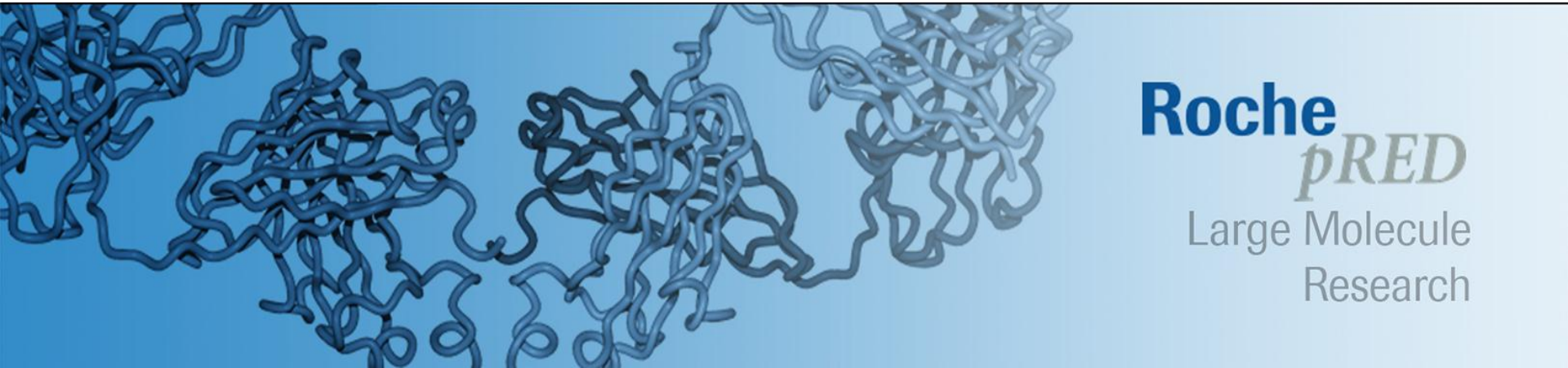
Roche Forschungsstandort Penzberg und Ausblick auf neue Produkte

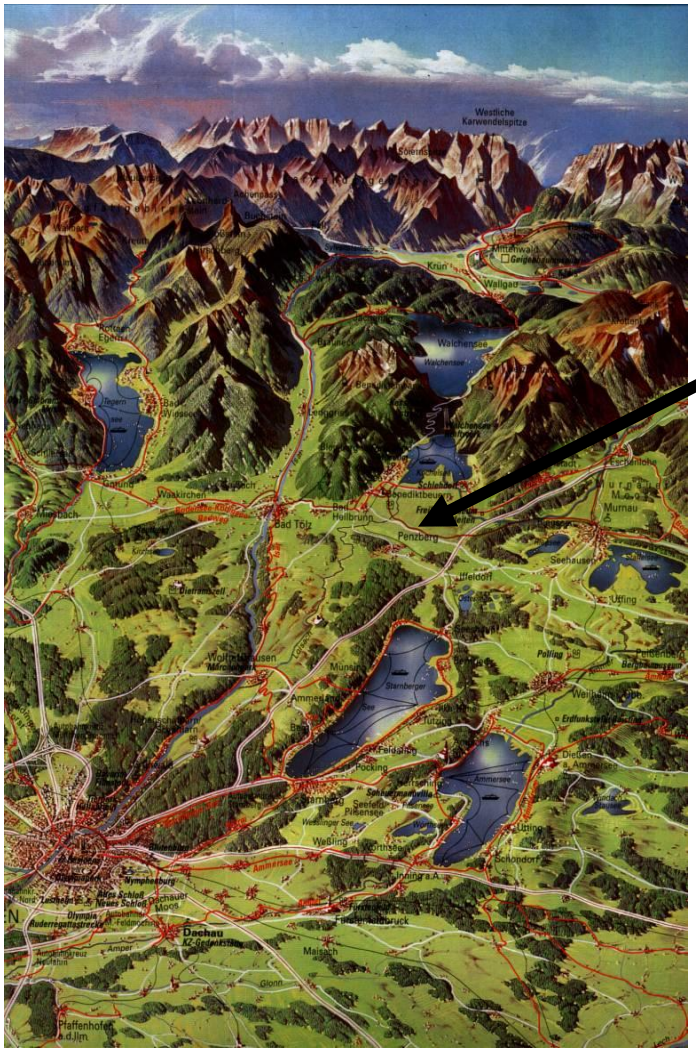
vfa.bio – Veranstaltung mit Patientenvertretern
Penzberg, 6. November 2013

Ralf Schumacher



Welcome to the Penzberg Site of Roche

Where we are



Penzberg

one of the largest Biotech-sites in Europe

situated near Munich and the Alps in Upper-Bavaria

Inhalt

- Roche in Penzberg
  - Diagnostik und Pharma
  - Forschung, Entwicklung und Produktion
- Therapeutische Proteine
- Neue Entwicklungen aus der Roche Forschung
  - Vom Labor in die Klinik

Roche in Penzberg

Eines der größten Biotech-Zentren Europas

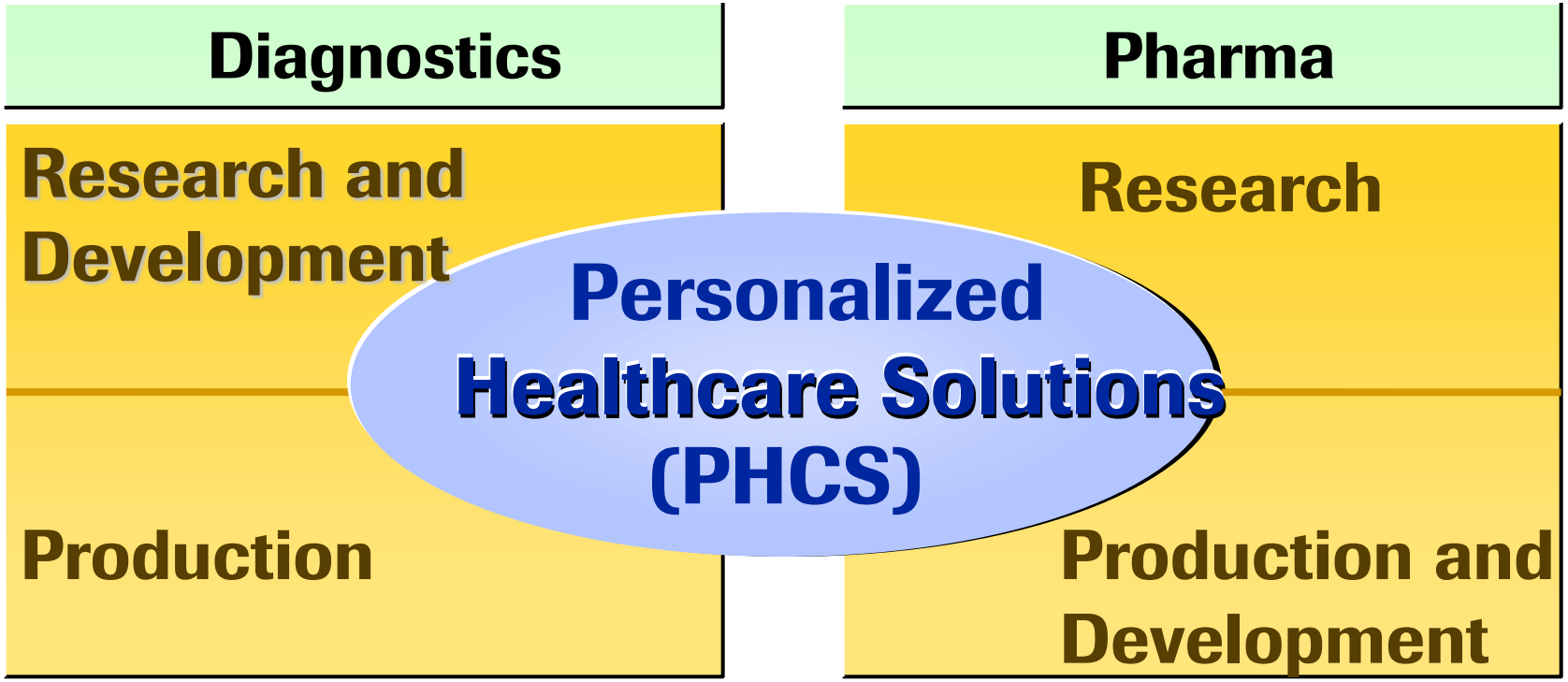
Divisionen:	Pharma und Diagnostics
Gründung:	1972
Beschäftigte:	> 5000 MA*
Fläche:	ca. 350.000 m^2
Investitionen 2012:	ca. 94 Mio. Euro
Investitionen 2000 – 2012:	ca. 1,806 Mrd. Euro

* Headcount inkl. Teilzeit- und befristete Stellen sowie Auszubildende und Praktikanten, Stand 12/2012

Roche at Penzberg

Where we are

We are the only Roche Biotech site that has the unique combination of both divisions on site



Historische Entwicklung
Über 40 Jahre Biotechnologie

1972

1974
Production: co-enzymes and substrates (e.g. NAD)

1975

1979
First enzyme cloned in E.coli:

GalDH

1982
Production: test kits based on recombinant enzymes

1985

1986
Development start: EPO

1990
Production start of first therapeutic protein: EPO

1995

1996
Dev. & Production:
-ECL technology

-Reteplase: first "from idea to patient" drug from Penzberg

1998
First Roche therapeutic mAb: Herceptin

2002
Production start: Pegasys

2007
Production start: Mircera

2012

2011
-Biomarker/CoDx Zelboraf

-10.000st batch for Elecsys

Roche in Penzberg

Biotech from Science to Patients

Site Penzberg

Pharma

Discovery
Cell Science
Bioinformatics
Molecule Design
Therapeutic Proteins
CD Media
Cell Banking
Clinical Supply
Manuf. Process Val.
Manuf. Process Dev.
Mircera
Pegasys
Herceptin
NeoRecormon

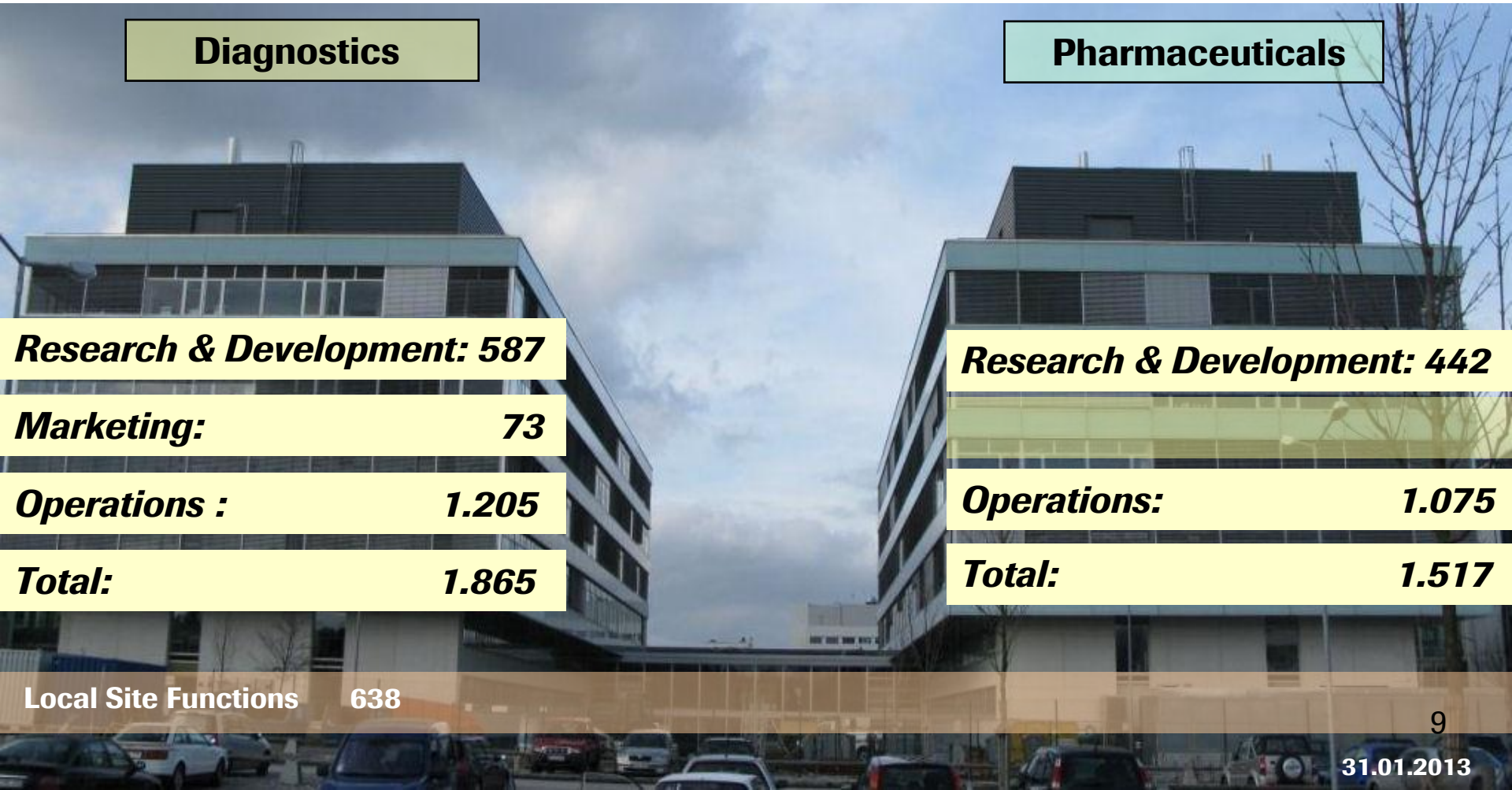
Diagnostics

Workflow Solutions
New Technologies
Stem Cell Tools
Rec. Proteins
Biostatistics
Nucleic Acid Purific.
Biomarker Assays
Custom Antibodies
Real-time PCR
Rare Reagents
Cobas Elecsys Family
Biochem. Reagents
Cedex HiRes
Light Cycler
MagNA Pure

Roche at Penzberg

with <u>both</u> Pharma & Diagnostics division on site

Headcount (FTE)



Diagnostics	
Research & Development:	587
Marketing:	73
Operations :	1.205
Total:	1.865

Pharmaceuticals	
Research & Development:	442
Operations:	1.075
Total:	1.517

Local Site Functions 638

Roche at Penzberg

Site overview Penzberg

Diagnostics production · Diagnostics research and development · Pharma production · Pharma research and development · Site Infrastructure

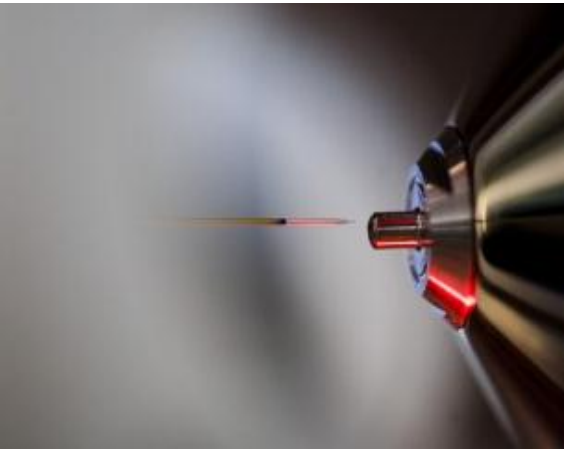
Pharma-Forschung und technische Entwicklung

Center of Excellence für therapeutische Proteine

- Kompetenzzentrum für die Erforschung, technische Entwicklung und frühe klinische Entwicklung von therapeutischen Proteinen für alle Krankheitsgebiete, die bei Roche im Fokus stehen
- Biologische und präklinische Forschung für onkologische Biopharmazeutika, einschließlich Biomarkern sowie gewebebasierter Forschung und Diagnostik
- Entwicklung technischer Prozesse
- Herstellung von Proteinwirkstoffen für präklinische und klinische Studien
- Entwicklung bis zur Marktdimension unter Einbezug der behördlichen Richtlinien und Zulassungen

Diagnostik–Forschung

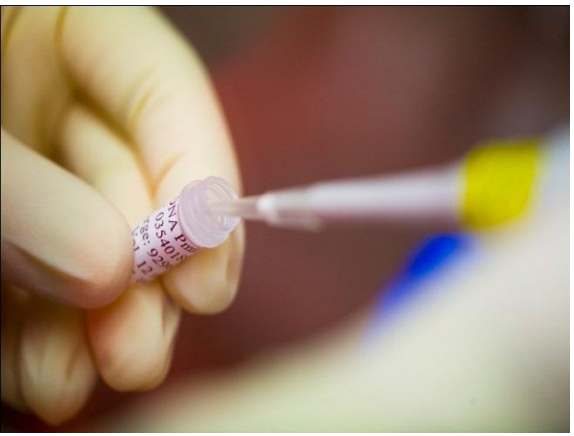
Zentrum für Forschung und Entwicklung



- Immunologie
- Klinische Chemie
- Systemintegration
- Genanalyse

Diagnostics Operations

Reagenzien für biochemische Forschung und Diagnostik



Produktion von Einsatzstoffen und Zwischenprodukten aus unterschiedlichsten Rohmaterialien unter Einhaltung der relevanten regulatorischen Vorgaben

Produktion von Kits und Bulkwaren für Forschungseinheiten und Industriekunden

Entwicklung von neuen Produkten mit Industriepartner (customized products)

Qualitätskontrolle für alle eingehenden und ausgehenden Produktchargen der Operations

Diagnostics Operations
Überblick Produkte

Mikrobielle Fermentation/Enzyme	Bakterien, Hefen, Pilze, Viren, Proteasen, Collagenasen, Marker-/Glukoseenzyme, Albumine, Immunoglobuline, Antigene, Streptavidin
Zellfermentation/ Protein-Chemie	CHO-Zellen, Hybridoma, Antiseren, Antikörper, Antikörper-Fragmente (PAK, MAK), Markierte AK, Modifizierte Proteine, Streptavidin-Beads
Chemie/ Biosubstanzen	Enzymsubstrate, Coenzyme, Farbstoffe, Oligonukleotide, Nukleotide, Nukleinsäuren, Peptide, Goldkonjugate, Magnetische Glaspartikel
Manufacturing	Reagenzien für PCR: MagNAPure, Lightcycler, Sequencing, Arrays; Biochemica, Mikrotiterplatten, Mastermixe
Qualitätskontrolle	Biochemische Analysemethoden, Diagnostische Funktionstests, Dokumentation
Management Support/ Effizienzinitiativen	Steuerung sämtlicher produktionsbezogenen Prozesse und Effizienzinitiativen

Pharma in Penzberg

- Produktion in Penzberg
- Forschung Therapeutische Proteine

Pharma-Biotech-Produktion

Biotechnologisch hergestellte Wirkstoffe

Wirkstoff	Marktprodukt	Indikation
Trastuzumab	Herceptin®	Brustkrebs Metastasierender Magenkrebs
Peginterferon alpha-2a	Pegasys®	Hepatitis B und C
Epoetin beta	NeoRecormon® (= EPO)	Blutarmut
Methoxy polyethylene glycol-epoetin beta	MIRCERA®	Blutarmut

weitere Produkte in der Entwicklung

Challenges and Opportunities in Drug Discovery

Heterogeneous disease causes and heterogeneous patient populations

→ hypothesis driven, specifically targeted approaches – supported with biomarkers, - omics approaches and strong disease understanding (preclin & clin), patient stratification is a MUST, patient selection based on biomarkers

High challenges for clinical development and launch

→ broad preclinical assessment (eg imaging), developing biomarker assays and translation into companion diagnostic

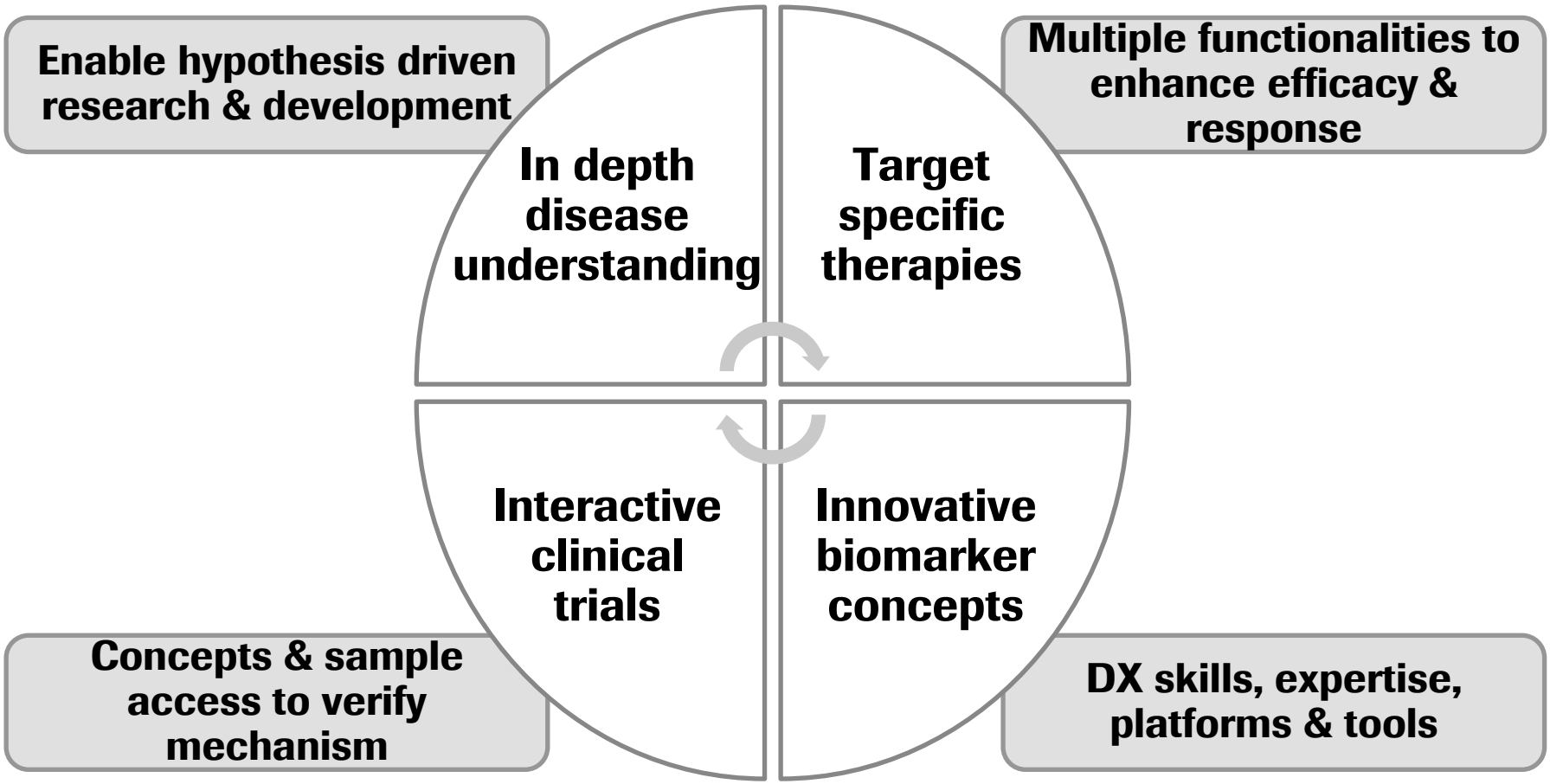
Long time from Hypothesis to poc and launch

→ increase confidence by starting biomarker work already in early preclinical phase integration from discovery knowledge into development design

Increasingly competitive environment

→ differentiation via in house validated targets, unique therapeutic modalities, rare profile Biologics, engineered modular Biologics; integrate biology and technology

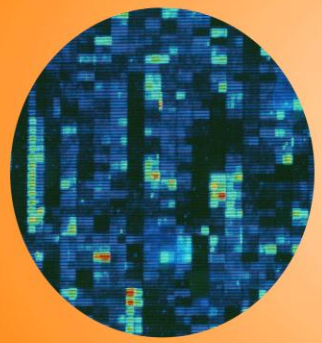
Modern drug discovery – driven by innovative target specific therapies and biomarker concepts



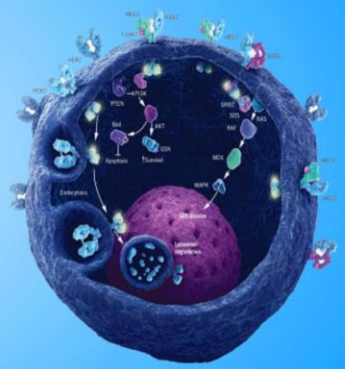
Roche uniquely positioned to drive PHC

Translating excellence in science into effective treatments for patients

Diagnostics

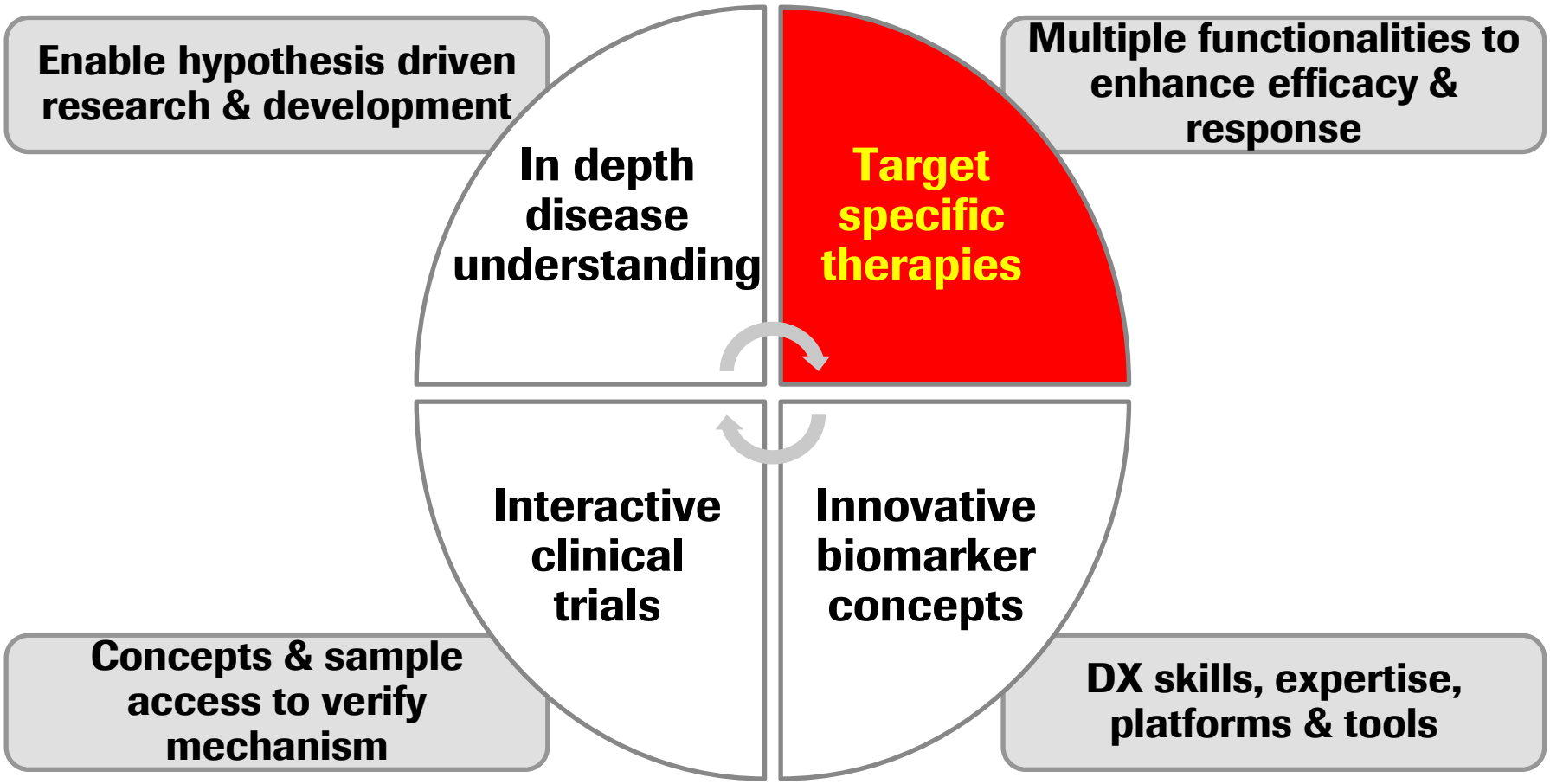


Pharmaceuticals



→ Combine expertise in molecular biology and technologies to benefit patient

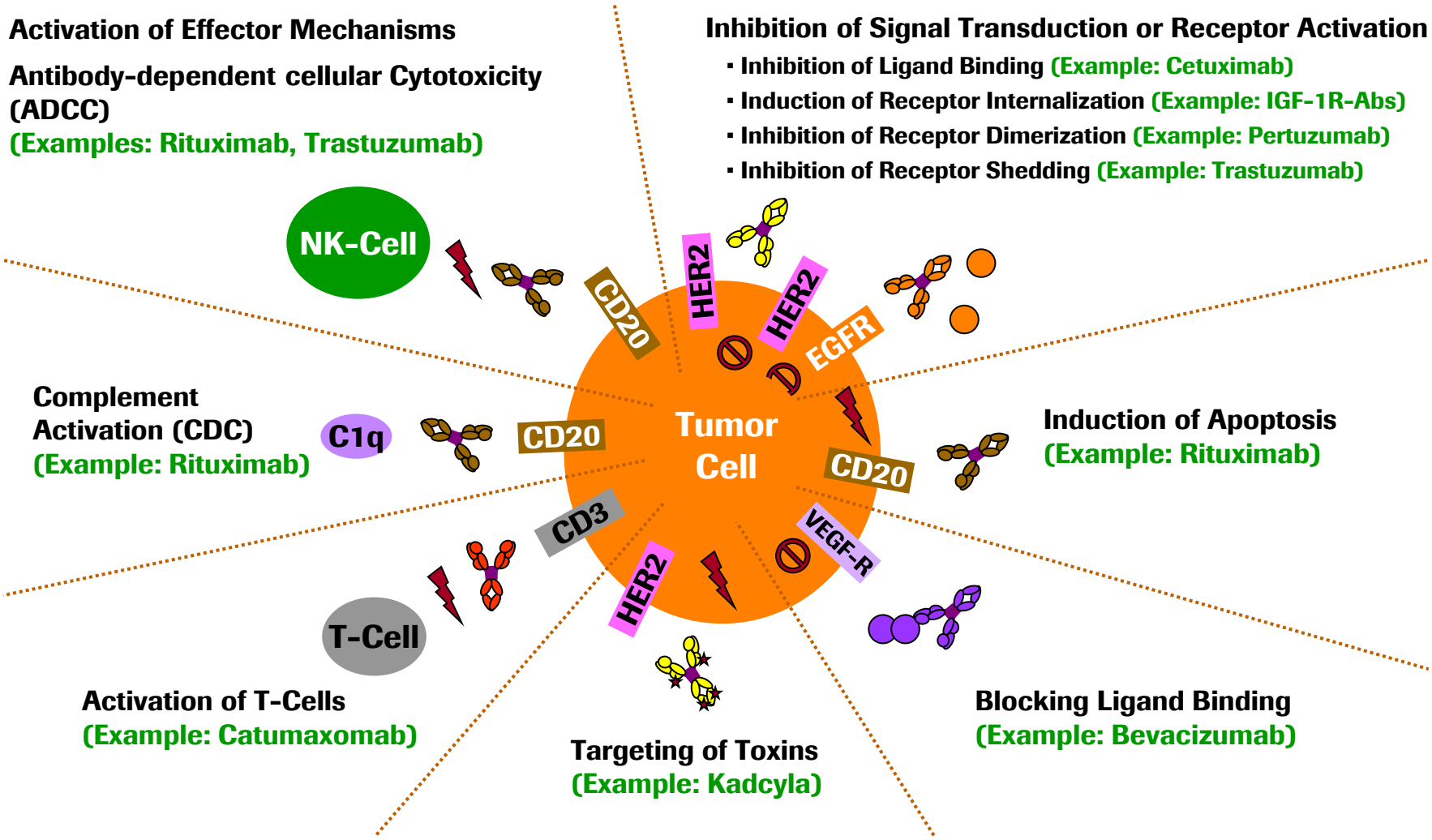
Modern drug discovery – driven by innovative target specific therapies and biomarker concepts



Therapeutic Proteins

- Therapeutic proteins (especially monoclonal antibodies) display high target selectivity and strong binding affinity
- The specific interaction with molecular targets allows to identify patients who may respond to the therapy
- Therapeutic proteins are developed in areas of high medical need
- Therapeutic Proteins are by far the fastest growing and promising business segment of innovative pharma products
- If a therapeutic effect is achieved the dose is in many cases not limited by side effects
- Main risk is target quality (efficacy in pivotal studies)

The Mode of Action of mabs is complex... and may involve contributions from multiple mechanisms



The *in-vivo* net contribution of different modes of action described for one mab is often incompletely understood and may also be different in different indications.

Modified from: Hasmann, M. et al. (2009) ChiuZ,

GAZYVA is designed to go beyond the revolution of MabThera/Rituxan by delivering superior efficacy

and

devoted to become the best-in-disease foundation for patients with B-cell malignancies

Type II anti-CD20 mAb[1]

↓

Increased Direct Cell Death[2]

Up to 50x in Direct Cell Death

Glycoengineered Fc Region[2]

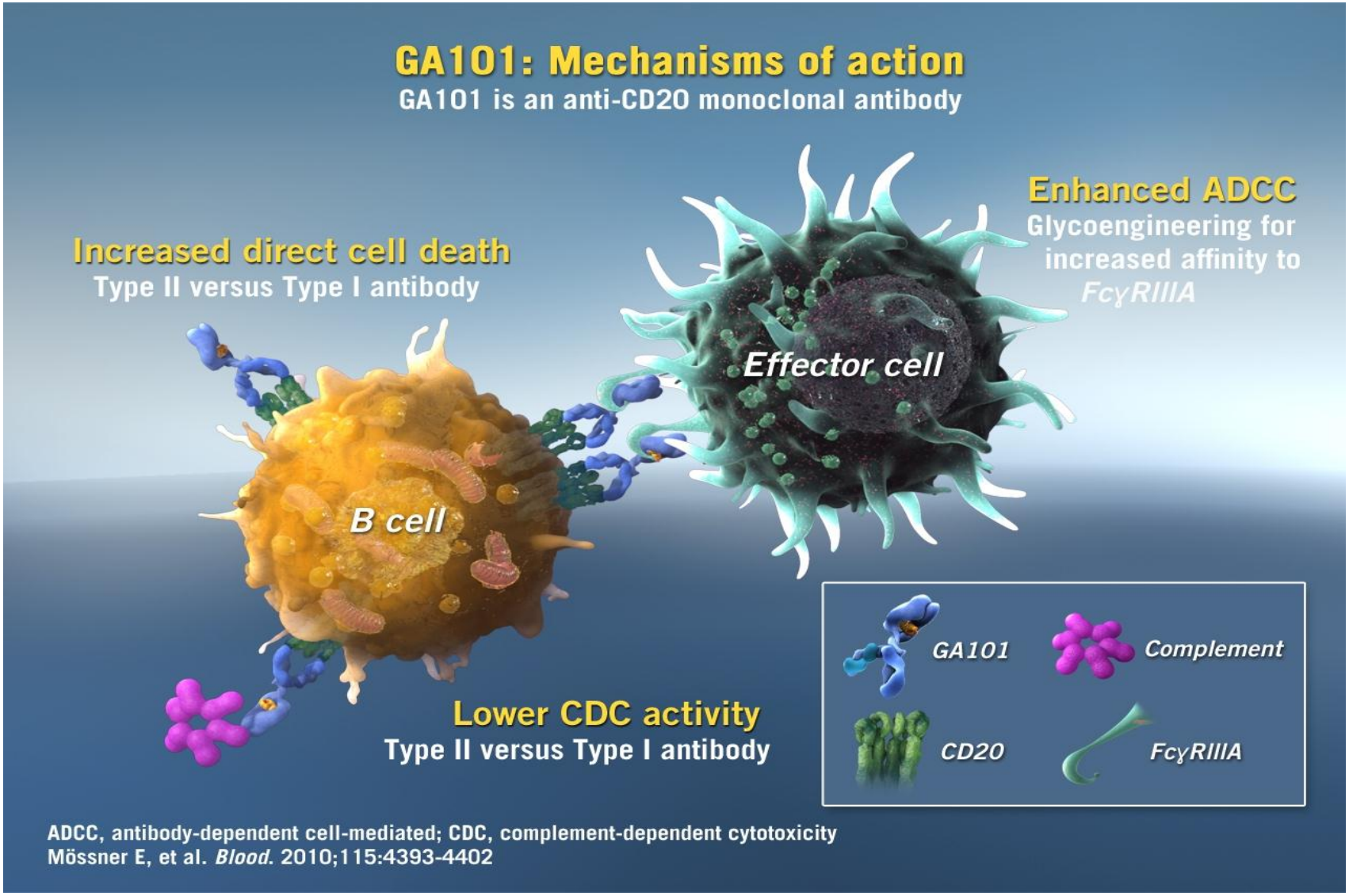
↓

Increased antibody-dependent cellular cytotoxicity (ADCC)[2]

Up to 100x in ADCC

Source: 1. Niederfellner G, *et al*. *Blood* 2011;118:3358–367. 2. Mössner E, *et al. Blood* 2010; 115:4393–4402 3. Alduaij W, *et al. Blood* 2011; 117:4519–4529.

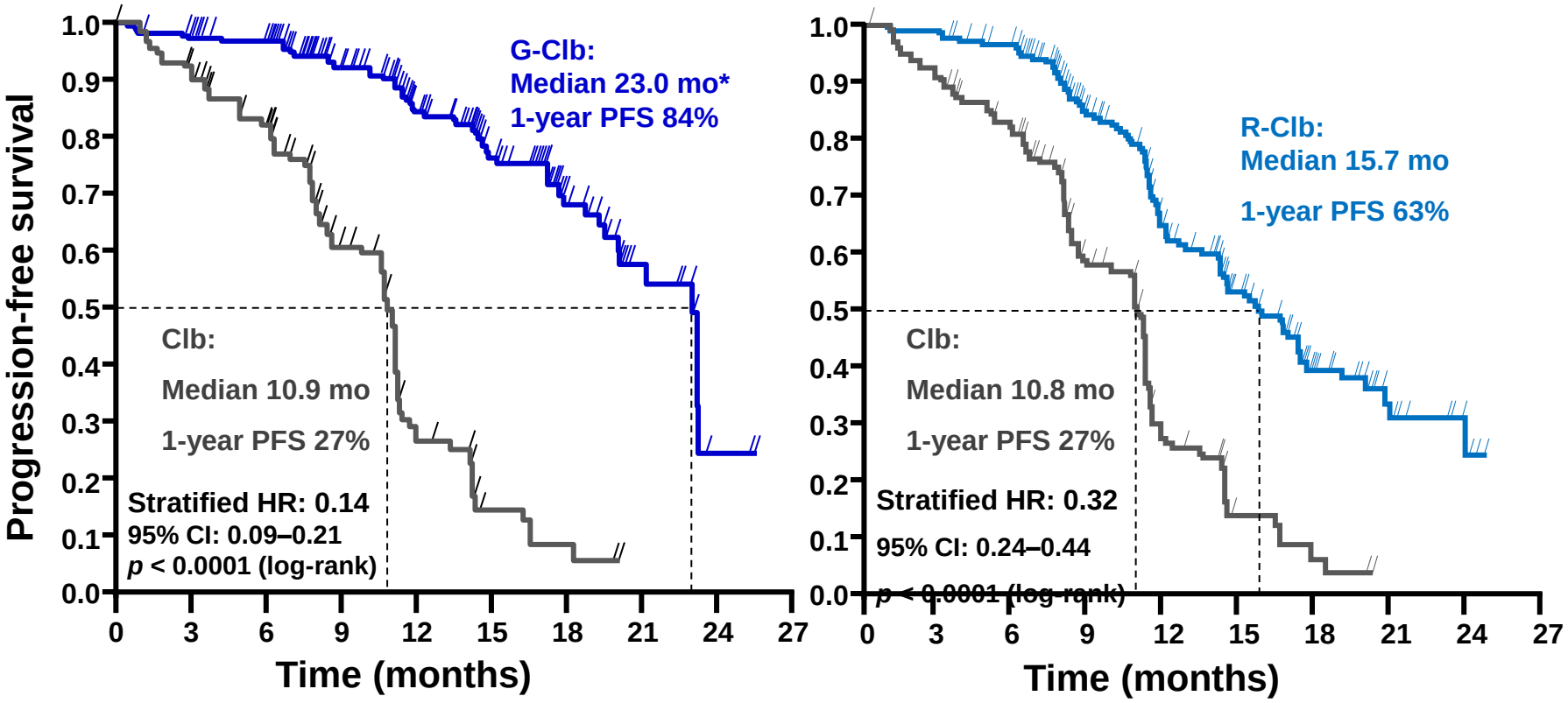
GAZYVA® Mechanisms of action



CLL11 1a & 1b – PFS (primary endpoint)

86% lower risk of progression, relapse or death in the G-Clb arm

68% lower risk of progression, relapse or death in the R-Clb arm



* In the G-Clb arm < 10% of patients had reached the median at cutoff; therefore, in contrast to the Clb arm the G-Clb median PFS could not be reliably estimated due to the few patients at risk at time of G-Clb median.

CI = confidence interval; HR = hazard ratio.

Doing now what patients need next