R&D Roundtable

Martin Mackay, President, R&D

June 14th, 2012

AstraZeneca

Our vision for R&D

Perfor-mance

- Approval of valued medicines
- Positive return on investment

Portfolio

- Consistent productivity
- High quality late-stage pipeline

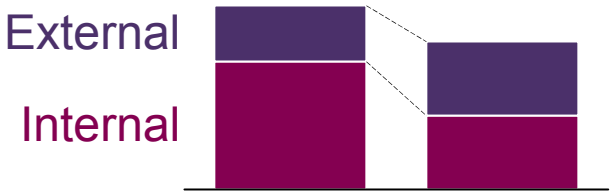
People

- Strong leadership cadre
- Smaller workforce

Operating Model

- Simpler footprint
- Innovative operating models

Cost



- Lower costs
- Higher external percentage

Transforming R&D 2010-12

Investing in the future of R&D

People

31 of the top 50 (60%) are new hires

Mene Pangalos
Innovative Medicines

Briggs Morrison
Global Medicines Development

Capabilities

>$200M over 5 years

- Personalised Healthcare
- Predictive Science
- Payer Evidence
- Clinical Trial Design

Portfolio

>40% of pipeline sourced externally

AMGEN

RIGEL

Bristol-Myers Squibb

Ardea Biosciences

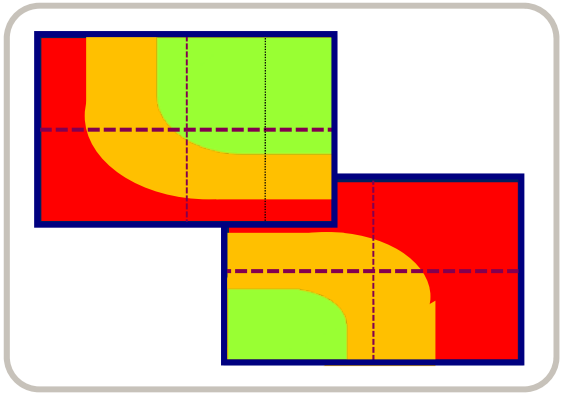
Transforming R&D 2010-12

Managing the cost of R&D

People	Property	Portfolio
23% reduction	21 ➔12 facilities	18% reduction

Building a high quality pipeline

5 Rs



Assurance Mapping

Real-World Evidence

Potential 2012-13 phase III investment decisions

Assets	Area under investigation
AZD6244 – selumetinib (MEK Inhibitor)	NSCLC / Melanoma
MEDI-1123 – tremelimumab (anti-CTLA-4 MAb)	Solid tumours
AZD8931 (erbB kinase inhibitor)	Breast cancer
CXL (beta lactamase inhibitor/cephalosporin)	MRSA
CAZ AVI (beta lactamase inhibitor/cephalosporin)	HAP/VAP
AZD9773 (anti-TNF-alpha polyclonal antibody)	Severe sepsis
MEDI-575 (anti-PDGFR-alpha MAb)	Glioblastoma / NSCLC
AMG-827 – brodalumab (anti-IL-17 MAb)	Psoriasis
MEDI-563 – benralizumab (anti-IL-5R MAb)	Asthma
AZD1981 (CRTh2 receptor antagonist)	Asthma

As of 31 Dec 2011

Late stage pipeline progress

Phase III	Submitted	New indications	Launched/Approved	
Naloxegol	BRILINTA ticagrelor tablets – Further markets	onglyza – Renal impairment USA, Europe	BRILIQUE ticagrelor tablets – Europe	BRILINTA ticagrelor tablets – USA, Canada, Brazil
CAZ AVI	Caprelsa (vandetanib) Tablets – Russia	onglyza – Add-on to insulin Europe	onglyza – China	kombiglyze XR ONCE A DAY – USA
Fostamatinib	forxiga (dapagliflozin) – Further markets	IRESSA gefitinib – 1st Line Japan	Nexium esomeprazole – Japan	Vimovo naproxen/esomeprazole magnesium – Europe, Canada, Brazil
IRESSA gefitinib – LCM	Symbicort budesonide/formoterol – COPD Japan	kombiglyze XR ONCE A DAY – Add-on to insulin USA	Caprelsa (vandetanib) Tablets – USA, EU	FASLODEX fulvestrant – Japan, India
FASLODEX fulvestrant – LCM	Symbicort budesonide/formoterol – SMART Asthma TBH Japan		FLUENZ nasal spray, suspension – Europe	Axanum acetylsalicylic acid/esomeprazole – EU
Lesinurad*	Zinforo ceftaroline fosamil – EU		RANMARK – Japan	komboglyze – EU
			FluMist Quadrivalent Influenza Vaccine Live, Intranasal – USA	

As of 31 Dec 2011
**subject to approval of Ardea acquisition*

Our priorities for R&D

1. Deliver the late-stage portfolio
2. Secure high value late-stage partnerships
3. Achieve 8-11 positive POCs in 2012-14
4. Maximise LCM and emerging markets

All at the right cost and demonstrating progressive return on invested capital

R&D Roundtable

Mene Pangalos, Executive VP, Innovative Medicines

June 14th, 2012

AstraZeneca

The people behind our science

Susan Galbraith
Oncology iMed

Track record of delivery in cancer biology and drug development

Joined from Bristol-Myers Squibb

Manos Perros
Infection iMed

Led Novartis Institute for Tropical Disease

Former VP and Head of Antiviral Research at Pfizer

Maarten Kraan
R&I iMed

Experienced rheumatologist and clinician

Formerly of Roche, Bristol-Myers Squibb and Schering-Plough

Mike Poole
Neuroscience iMed

Twenty years experience in pharmaceutical clinical research

Former Chief Medical Officer at Link Medicine

Gunnar Olsson
CVGI iMed

Over 30 years of experience in cardiology

With AstraZeneca since 1989

Clive Morris
New Opportunities iMed

Former late stage development director for Oncology within Clinical Development

Accountability at every stage

Martin Mackay President R&D

Innovative Medicines (IM) **Global Medicines Development**

Target Selection → Proof of Concept

Late-stage development

Internal and external opportunities

IM Research Board

Product Development Committee

Product Review Board

Market

Portfolio Investment Board

Driving quality, not quantity

Right target

Right tissue/
Right exposure

Right safety

Right patients

Right commercial

Impact

- 30% decrease in IM portfolio volume
- 83% of projects stopped in pre-clinical phases

Benefits

- Increasing our focus on key projects and competitive position
- Increasing the odds of pipeline to deliver
- Removing low value projects early
- Staffing projects to be competitive
- Freeing resources to innovate, and re-invest in business priorities

Small molecule led NME's

Phase 1	Phase 2	Phase 3/registration
AZD5363 (AKT) Solid tumors	AZD6244 (Selumetinib) (MEK) Solid tumors	Caprelsa™ (VEGFR/EGFR) MTC
AZD3514 (AR down regulator) Prostate cancer	Fostamatinib (SYK) Haematological malignancies	Fostamatinib (SYK) Rheumatoid arthritis
AZD2014 (mTOR1&2) Solid tumors	AZD8931 (erbB) BC chemo combi/solid tumors	Forixga (SGLT2) Diabetes
AZD1480 (JAK1/2) Solid tumors	AZD4547 (FGFR) Solid tumors	Brilinta™ (ADP) Arterial thrombosis
Olaparib (PARP-gBRCA) Solid tumors	AZD8683 (Muscarinic antagonist) COPD	Naloxegol (Oral peripherally acting opiod antagonist) OIC
AZD6244/MK2206 (Selumetinib) (MEK/AKT) Solid tumors	AZD5423 (iSEGRA) COPD	Zinforo (Ceftaroline) Pneumonia/skin infections
AZD2115 (MABA) COPD	AZD5069 (CXCR2) COPD	CAZ AVI (BLI /cephalosporin) SBI
AZD2820 (MC4r) Obesity	AZD2423 (CCR2b) COPD	
CAT-354 (Tralokinumab) (IL-13) Ulcer. colitis	AZD1981 (CRTh2) Asthma/COPD	
AZD5213 (H3R) Alzheimer's/ADHD	AZD4017 (11BHSD) Glaucoma	
AZD3839 (BACE1) Alzheimer's	AZD2927 (ion channel blocker) Atrial fibrillation	
AZD3241 (MPO) Parkinson's Disease	AZD6765 (NMDA) MDD	
AZD1446 (a4b2 NNR) Alzheimer's	AZD3480 (a4b2 NNR) AD	
AZD5847 (Oxazolidine antibacterial inhibitor)TB	AZD2423 (CCR2b) Pain	
AZD5099 (GyrB) Serious infections	CXL (BLI /cephalosporin) MRSA	
	AZD9773 (aTNF polyclonal) Severe sepsis	

Legend

- Oncology
- Respiratory & Inflamm.
- CVGI
- Neuroscience
- Infection

As of 31 Dec 2011
Does not reflect partner projects

‘Hot’ science ...

CXCR2 (AZD5069) – Phase IIa

Severe Asthma

OPPORTUNITY

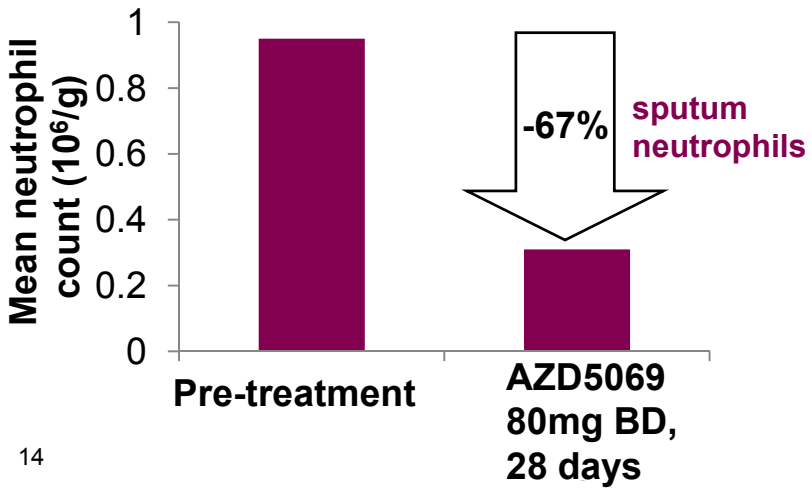
- Asthma is one of the most prevalent chronic conditions, affecting over 300 million worldwide. Every decade, it’s prevalence increases 50%.

DIFFERENTIATION POTENTIAL

- First-in-class COPD therapy and reducing exacerbations in severe asthma

Proof of Mechanism achieved – Phase IIa study showed 67% reduction in neutrophils from baseline

Decreased lung neutrophil counts in Phase IIa



NMDAr (AZD6765) – Phase IIb

Major depressive disorder (MDD)

OPPORTUNITY

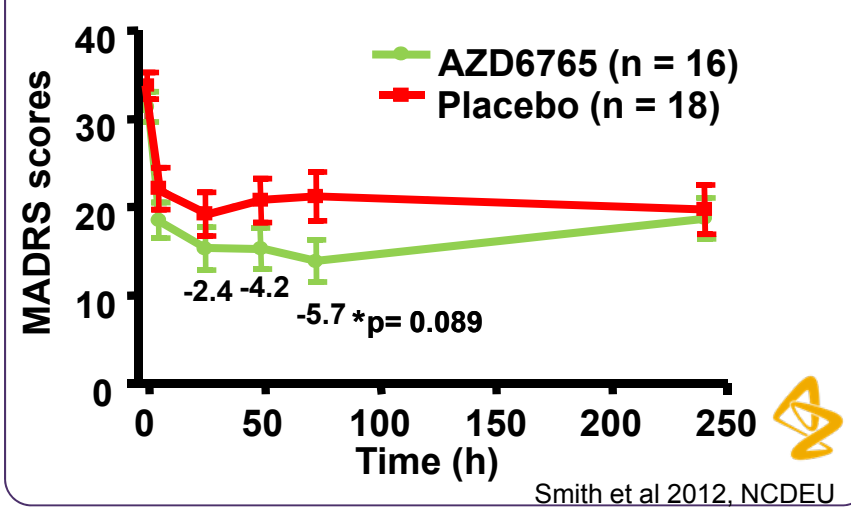
- Globally 450 million people suffer a mental or behavioral disorder. By 2020 it is estimated that depression will be the leading cause of disease burden.

DIFFERENTIATION POTENTIAL

- Treatment for refractory depression that could occupy a unique market position – following ineffective generics and before expensive hospital procedures

Efficacious in Phase IIa without psychomimetic effects – confirmed with fMRI and gamma-EEG; well-tolerated intermittent IV infusions

Single infusion very well tolerated in Phase IIa



Smith et al 2012, NCDEU

Partnering for success

Progress with the virtual iMed

Optimised resources

- Small headcount
- Simplified footprint
- Flexible collaborations replacing brick and mortar labs
- Cost-effective suppliers
- Sharing risk & cost

Improved productivity

- Leadership in place
- Autonomous drug ‘hunters’
- Based in major neuroscience hubs
- Rapid, efficient execution

Partnering with the best

- Proprietary discovery across network of partners
- Tapping into richest science available
- Access to AZ capabilities and global reach
- Sharing successes

Axerion Therapeutics

The Feinstein Institute for Medical Research
North Shore-Long Island Jewish Health System
North Shore LIJ

UBC

Washington University in St. Louis

Weill Cornell Medical College

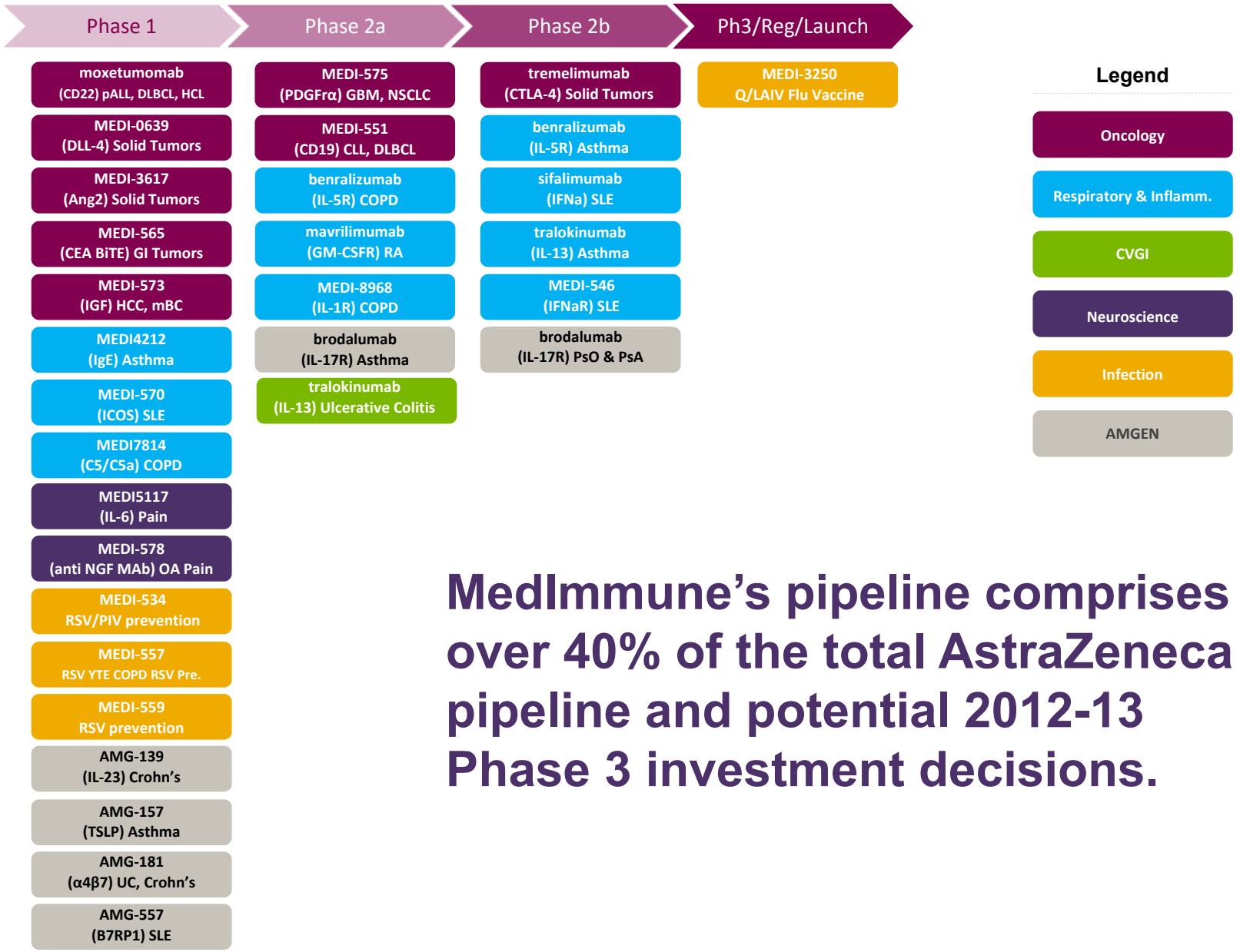
R&D Roundtable

Bahija Jallal, Executive VP R&D, MedImmune

June 14th, 2012

AstraZeneca

A pipeline poised to advance into phase III



MedImmune's pipeline comprises over 40% of the total AstraZeneca pipeline and potential 2012-13 Phase 3 investment decisions.

New approaches to building the R&D pipeline

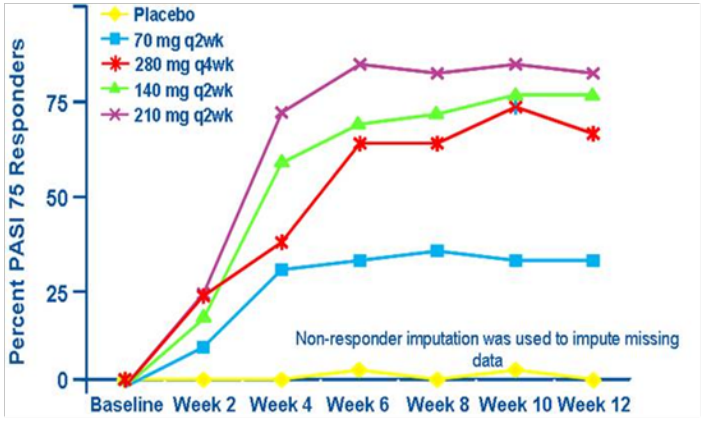
MedImmune AMGEN

INNOVATIVE AMGEN PARTNERSHIP

- MedImmune and Amgen are jointly developing and commercializing five monoclonal antibodies from Amgen's inflammatory disease portfolio
- The assets have novel profiles with the potential to deliver multiple indications per asset
- The lead asset in the collaboration is Brodalumab (AMG827) in Phase 2 development for psoriasis, psoriatic arthritis, and asthma with Phase 3 investment decisions upcoming

Asset	Indications	Phase
Brodalumab (AMG 827)	Psoriasis & Psoriatic Arthritis	2b
	Asthma	2a
AMG 139	Crohn's	1
AMG 157	Asthma	1
AMG 181	Ulcerative Colitis & Crohn's	1
AMG 557	SLE	1
All Assets	LCM	TBD

Brodalumab Efficacy in Psoriasis



Benralizumab (MEDI-563): Asthma (Phase 2b)

Anti IL-5 receptor mAb that depletes eosinophils and basophils

UNMET MEDICAL NEED

- Eosinophilic asthma represents ~40-60% of all patients with asthma and is characterized by more frequent exacerbations and higher risk of near-fatal events

MECHANISM OF ACTION

- MEDI-563 binds with high affinity to the IL-5 receptor alpha thereby depleting eosinophils and basophils. It is believed that reduction in sputum eosinophil count is associated with better asthma control and increases in sputum eosinophil counts are associated with asthma/COPD exacerbations

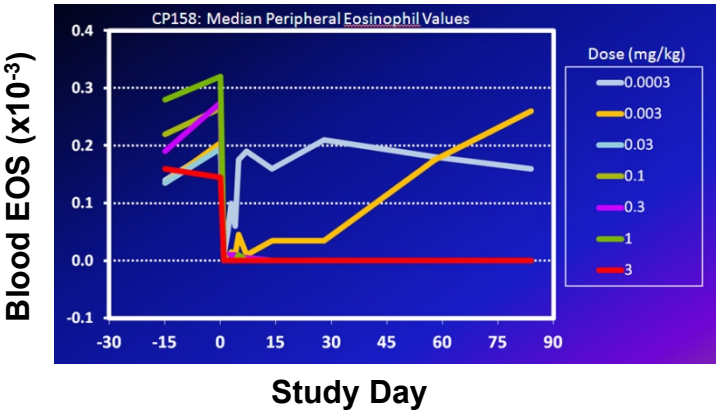
DIFFERENTIATION

- Incorporation of PHC strategy
- Improved outcomes vs. SoC/competitors
- Convenience of dosing vs. SoC

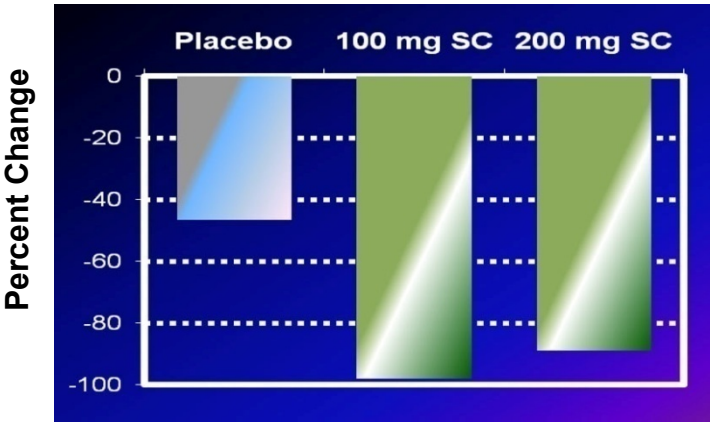
BIOLOGICS MARKET SIZE

- Estimated at $9-13B

Effect on Blood Eosinophils in Asthma Patients



Effect on Airway Eosinophil Values



Sifilimumab (MEDI-545): SLE (Phase 2b)

Anti IFNα mAb that prevents signaling through the Type I IFN receptor

UNMET MEDICAL NEED

- There is a significant unmet need in SLE for therapies that can reduce long-term steroid use and its associated side effects. Type 1 IFNs play a key role in SLE disease pathogenesis with IFN-α being an important Type 1 IFN subtype

MECHANISM OF ACTION

- MEDI-545 binds to IFN-α and prevents signaling through the Type I IFN receptor. IFN-α activates multiple cell types including monocytes, dendritic cells, neutrophils, T cells and B cells, and drives multiple pathways believed to be central to SLE

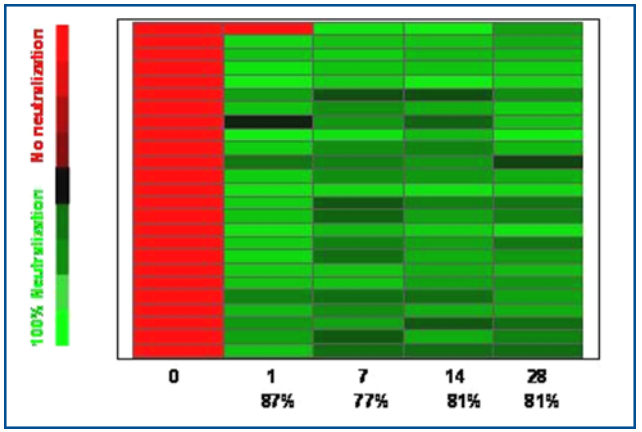
DIFFERENTIATION

- Improved outcomes vs SoC
- Reduced chronic steroid use
- Incorporation of PHC strategy

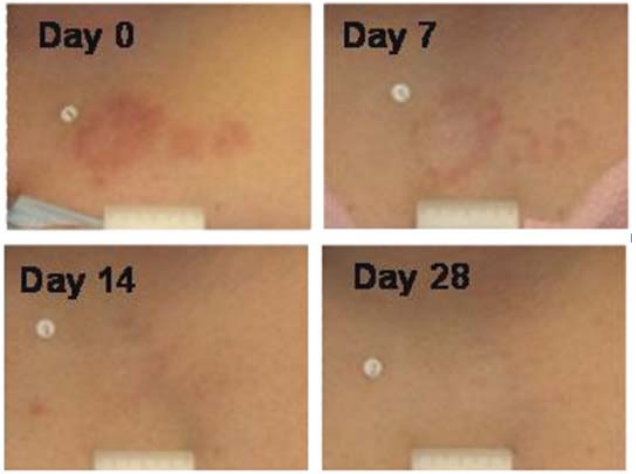
BIOLOGICS MARKET SIZE

- Opportunity estimated at $4-5B

Inhibition of type I IFN-inducible genes (Day 0–28)



Effect on SLE Skin Lesion (Day 0-28)



Moxetumomab pasudotox (CAT-8015): ALL (Ph 1b)

Anti CD22 immunotoxin that uniquely delivers toxins to malignant B-cells

UNMET MEDICAL NEED

- Anti-CD20 therapy with rituximab has improved outcomes for cancer patients. However, many patients relapse and stand to benefit from new approaches

MECHANISM OF ACTION

- Moxetumomab has a unique MoA whereby it selectively binds to CD22, is internalized, and is processed which releases the cytotoxic portion leading to cancer cell death

DIFFERENTIATION

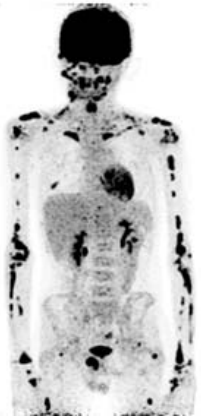
- Targeted therapy: CD22 target is broadly expressed and internalized in B-cell malignancies making it an ideal target for immunotherapy
- Demonstrated single agent clinical activity in both pediatric ALL and Hairy Cell Leukemia

BIOLOGICS MARKET SIZE

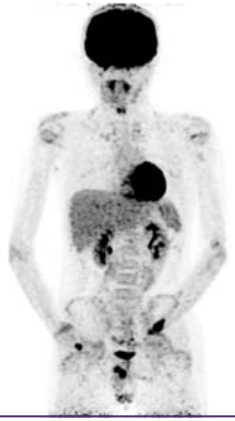
- Opportunity estimated at $1B

Activity in Pediatric ALL

Pre Treatment



Post Treatment



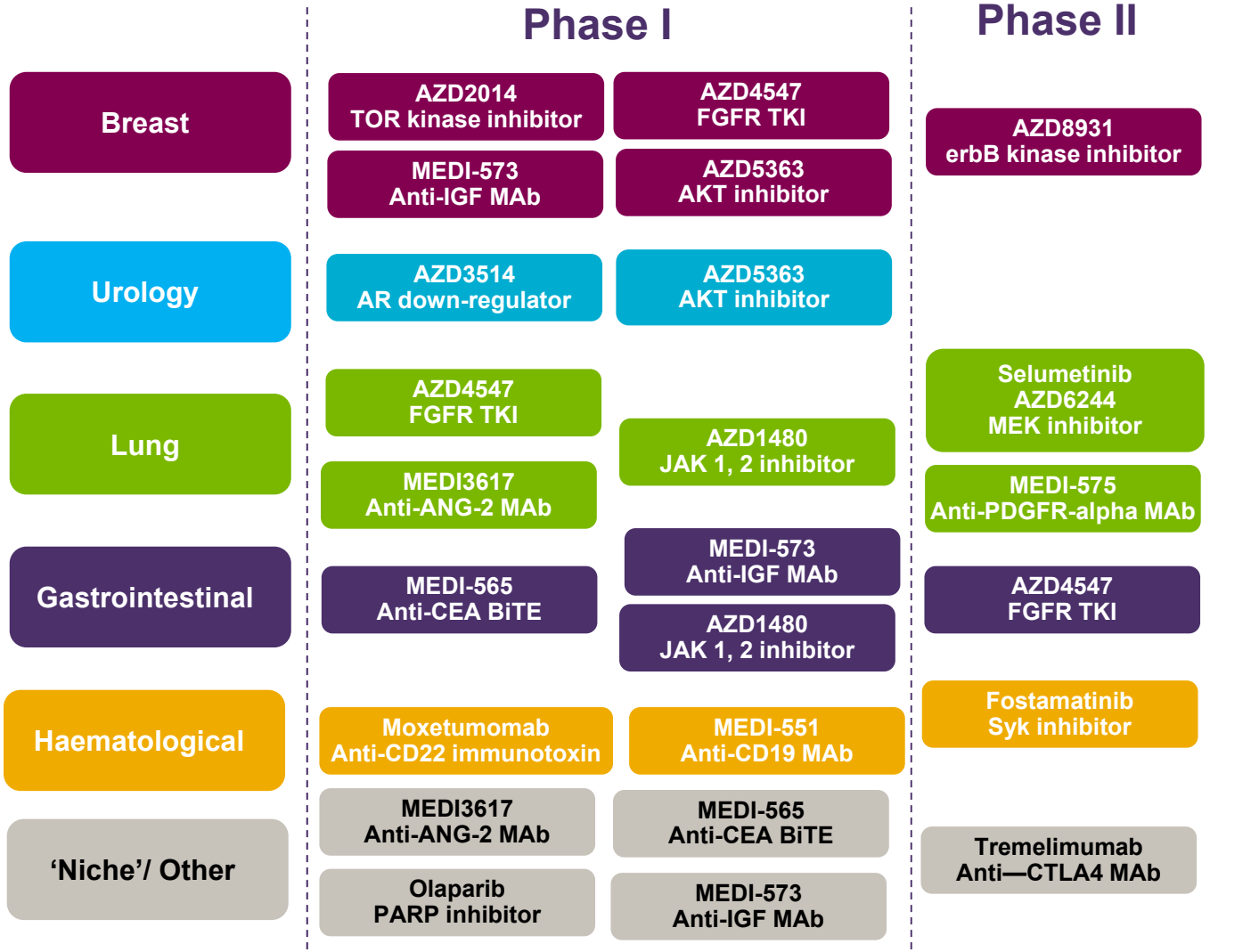
R&D Roundtable

Susan Galbraith, iMed Head, Oncology

June 14th, 2012

AstraZeneca

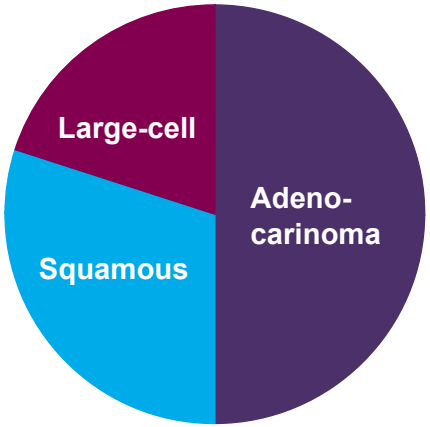
Our oncology pipeline



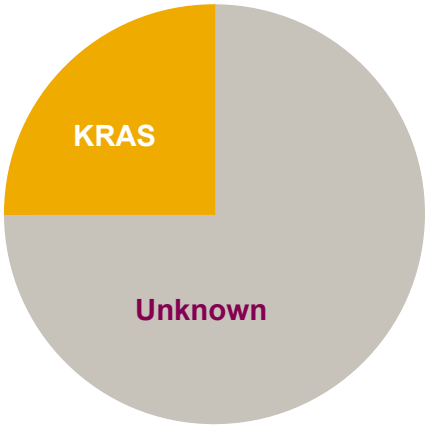
As of 31 Dec 2011

Lung Cancer – The first solid cancer diagnosed by genetic driver and treated by genetically targeted agents

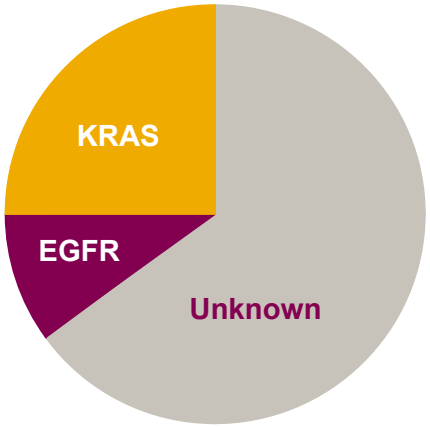
Historical View → **1987** → **2004** → **2012**



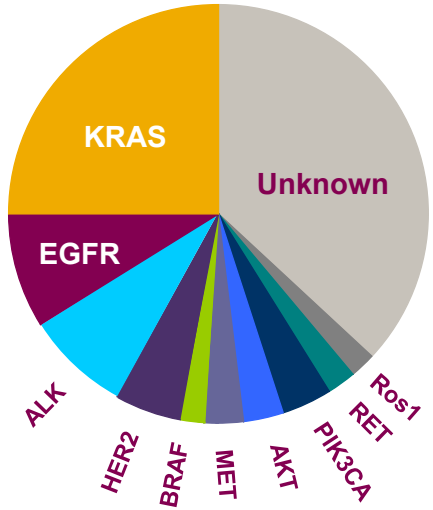
- Worldwide, lung cancer is the most common cause of cancer-related death (1.3M deaths)
- Traditional classification used morphology
- The most common types of Non-small Cell lung cancer described above



- 1987: Discovery showed that NSCLC cells can harbor a single specific mutated KRAS oncogene
- KRAS is thought to be the primary genetic "driver" leading to cancer



- 2001-04: AstraZeneca in collaboration with external groups show that clinical response to Gefitinib (IRESSA) correlates with EGFR mutations



- 2012: Global genomics initiatives (e.g., TCGA) identify multiple additional primary genetic "drivers"
- Majority of lung cancer cases now have a 'molecular diagnosis' with further segmentation inevitable

MEK inhibitor

AZD6244 (Selumetinib) – Treatment for lung cancer

OPPORTUNITY

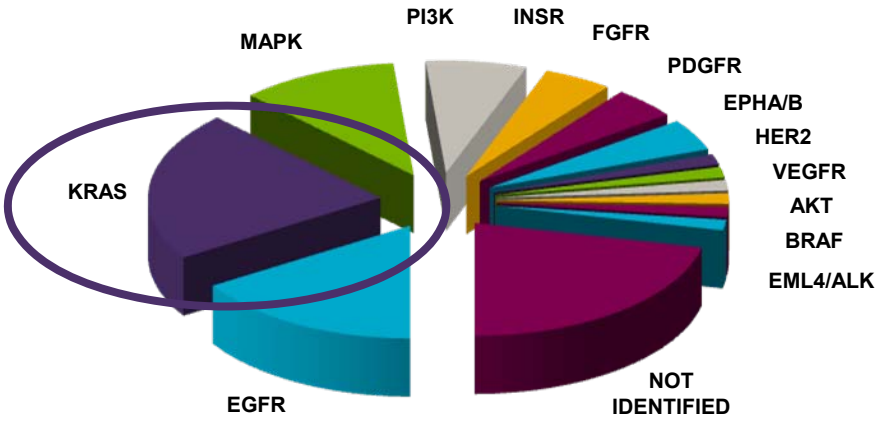
- **KRAS mutation positive non-small cell lung cancer (NSCLC) represents ~20% of lung cancer and is a disease associated with a poor prognosis**

DIFFERENTIATION POTENTIAL

- To drive and lead the establishment of MEK dependency as a key cancer treatment paradigm

SCIENTIFIC RATIONALE

- MEK/ERK pathway is activated as a consequence of KRAS mutation in NSCLC
- KRAS mutations are associated with resistance to Standard of Care and no effective follow-on therapies
- AZD6244 is a potent and selective inhibitor of MEK1/2



Distribution of gene changes in NSCLC

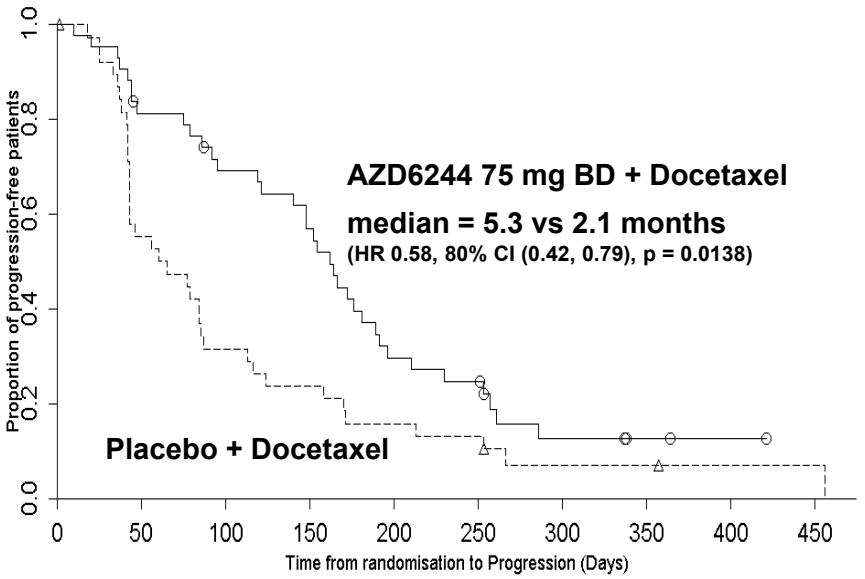
MEK inhibitor

AZD6244 (Selumetinib) – Treatment for lung cancer

WHY WE BELIEVE IN THIS APPROACH

- Phase I achieved Proof of Mechanism and Principle at tolerated dose
- Significant improvement in PFS with AZD6244/ chemotherapy combination vs chemotherapy alone in Phase IIb
- PHC strategy with Roche Molecular Systems to recruit patients with KRAS mutation only

	AZD6244 + docetaxel (N=43)	Placebo + docetaxel (N=40)
Response	16 (37%)	0
Non-response	27 (63%)	40 (100%)



Improved progression-free survival demonstrated and trend to increased OS (median 9.4 vs 5.2 months) following AZD6244 combination treatment in Phase IIb

Fibroblast growth factor receptor (FGFR) inhibitor

AZD4547 – Treatment for gastric, lung and breast cancers

OPPORTUNITY

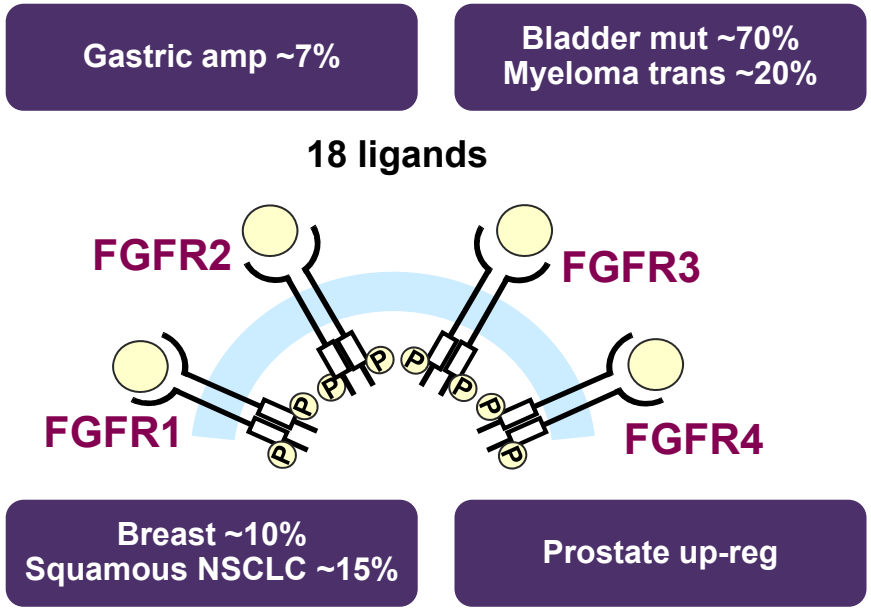
- **Disregulation of FGF/ FGFR signalling is associated with early relapse and poor survival, particularly in patients with gastric tumours**

DIFFERENTIATION POTENTIAL

- A novel targeted therapy for FGFR-amplified cancers

SCIENTIFIC RATIONALE

- FGFR maintains the malignant properties of tumour cells – growth, survival and angiogenesis
- Disregulation of FGF/ FGFR occurs in several tumour subsets due to gene amplifications/rearrangements/mutations



Proportion of tumour subsets with FGFR amplification/ mutations

Fibroblast growth factor receptor (FGFR) inhibitor

AZD4547 – Treatment for gastric, lung and breast cancers

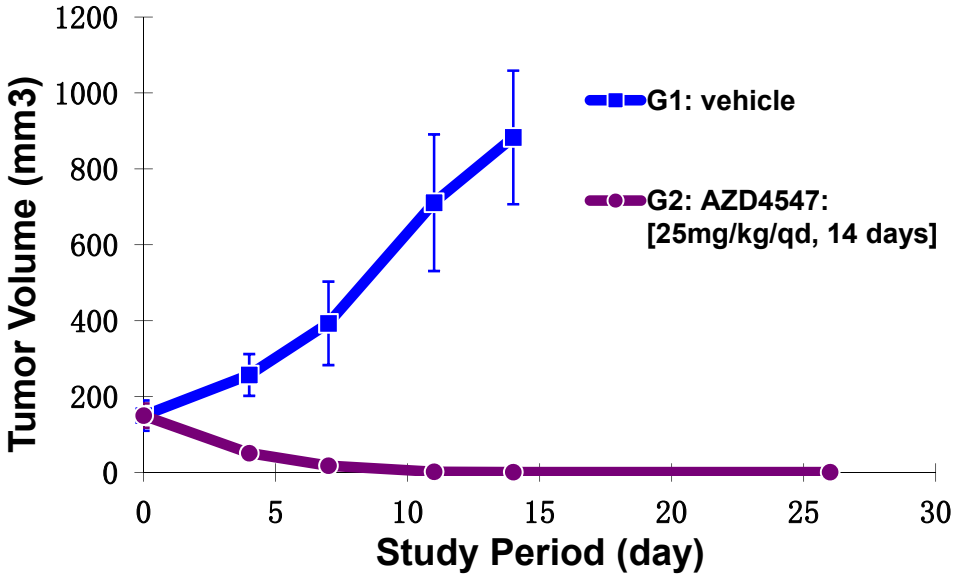
WHY WE BELIEVE IN THIS APPROACH

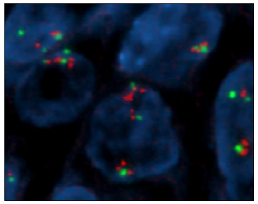
- Primary explant models from patients' tumours with FGFR gene amplification show profound tumour regression with AZD4547
- Diagnostic development in Phase I enables faster transition to Phase III
- Tumour regression seen in a patient with squamous lung cancer and FGFR amplification in Phase I

STATUS

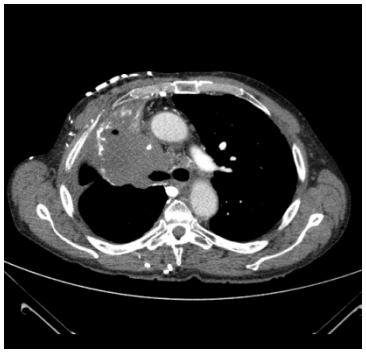
- Potential Phase IIb ID 2012-13 in Squamous Lung cancer
- PHC strategy to prospectively select patients with FGFR gene amplification using FISH diagnostic assay

Lung primary explants with FGFR1 gene amplification regress when treated with AZD4547 *in vivo*





FISH assay



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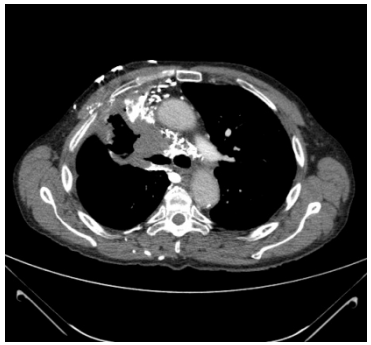


9/5/2012

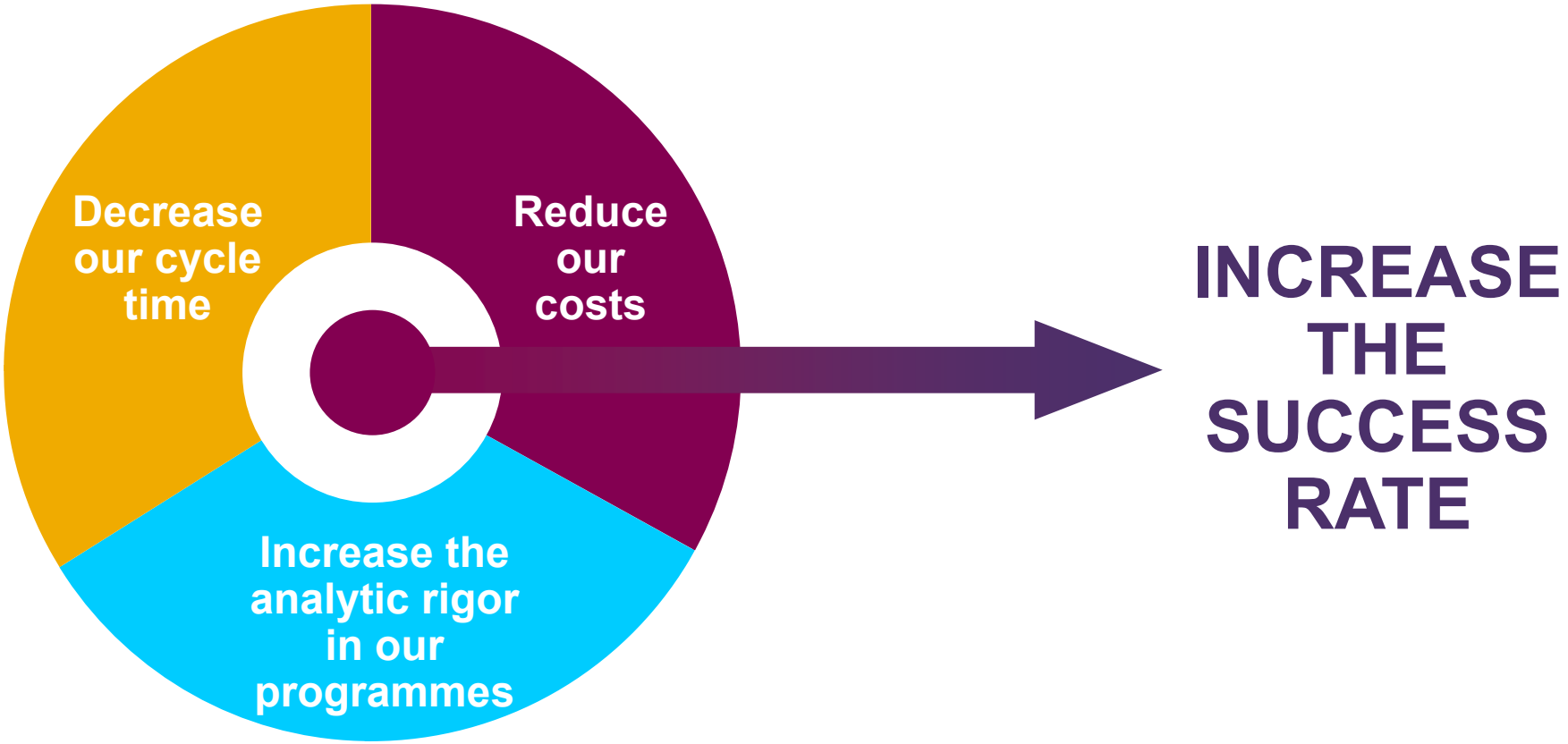
R&D Roundtable

Bill Mezzanotte, GMed Head, Respiratory, Inflammation and Neuroscience

June 14th, 2012

AstraZeneca

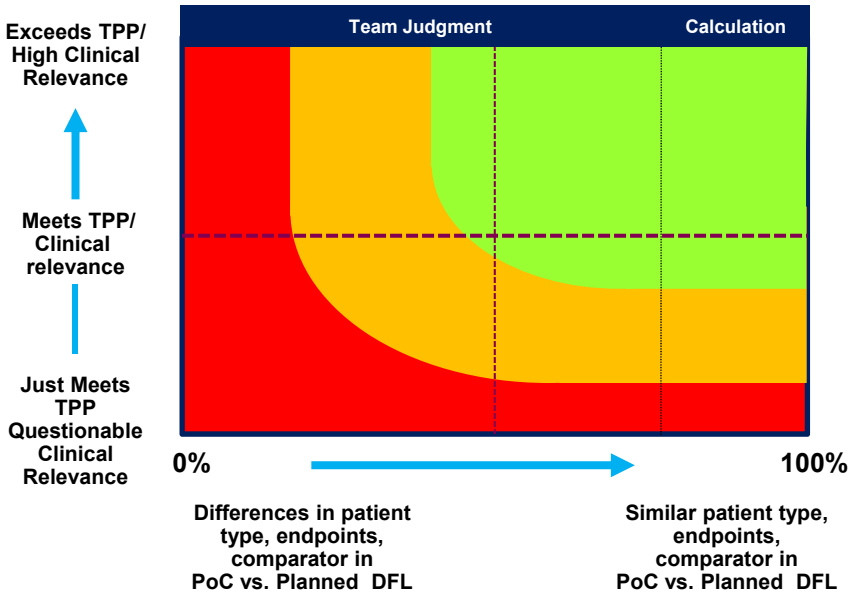
Increasing our success in late stage development



Phase III heat maps and probability of success

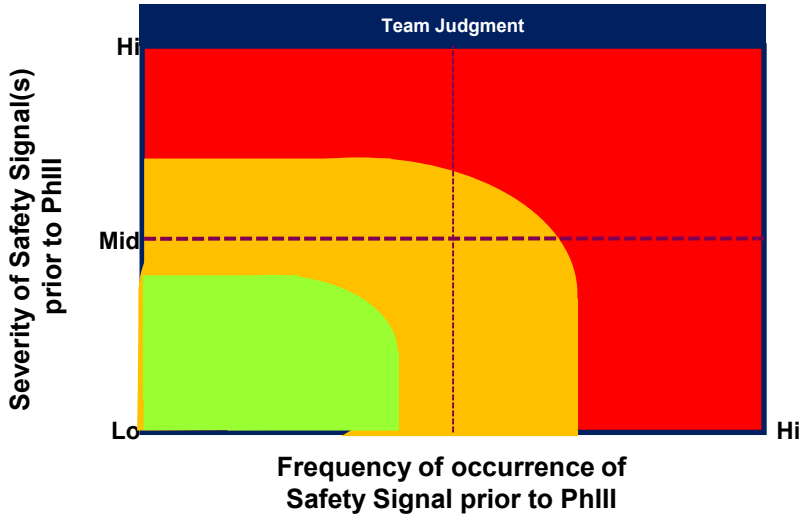
Efficacy map

1. What is the magnitude of your PoC Clinical signal relative to your base TPP?
2. How similar is your planned Phase III Clinical Programme to your PoC trial?



Safety map

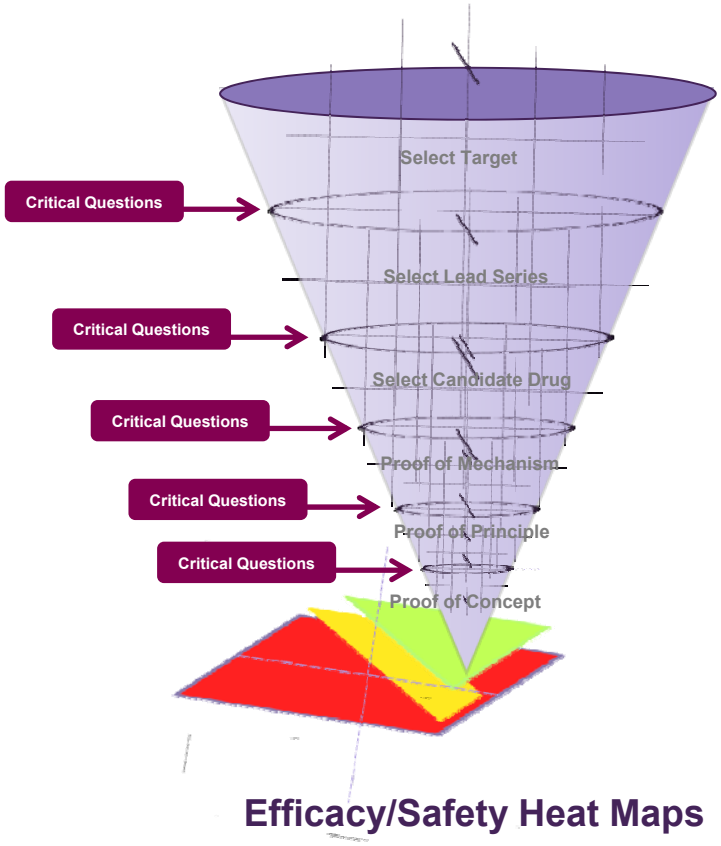
1. What is the severity of your safety signal(s) prior to PhIII?
2. What is the frequency of safety signals prior to PhIII?



Repeated Critical Evaluation Over Time Helps to Identify the Most Promising Molecules

Pre-Clinical

Phase III



Efficacy/Safety Heat Maps

High uncertainty
Low knowledge

Low uncertainty
High knowledge

Regulatory rigour for greater success

BRILINTA:

First Regulatory Approval Achieved in Europe —December 2010

Achieved regulatory approvals in 38 countries across 5 continents within 6 months of first approval

External preparedness

Environmental factors

Competitive intelligence

AZ and health authorities interactions

Internal preparedness

Regulatory peer review

Regulatory feedback

Regulatory timeline

Increasing payer outcomes

We deliver clinical and economic evidence for payers to understand the value of our medicines in achieving better, cost effective healthcare

Payer Insights

- Customer engagement
- Payer research
- Payer advisory boards

Payer Analytics

- RCT design & analysis
- Health economic modelling
- Specialist statistics (Payer Analysis Plan)
- Informatics

Payer Evidence Strategy

- Product strategy development
- Payer scientific advice
- Global reimbursable dossier generation
- Informatics

Real World Evidence

- Customer & partner engagement
- RWE study design & analysis
- Informatics

Strategic & Operational Pricing

- Price modelling
- Pricing research & analogue analysis
- Contracting and price negotiation

Impressive clinical trial capability

BRILINTA PLATO Trial

Real World Design & Head to Head Superiority

Acute Coronary Syndrome

- Trial design reflected ACS treatment decisions – 18,700 patients in 43 countries
- Superiority achieved against current ACS standard of care
- Payer and physician needs addressed in study outcomes

ONGLYZA SAVOR TIMI-53 Trial

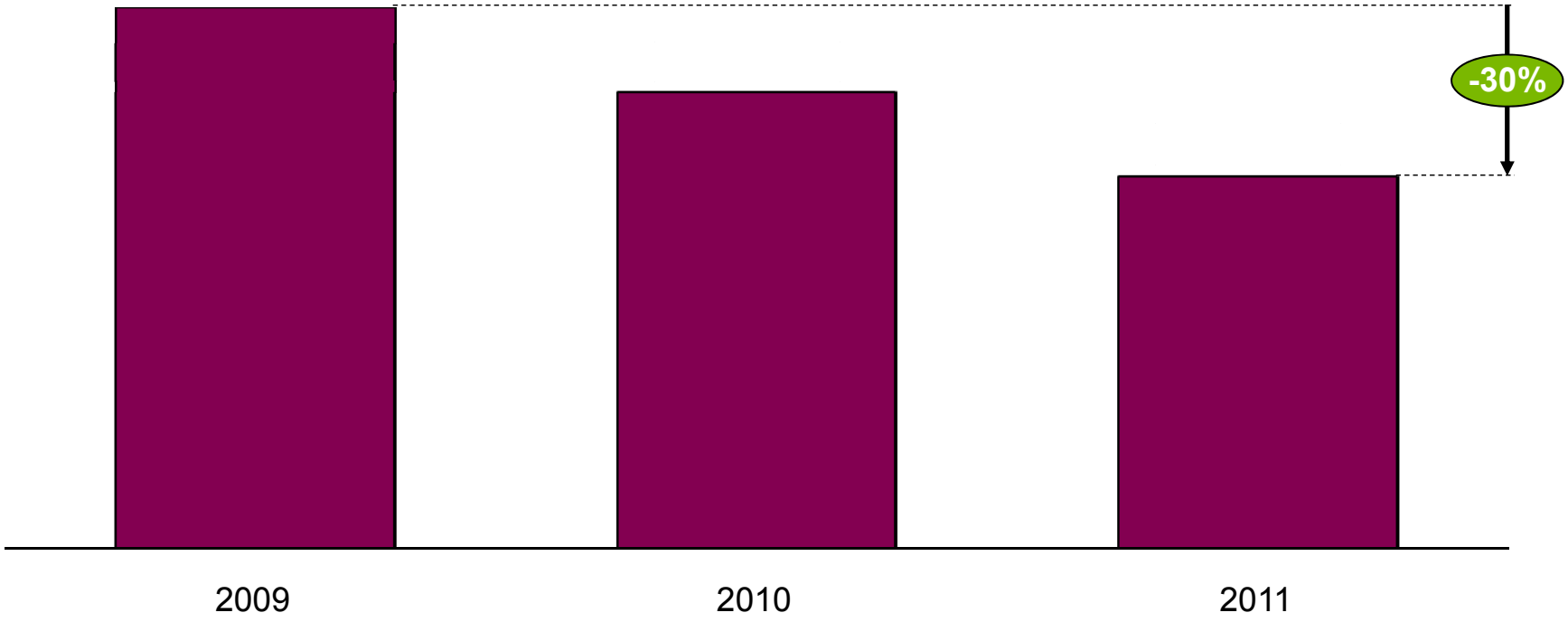
Elegant Design to Foster Recruitment Speed

Adults with Type 2 Diabetes

- Fast study recruitment – 16,500 patients completed in 19 months
- Event-driven trial design powered for superiority
- Complies with new FDA T2DM guidance regarding long-term CV risk

Significant improvement in R&D productivity: Example: Cost per patient

AZ has reduced "cost per patient" by more than 30% in the period 2010-2012



Source: R&D Clinical June 2012