

A New Age In Drug Development: Rising to the Challenge

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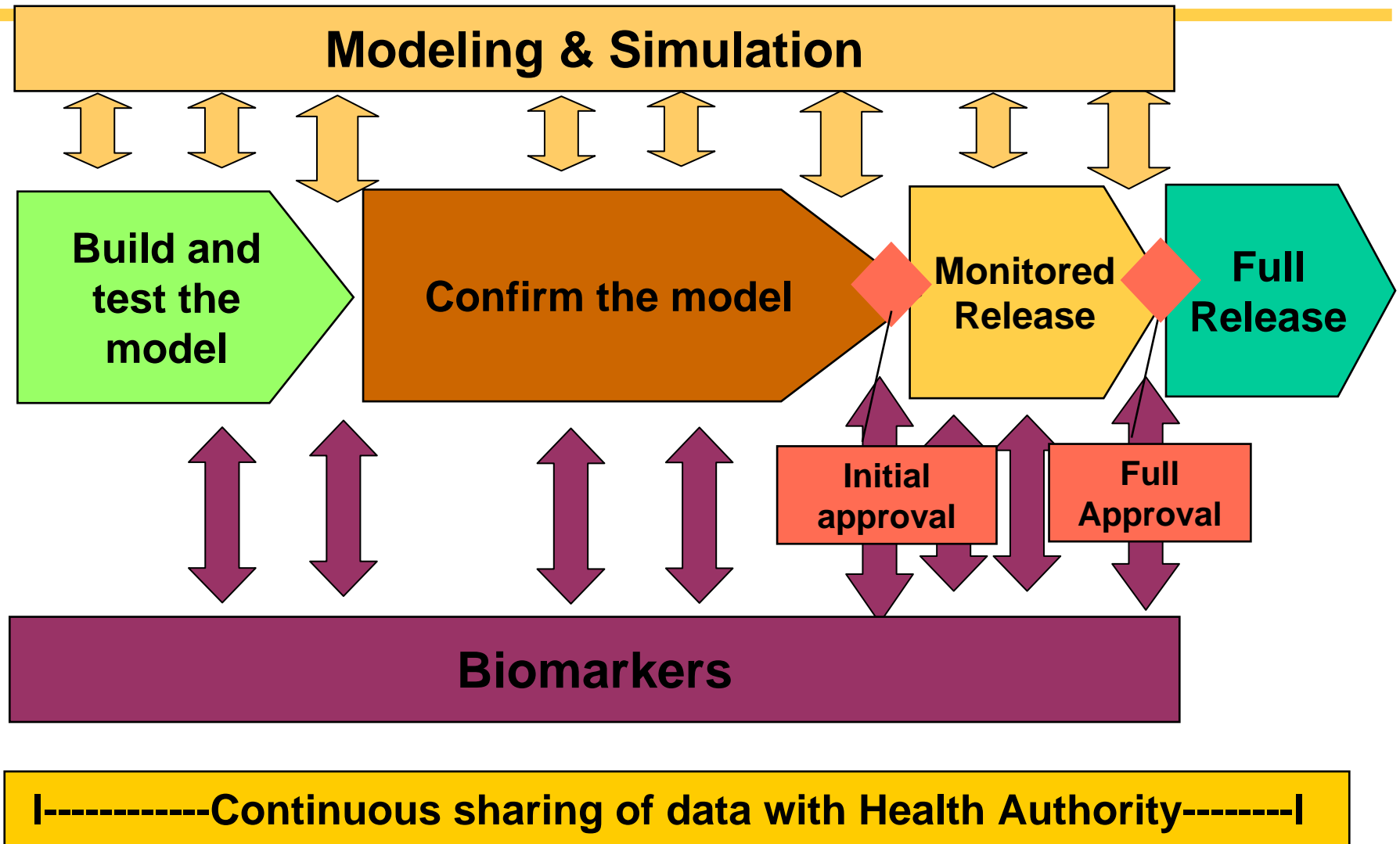
Novartis Pharma AG



Key Drivers to Transform Development

- 1 **Modeling and simulation**
- 2 **Rapid compound selection in man**
- 3 **Biomarkers**
- 4 **Innovative clinical trial design**
- 5 **Innovative approaches to initial registration**
- 6 **Integrated safety assessment & risk management**
- 7 **Quality by design manufacturing**

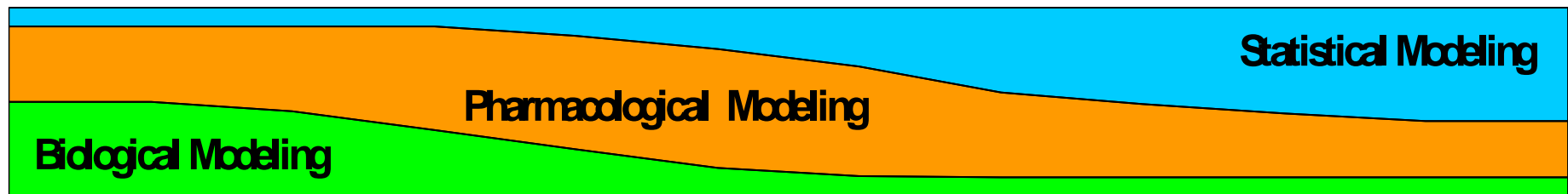
A New Age of Drug Development?



Integrating Knowledge for Model-based Drug Development

Genes...Cells...Tissues...Systems...Patients...Populations

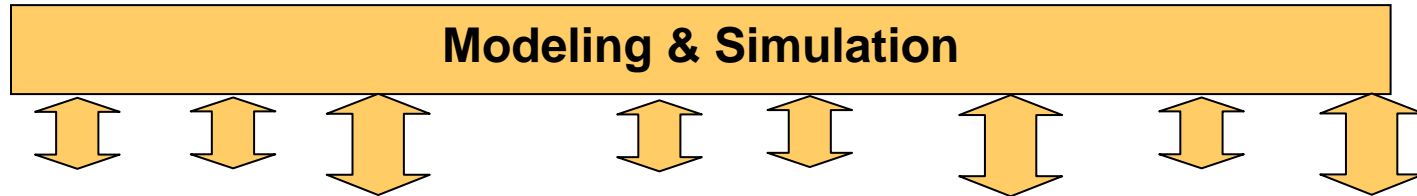
Development time axis



Integrated approach to Modeling & Simulation:


- **Biological modeling** – model pathways of disease as targets of intervention
- **Pharmacological modeling** – determine relationships for dose, exposure, response
- **Statistical modeling** – assesses development strategies and trial designs in populations

Model-based Drug Development

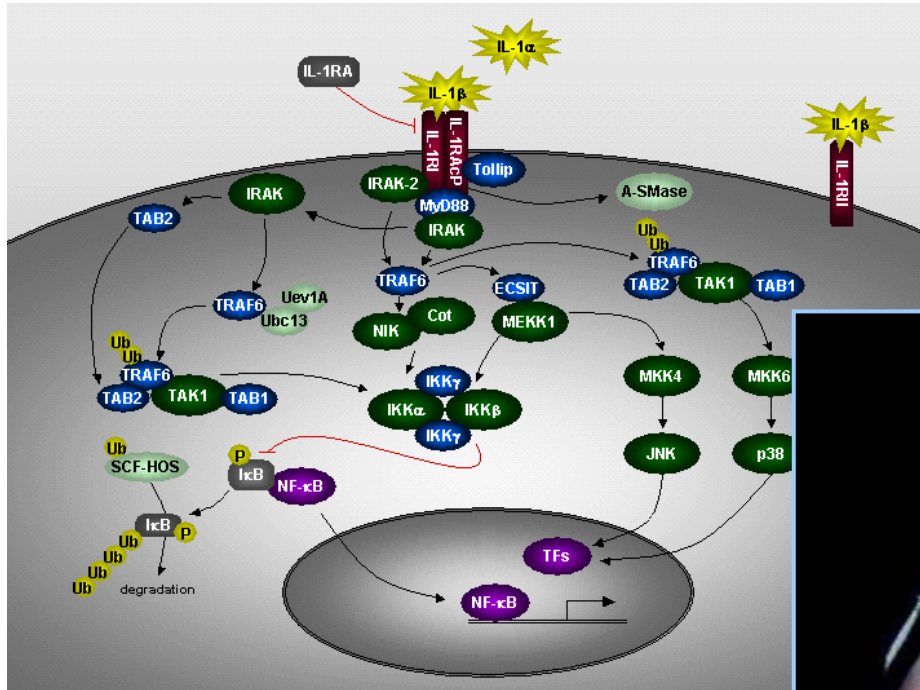


- Systematically integrate modeling & simulation (M&S) throughout the development process -- from research to marketing – to enhance decision-making
- Quantitatively characterize the causal chain (where physiological models are available) of disease progression and the impact of drug action (efficacy/safety)
- Guide development strategies, dose selection, trial design

Health Authorities:

- 
- accept industry-generated drug and disease models as a tool for communication of proposed clinical development plans at pre-IND and End of Phase II meetings
 - accept causal and model-based evidence, together with clinical results, as sufficient evidence for regulatory decision-making

Proof-of-Concept: IL-1 Molecular Pathways to Patients



Muckle Wells syndrome – IL-1 Genetic Disease

Targeted Development in Muckle Wells syndrome

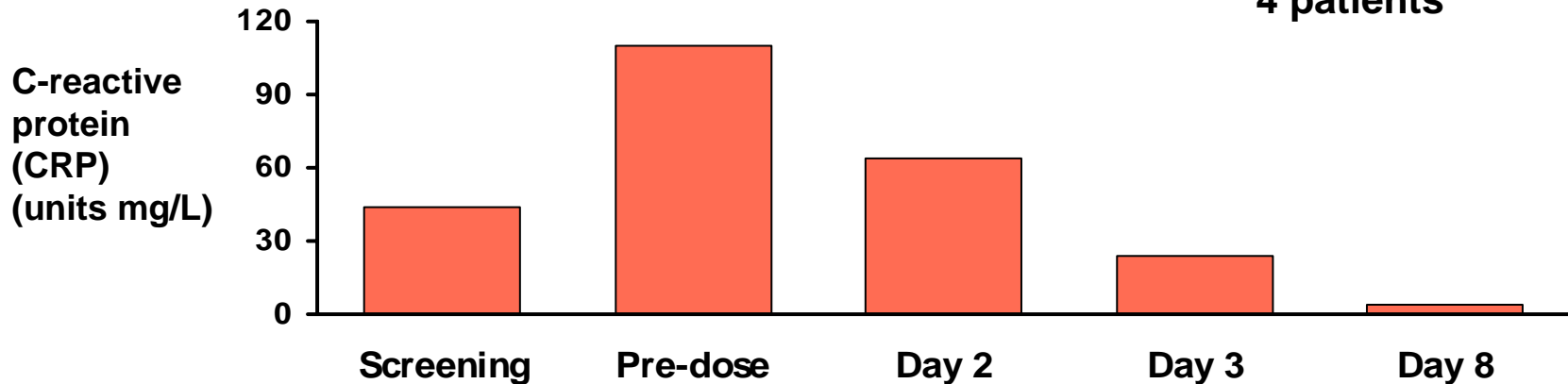


Baseline

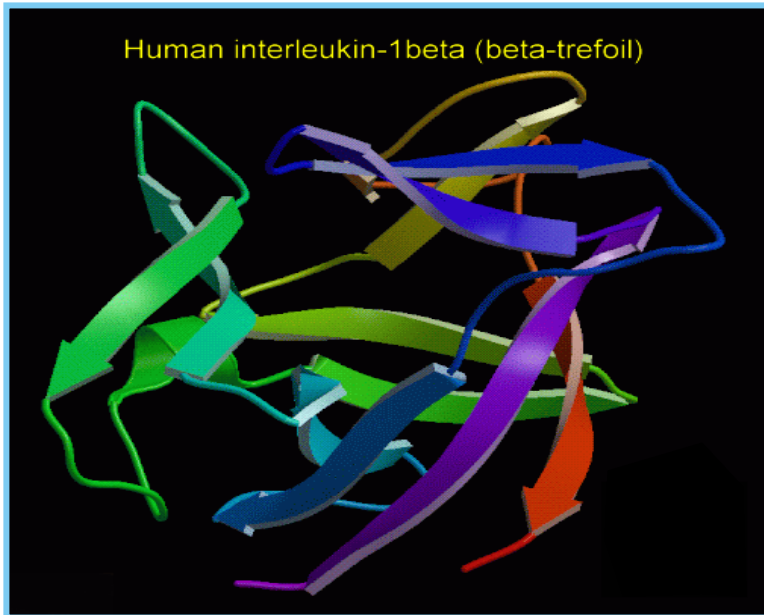


24 hours

- 64 year-old woman with NALP3 mutation
- Rash resolved completely within 1 day of commencing ACZ885
- Compelling Proof-of-Concept results from 4 patients



A Rich Potential for Treating IL-1 related Diseases

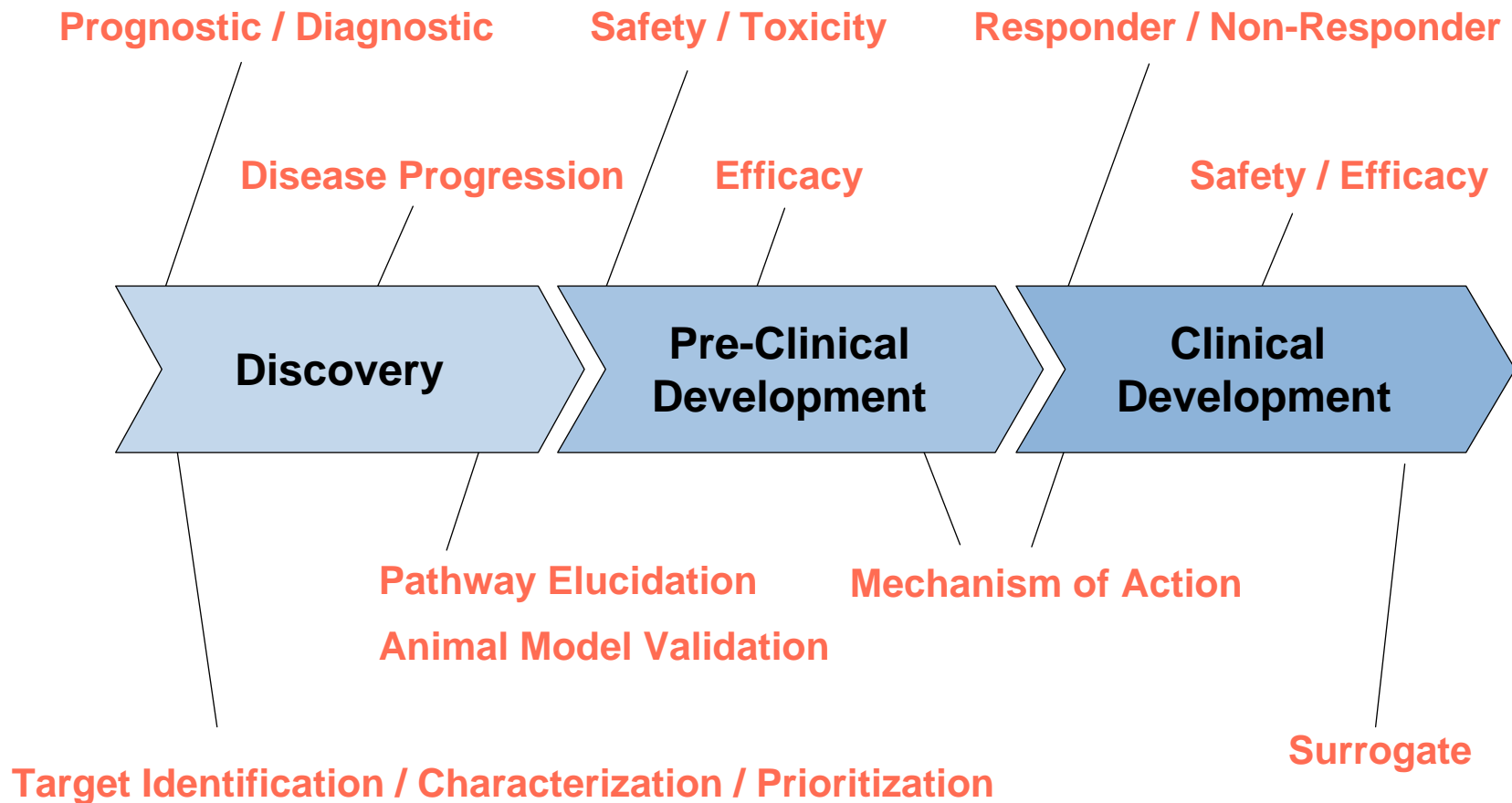


- Primary Pulmonary Hypertension
- Acute Coronary Syndrome
- Rheumatoid Arthritis
- Type I Diabetes
- Osteoarthritis
- COPD¹
- Asthma
- Psoriasis
- Sepsis

Translational Medicine: Earlier Decision Making in Proof of Concept Phase

- Targeted development followed by rational expansion of indications based on pathway analysis
- Earlier demonstration of proof of activity in humans
- Targeted development drives the lead indication forward rapidly and exposes mechanistic flaws at an early stage
- Dependent on improved tools for predictive toxicology and use of biomarkers for medical utility and safety

Biomarkers in Drug Development



Biomarkers and Surrogate Markers: Opportunities for Collaboration with Health Authorities

- Establish an inventory of “validated” or “accepted” biomarkers
- Use of epidemiologic data to link markers to disease outcome
- Establish models to transition biomarkers to fully validated surrogate endpoints
- Provide guidance on and facilitate use of biomarkers for regulatory decision making to foster timely availability of innovative medicines to patients
- Facilitate the development of diagnostics for identification of appropriate patients for medical intervention



From Concept to Action: Industry

Goal: Transform drug development through integration of innovative approaches and technologies in close partnership with regulatory authorities

Science & Technology

Integrate relevant scientific and technological advances in drug development process

Safety

Improve evaluation systems to detect signals earlier and manage risk effectively

Information Technology

Establish standards and tools for efficient data integration and sharing

External Stakeholders

Engage HAs regarding standards and policies for use of new technologies in drug development

From Concept to Action: Health Authorities

Goal: Transform regulatory paradigm through integration of innovative approaches and technologies in close partnership with industry

Role

Expand role as a scientific partner and development enabler

Infrastructure

Establish framework to support data sharing & more flexible and earlier scientific interactions

Regulatory Science

Embrace scientific & technical innovations and incorporate into guidance documents and regulatory decision-making

Regulatory Innovation

Establish review & approval processes that enable early access to innovative medicines

All Can Benefit From Success

By transforming drug development through...

- Powerful, new and validated scientific and technical methods/tools
- Innovative development and regulatory approaches

... **HAs** will gain greater confidence in the data used to approve marketing applications

... **Physicians** will have better evidence for treatment decisions

... **Patients** will have rapid access to innovative, effective and better understood therapies

... **Pharma** will achieve robust product development pathways that are more efficient and predictable