells (decreased cytokines, chemokines, metalloproteases, elevated protease inhibitors[3, 4]

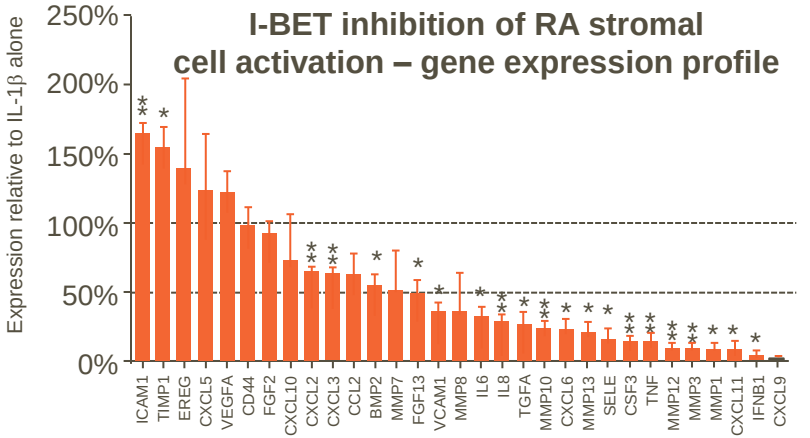
1.Chan *et al*. 2014 EJ Imm., 2. Park-Min *et al*. 2014 NatCom,
3. Xiao *et al.* 2015 Rheumatology, 4. Klein *et al.* 2014 ARD

Status:	Phase II start 2016
Indication:	Therapy Resistant RA
Planned Filing:	2021-2025

I-BET resets disease in rat collagen-induced arthritis



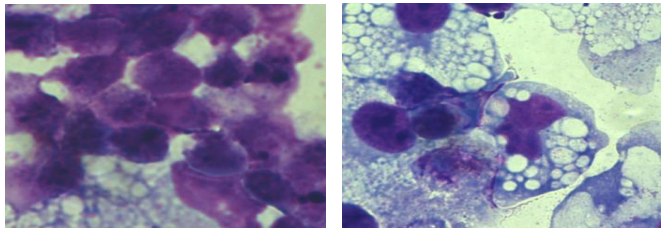
I-BET inhibition of RA stromal cell activation – gene expression profile



GSK2879552 LSD1 inhibitor: Early signal of efficacy in SCLC

- Preclinical data give reason to believe
- Clinical studies ongoing in Small Cell Lung Cancer and Acute Myeloid Leukaemia
- Signal of significant progression-free survival for some patients

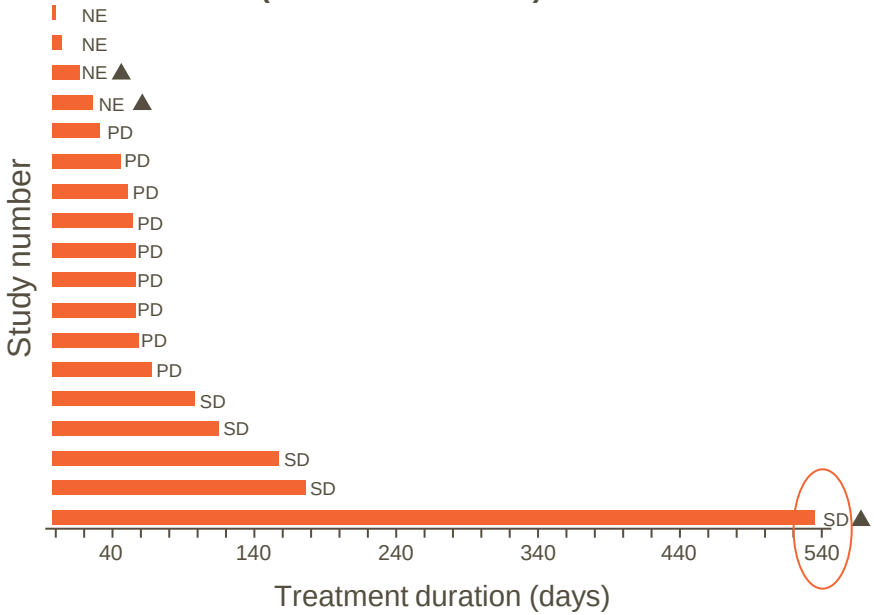
Untreated **10 nM GSK552**



MLL-AF9 mouse derived leukemia cells treated for 6 days *in vitro*

Status:	Phase I
Indications:	AML, SCLC
Planned Filing:	2020

Plot of duration of treatment (days) with Tumour Response (RECIST 1.1 criteria) SCLC



Best confirmed response –PR: Partial Response, SD: Stable Disease, PD: Progressive Disease, NE: Not Evaluable
Triangles indicate ongoing subjects

GSK, data on file.

Immuno-Oncology: NY-ESO T-Cell Therapy

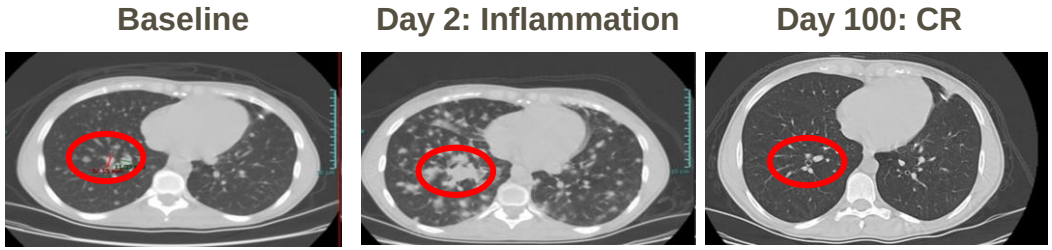
- TCR T-cell therapy
- 50% ORR seen in sarcoma
- Ongoing studies in ovarian and other solid tumours and haematological malignancies
- Planned studies in combination with checkpoint modulators
- Collaboration with Adaptimmune

Status:	Phase I/II
Indications:	NY-ESO-1 positive Cancers: Sarcoma, Myeloma, NSCLC, Melanoma, Ovarian Cancer

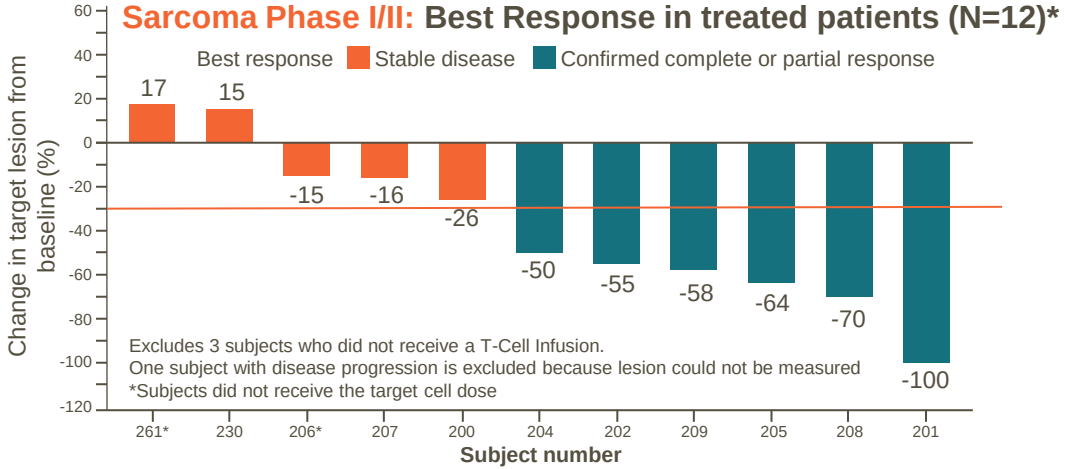
Filing strategy to be agreed with Adaptimmune

Note: GSK3377794 subject to exercise of option by GSK

Sarcoma Phase I/II: Individual patient complete response (CR)



Sarcoma Phase I/II: Best Response in treated patients (N=12)*

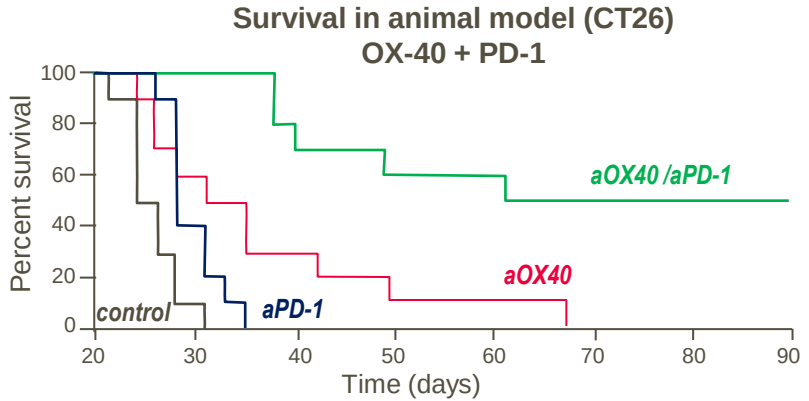


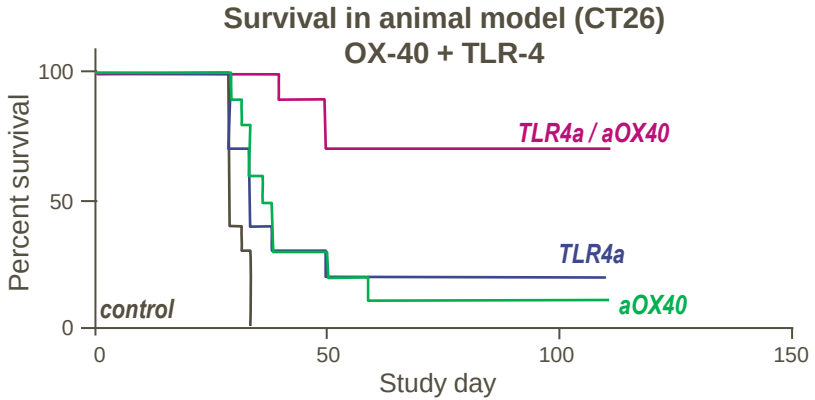
GSK, data on file.

Immuno-Oncology: GSK3174998 OX40 agonist mAb

- GSK3174998 is one of four humanised OX-40s in clinic
- Dual mechanism: enhancing effector T-cell and suppressing T-regs
- Phase I Study started in eight cancers
- Combination with Merck PD1 in 2016
- Combination with GSK TLR4 in 2017
- Collaboration with MD Anderson

Status:	Phase I
Indications:	Solid tumours, Heme Malignancies
Planned Filing:	2020





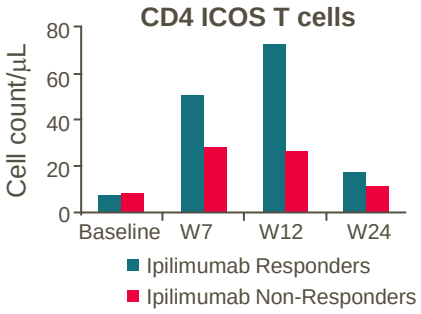
GSK, data on file.

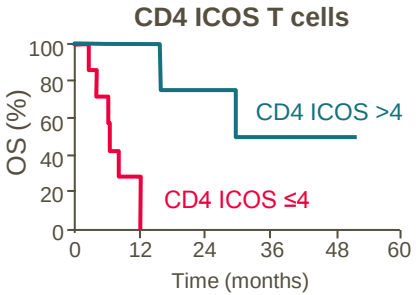
Immuno-Oncology: GSK3359609 first-in-class ICOS agonist antibody

- Universal mechanism across multiple cancers
- Patient selection biomarker
- Enhances T-cells associated with survival
- Use after CTLA-4 and PD-1 in unresponsive or refractory patients
- Possible anchor for use in combinations
- Collaboration with INSERM

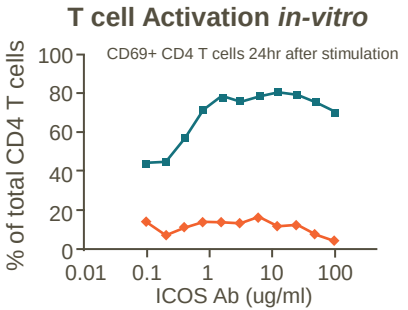
Status:	Phase I start Q1 2016
Indications:	Solid tumours, Heme Malignancies
Planned Filing:	2020

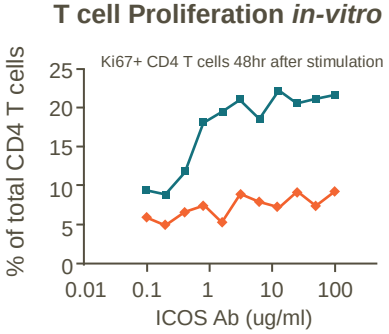
ICOS in ipilimumab-treated patients





GSK3359609



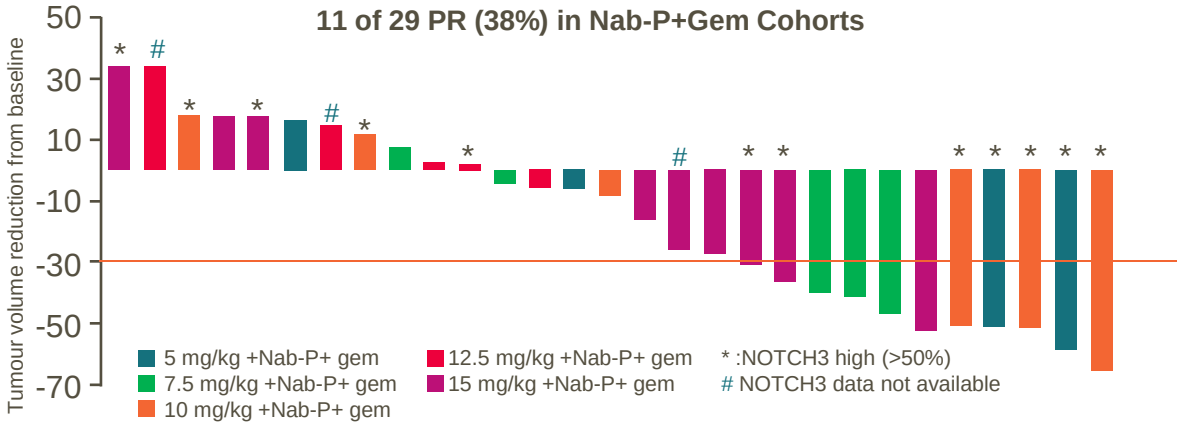


DiGiacomo, Clin Immunol Immunother 2013

Cancer Stem Cells: tarextumab (anti-Notch 2/3)

- Inhibition of Notch 2/3 Receptors in cancer stem cells
- Phase Ib: Overall response rate of 38%
- Ongoing randomised Phase II studies in pancreatic cancer and SCLC
- Phase II read-out 2016
- Collaboration with OncoMed

ALPINE (Phase Ib) Pancreatic Cancer:
gemcitabine/Abraxane* + tarextumab
Dose range: TRXT from 5 to 15mg/kg Q2W



Attractive signal over 23% ORR of Gem/Abraxane SOC in hard-to-treat cancer

O'Reilly *et al*. 2015 Gastrointestinal Cancer Symposium

Status:	Phase II
Indications:	Pancreatic cancer and Small Cell Lung Cancer
Planned Filing:	2020

Note: tarextumab subject to exercise of option by GSK
*Abraxane is a trademark of Abraxis Bioscience LLC

Oncology R&D strategy

Focusing on 3 areas fundamental to oncology

Cancer Epigenetics

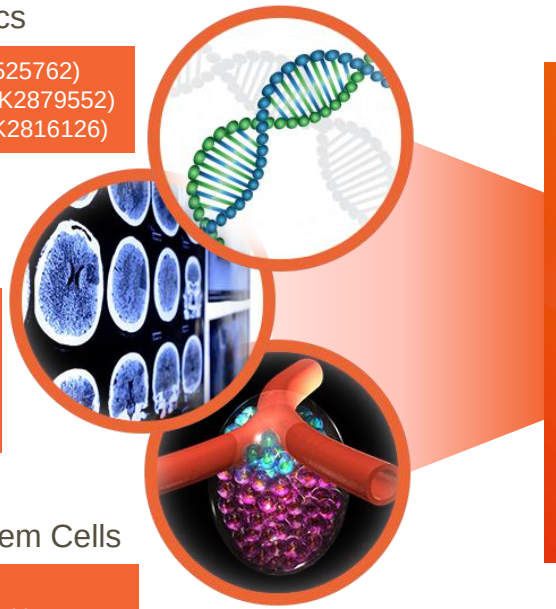
- BET inhibitor (GSK525762)
- LSD-1 inhibitor (GSK2879552)
- EZH2 inhibitor (GSK2816126)

Immuno-Oncology

- NY-ESO-1 TCR-T
- OX40 agonist (GSK3174998)
- ICOS agonist
- TLR4 agonist

Cancer Stem Cells

- Notch2/3 (tarextumab)
- Notch1 (brontictuzumab)



GSK Pipeline

Long-Term Survival & Cures

- Epigenetics
- Immuno-oncology
- Stem cells

Reprogram Cancer Cells

- Epigenetics

Stimulate Anti-tumour Immunity

- Immuno-oncology

First in Class Medicines & Combination Therapy

- Epigenetics
- Immuno-oncology
- Stem cells

Oncology – Pipeline snapshot

BET inhibitor (GSK525762)	*Solid tumours, Heme Malignancies*
LSD-1 inhibitor (GSK2879552)	*AML, SCLC*
EZH2 inhibitor (GSK2816126)	*Solid tumours, Heme Malignancies*
PRMT5 inhibitor (GSK3326595) †	*Solid tumours, Lymphoma*
Novel small molecule targets (X6)	
NY-ESO-1 TCR-T †	*Sarcoma, Multiple Myeloma, NSCLC, Ovarian, Melanoma*
OX40 agonist (GSK3174998) †	*Solid tumours, Heme Malignancies*
ICOS agonist (GSK3359609) †	
TLR4 agonist (GSK1795091)	
CAR-T and TCR-T targets (x6)	
Novel small molecule targets (x2)	
ImmTacs (x4) †	
mAb-dAbs and dual-specific Abs (x5)	
Notch2/3 (tarextumab) †	*Pancreatic, SCLC*
Notch1 (brontictuzumab) †	*Solid tumours, Heme Malignancies*
BCMA ADC (GSK2857916)	*Multiple Myeloma*
FGF Ligand Trap (GSK3052230) †	*Mesothelioma, NSCLC*

- Epigenetics
- Immuno-Oncology
- Stem Cells
- Other targeted therapies

† Collaboration with a third party.

Assets profiled at R&D day by planned filing date

See www.gsk.com for full clinical pipeline

2014 to 2017: 6 NMEs & 5 PLEs

Nucala (mepolizumab) *IL-5 mAb* **Severe Asthma**	sirukumab *IL-6 mAb* **Rheumatoid Arthritis**
mepolizumab *IL-5 mAb* **COPD**	GSK2696273 *Ex-vivo stem CGT* **ADA-SCID**
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fluticasone furoate+vilanterol +umeclidinium *ICS/LABA/LAMA* **COPD**	GSK2696275 *Ex-vivo stem CGT* **Wiscott-Aldrich Syndrome**
dolutegravir + rilpivirine *Integrase inhibitor + NNRTI* **HIV**	GSK2998728† *TTR production inhibitor* **FAP**
Benlysta Subcutaneous *BLyS mAb* **SLE**	

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mepolizumab *IL-5 mAb* **Nasal Polyposis**	tarextumab† *Notch 2/3 mAb* **Pancreatic Cancer, SCLC**	GSK2398852+ GSK2315698 *SAP mAb + SAP depleter* **Amyloidosis**
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2021 to 2025: 17 NMEs & 5 PLEs

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GSK3191812 *TSLP dAb* **Asthma**	belimumab + CD20 *BLyS+CD20* **Sjogren's Syndrome**	GSK3050002 *CCL20 mAb* **Psoriatic Arthritis**	

- Respiratory
- HIV / Infectious Diseases
- Immuno-Inflammation
- Oncology
- Rare Diseases
- Other

† Subject to exercise of option
# Subject to collaborator agreement
^ EU filing
* USAN, INN approval pending

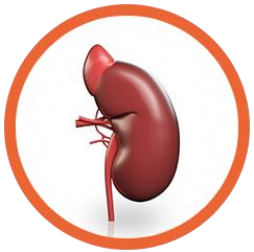
Rare Diseases

Amyloidosis and Cell and Gene Therapy

Amyloidosis: a complex protein deposition disease process with ~50% mortality at 3 years

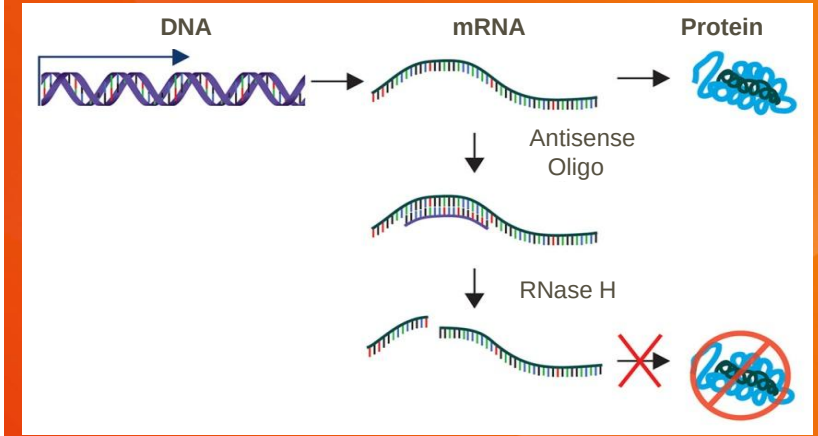
- AL amyloidosis – monoclonal immunoglobulin light chains (plasma cell dyscrasia) (~70% of all cases)
- ATTR amyloidosis – hereditary disease caused by variant transthyretin (TTR) protein
  – acquired disease caused by wild type TTR (senile amyloidosis)
- AA amyloidosis – complication of chronic inflammation or infection
- **Implication in other disease states**. Growing recognition of its importance

Accumulation of amyloid deposits damages vital organs causing disease

Peripheral / visceral nerves	Kidney	Heart	Liver
			
TTR	**AA, AL, TTR**	**AL, TTR**	**AL, AA**

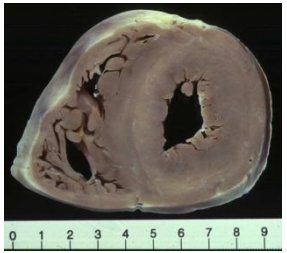
Two fundamental approaches to treatment: prevent amyloid formation and remove amyloid deposits

"Gene silencing" by antisense oligonucleotide

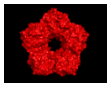


- **Knockdown of TTR gene prevents production of mutant and wild type TTR protein**
- **Prevents formation of amyloid deposits in vital organs**
- **GSK2998728 in collaboration with Isis Pharmaceuticals**

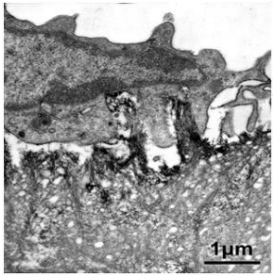
Removal of amyloid deposits by macrophage-mediated clearance



Serum amyloid P component (SAP) in blood and all amyloid deposits



SAP removed from plasma by GSK SAP depleter but still decorates deposits in organs



Anti-SAP mAb can then target SAP in amyloid deposits

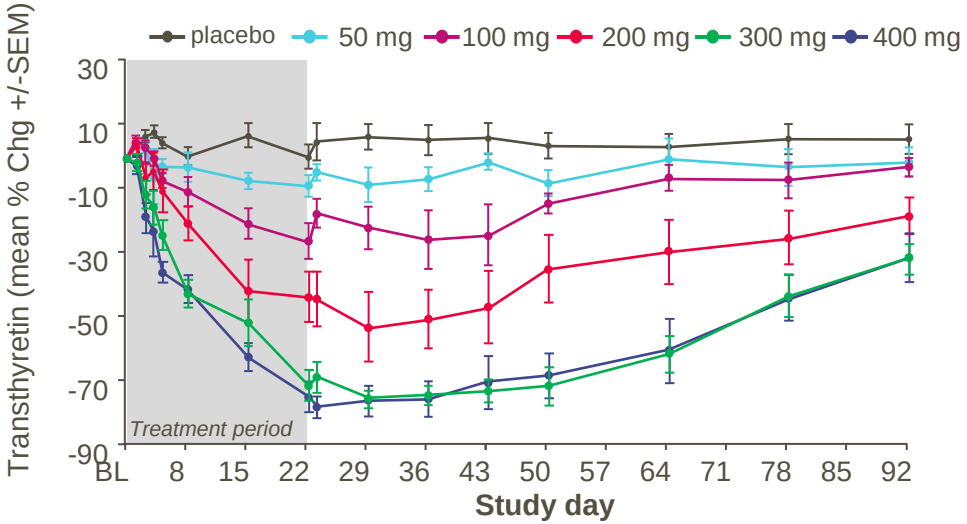
Antibody binding triggers amyloid clearance by macrophages

Organ function is restored

GSK2998728 RNA targeted transthyretin (TTR) knockdown

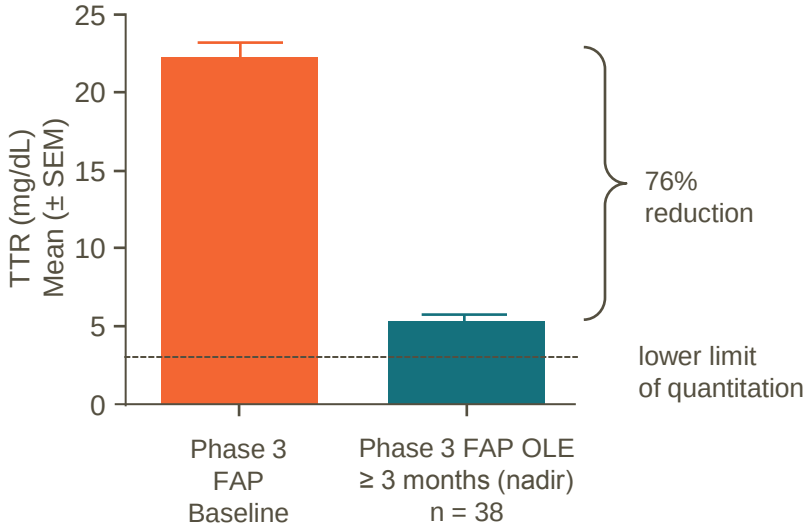
~80% TTR knockdown

Mean change - Time profile following 3 loading doses week 1, then 1 weekly dose (n=65; healthy volunteers)



TTR reductions observed in Phase III FAP open label extension

Mean max TTR reduction = 76%
Max TTR reduction = 92%



Status:	Phase III
Indication:	Familial amyloid polyneuropathy (FAP); Familial and wild-type amyloid cardiomyopathy (TTR CM)
Filing:	2017 (FAP), 2020 (TTR CM)

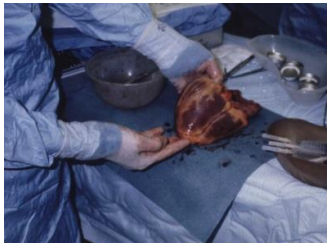
GSK: data on file

Note: GSK2998728 is a collaboration with Isis Pharmaceuticals and subject to exercise of option by GSK

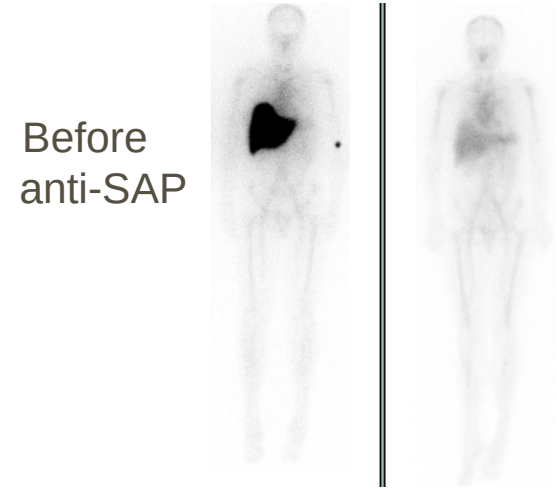
Ackermann et al. International Symposium on Amyloidosis. 2012, poster #0P73

CPHPC + Anti-SAP mAb for systemic amyloidosis

- Directly targets amyloid deposits that cause disease
- Proof of concept in systemic amyloidosis
  - Regression of amyloid in liver, kidney, spleen, etc
- Potential for accelerated approval
- US breakthrough status application planned
- Use in cardiac AL and ATTR amyloidosis
- Example of academic partnership model
- Collaboration with Pentraxin



Reason to believe – amyloid imaging



Liver ECV (median normal 29%)	36.0	29.0
Liver Stiffness (median normal 5.3 kPa)	5.7	2.8
% of tracer in liver	61.1	17.4

Therapeutic clearance of amyloid by antibodies to serum amyloid P component

Richards *et al*. N Engl J Med 2015; 373:1106-1114

Amyloidosis: a comprehensive R&D approach

- Similar prevalence to Pulmonary Arterial Hypertension
  - Approximately 30,000 cases but currently under-diagnosed
- Fundamental mechanism in diverse but medically important disease states
- GSK approaches address both removal of existing deposits and prevention of accumulation
- World class expertise – ability to maximise the opportunity from our leadership position
  - Oral SAP depleter/ anti fibril approaches

GSK's dual approach to amyloidosis

1. "Gene silencing" by antisense oligonucleotide

TTR to prevent formation of amyloid deposits in vital organs

2. Removal of amyloid deposits by macrophage-mediated clearance

Anti-SAP mAb to target SAP in amyloid deposits

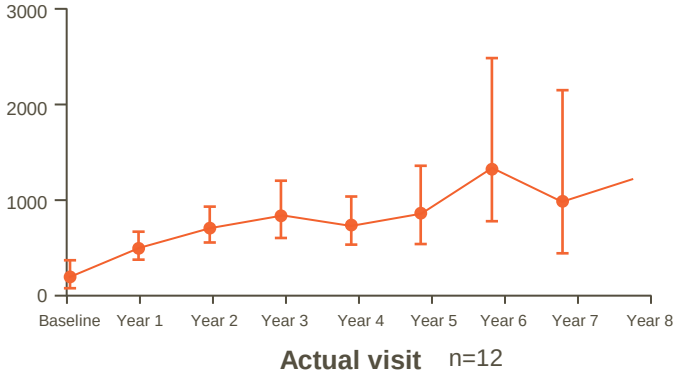
GSK2696273 for adenosine deaminase severe combined immunodeficiency: 100% survival at median 7 year follow up

Severe Combined Immuno-Deficiency (SCID)

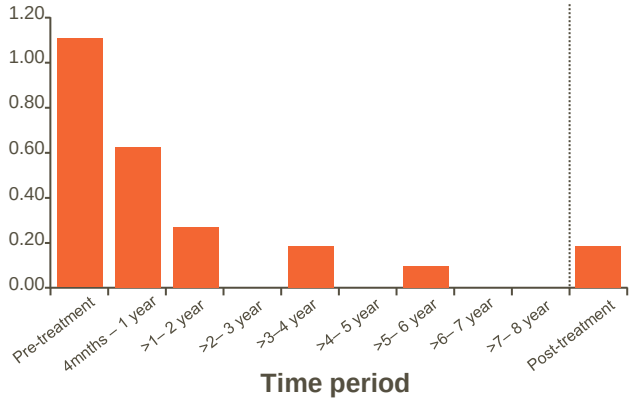
- Fatal
- Life-threatening opportunistic infections

Status:	Filed in Europe
Indication:	ADA SCID
Planned Filing:	US filing 2017

Increased T cell count



Reduced infections



GSK2696273 is a collaboration with Telethon and Ospedale San Raffaele

Cicalese *et al*. ESID 2015, poster #0779.

Gene therapy works in different monogenic diseases

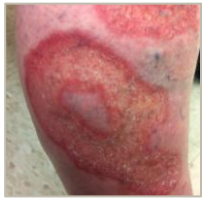
Innovative collaboration with Telethon and Ospedale San Raffaele

- World first *ex vivo* autologous stem cell gene therapy filed
- Filing strategy agreed for 2 more
- Beta thalassaemia study started
- Building GSK platform capability in cell and gene therapy. New alliances and internal platform build
- Cell gene therapy approaches in oncology and potentially other areas. IP estate and know-how accumulating

Pipeline of products

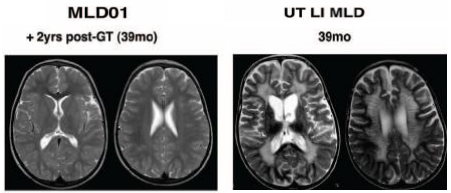
- ADA SCID [a]
- Metachromatic Leukodystrophy [a]
- Wiskott-Aldrich Syndrome [a]
- Beta thalassemia [b]
- MPS1 [b]
- Chronic Granulomatous disease [b]
- Globoid Cell Leukodystrophy [b]

[a] Licensed from Telethon and Ospedale San Raffaele
[b] GSK holds an option to license programme from Telethon and Ospedale San Raffaele



Wiskott-Aldrich Syndrome (WAS)

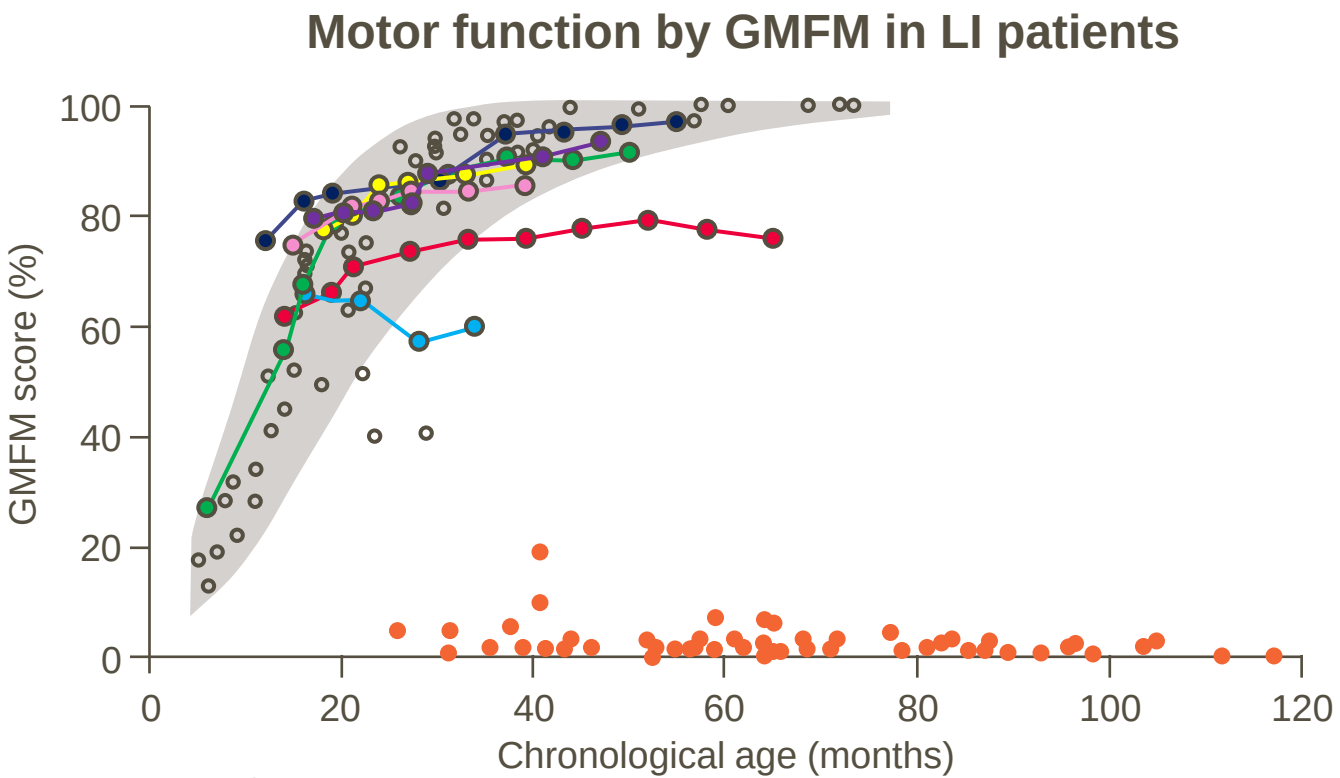
- Thrombocytopenia
- Infections
- Autoimmune disease
- Lymphoma



Metachromatic Leukodystrophy (MLD)

- Fatal
- Rapid loss in cognitive & motor function, followed by death

Cell Gene Therapy clinical effect in MLD



Biffi *et al*. ESCGT 2015 presentation

Introducing our experts

GSK's leading scientists in immuno-inflammation, cancer research, amyloidosis and CGT

Paul-Peter Tak

Senior Vice President,
Head Immuno-
Inflammation (II) TAU

Ravi Rao

Vice President, Medicines
Development Leader &
Head Unit Physician II

John Bertin

Vice President,
Head Pattern Recognition
Receptor DPU

Axel Hoos

Vice President, Head
of Immuno-Oncology

Chris Carpenter

Vice President, Head
Cancer Epigenetics DPU

Duncan Richards

Vice President, Head Academic
DPU

Sven Kili

Vice President, Development
Head for Gene Therapy

Assets profiled at R&D day by planned filing date

See www.gsk.com for full clinical pipeline

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Benlysta Subcutaneous *BLyS mAb* **SLE**	

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- HIV / Infectious Diseases
- Immuno-Inflammation
- Oncology
- Rare Diseases
- Other

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Q&A