Physiomics plc Showcase Presentation BioTrinity May 2014

PHYSIOMICS
rational therapeutics

Copyright Physiomics PLC
Private and Confidential

Introduction to Physiomics plc

- **Business**
  - Founded 2001, Listed on AIM (2004), based in Oxford, UK
- **Focus**
  - Predictive models to:
    - Improve the success rate of drug discovery and development projects
    - Reduce timelines
    - Save money
    - Make better decisions
- **Particular focus in oncology**
  - Unique Virtual Tumour model

Copyright Physiomics PLC

Physiomics Products and Services

Target validation

Mechanism of action studies

Lead selection

Virtual Tumour

Virtual Tumour Clinical

DrugCARD – Combinations and regimens database

Cardiac toxicity prediction service

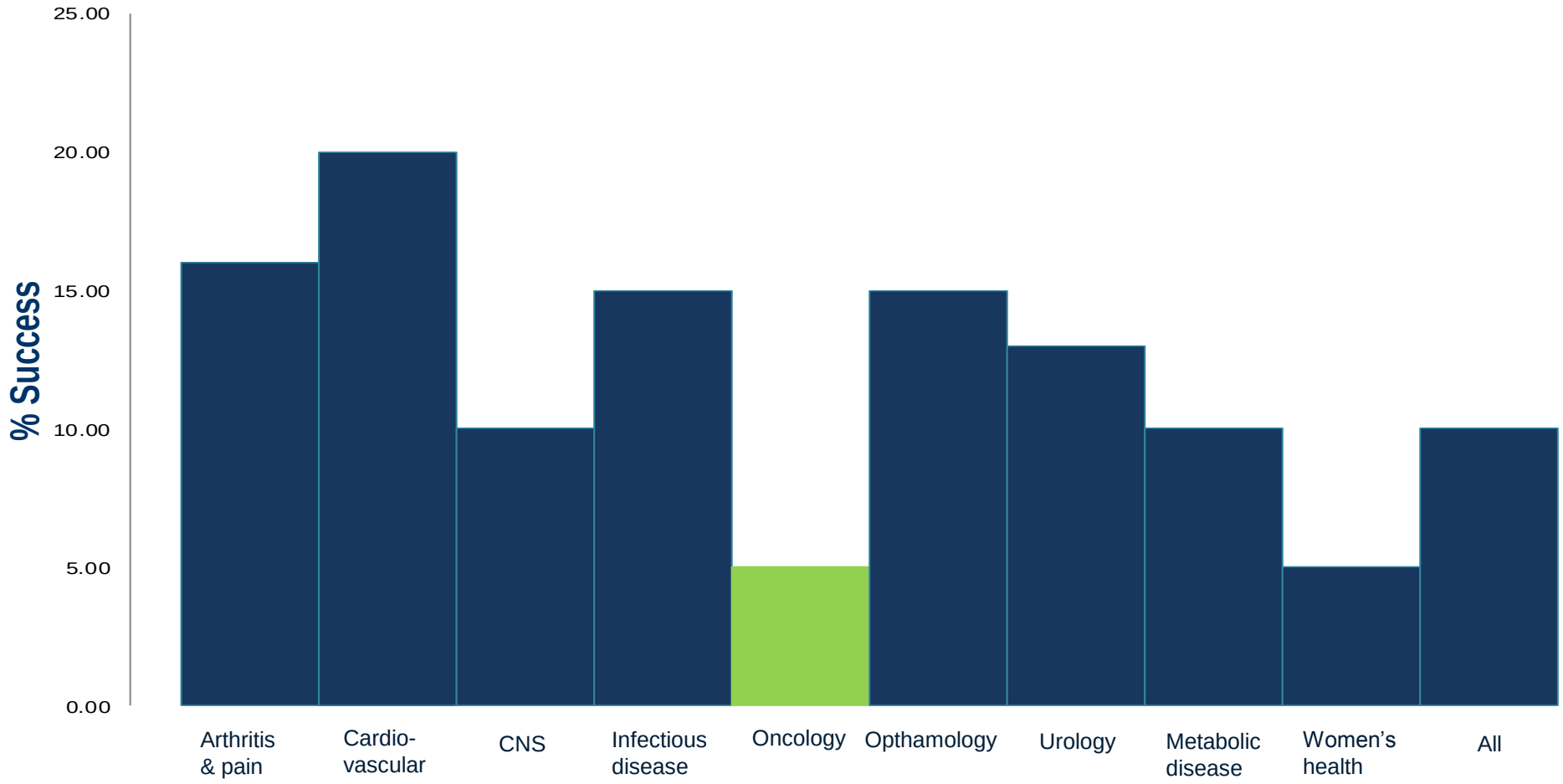
Preclinical PK/PD

Population PK/PD

Copyright Physiomics PLC
Private and Confidential

Target Market

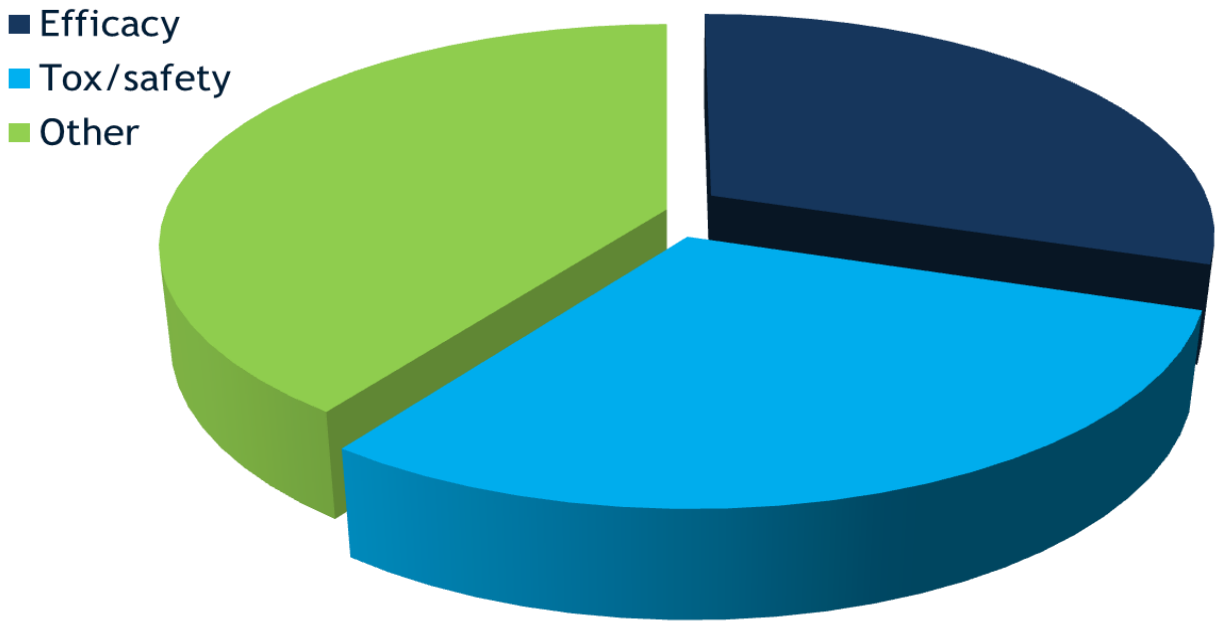
- **Physiomics currently focuses on services for oncology (cancer), where there has historically been a low success rate**



Kola and Landis, *Nature Reviews Drug Discovery* (2004) 3:711-715

Copyright Physiomics PLC
Private and Confidential

Target Market



- **Our technology has the potential to increase the success rate by:**
- **Optimising efficacy – responsible for ~ 30% of attrition**
- **Improving toxicity profile – toxicity and clinical safety responsible for ~ 30% of attrition**

Kola and Landis, *Nature Reviews Drug Discovery* (2004) 3:711-715

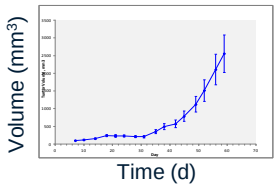
Copyright Physiomics PLC
Private and Confidential

Virtual Tumour Preclinical

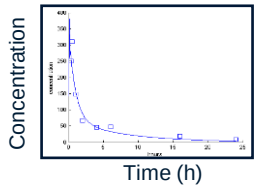
Copyright Physiomics PLC
Private and Confidential

Virtual Tumour Mechanics

1) Cell line growth data: control xenograft growth curves

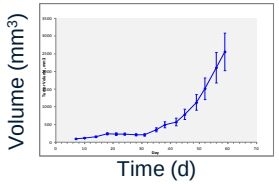


2) Compound PK data: plasma/tumour time courses

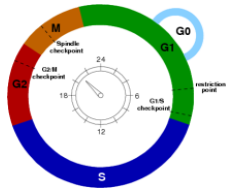


3) Compound PD data:

- xenograft inhibition data (growth curves)

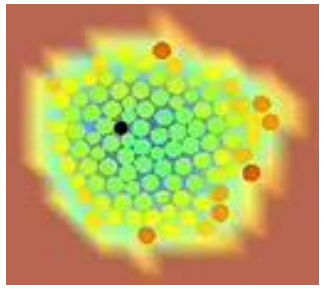


- **biomarker data** (cell cycle, cell death, target biomarkers)



Required data
Optional data

Virtual Tumour

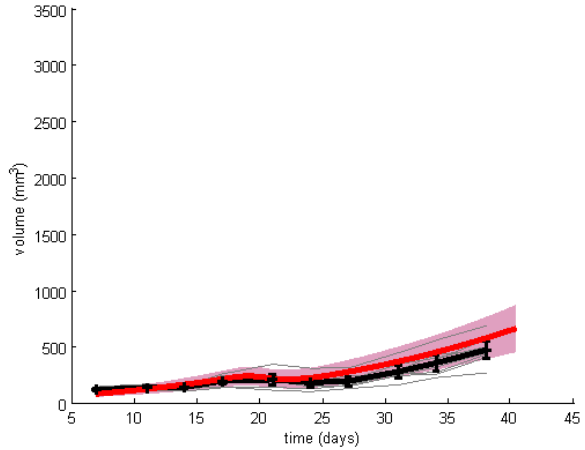


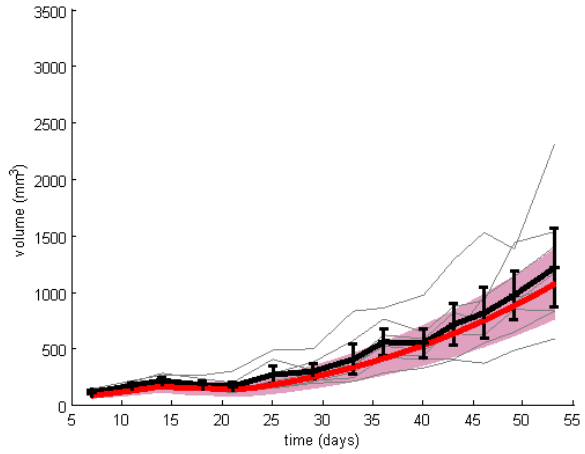
proprietary cell population model

Predicted
Mean
Confidence interval

Experiment
Individual mice
Mean and standard error

Tumour growth inhibition for selected schedules

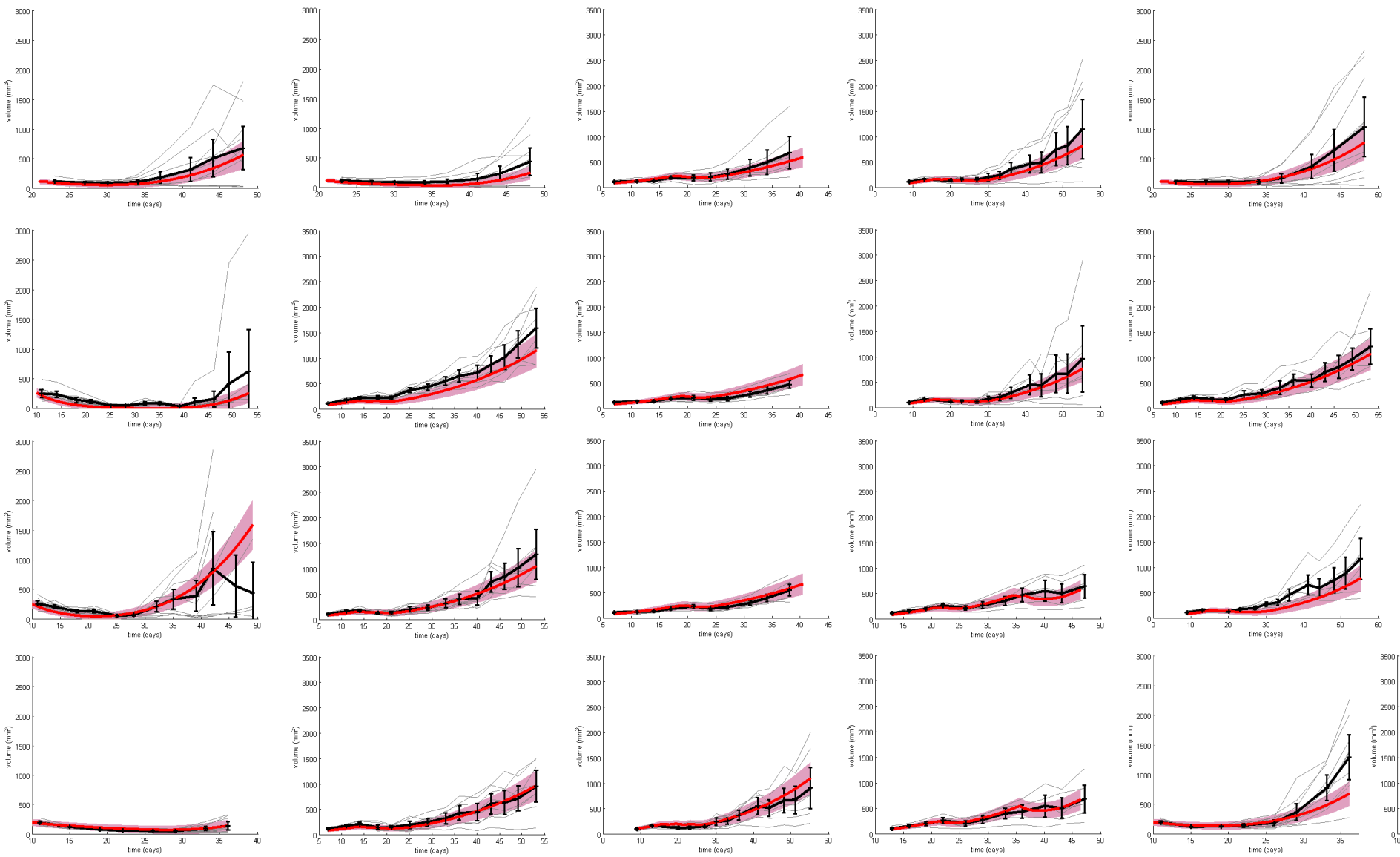




Copyright Physiomics PLC
Private and Confidential

Case Study – Blind Validation for Large Pharma

19/21 Different Combination Dosing Schedules Predicted Accurately



Predicted

Mean → Confidence interval

Experiment

Individual mice

Mean and standard error

- ***DNA repair inhibitors***
- ***Targeted agents***
- ***SOC's***

Copyright Physiomics PLC
Private and Confidential

Virtual Tumour Pre-Clinical - Summary

- **Preclinical Virtual Tumour**
  - Predicts the change in mean tumour volume over time
  - Over 35 preclinical studies have confirmed the predictive capability of the model
    - *Modelled over 200 xenograft experiments*
  - Three large pharma customers
    - *Lilly licensed the progenitor of the Virtual Tumour platform*
    - *Two other pharmas (one top five) actively engaged in preclinical Virtual Tumour projects*
- **Strong demand to translate regimen optimisation into the clinic**

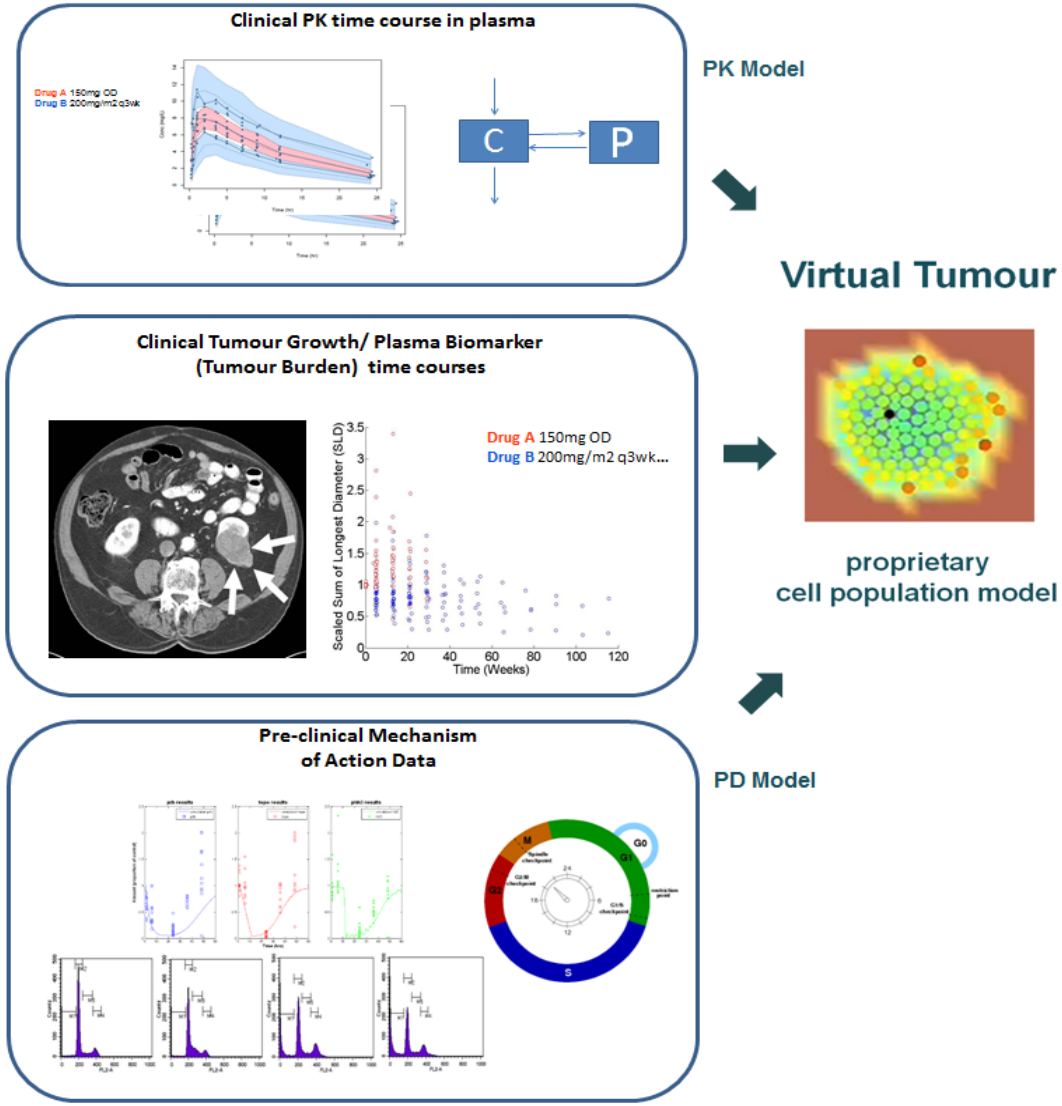
Copyright Physiomics PLC
Private and Confidential

Virtual Tumour Clinical

Copyright Physiomics PLC
Private and Confidential

Virtual Tumour Clinical Development

- Biomedical Catalyst grant from the UK Technology Strategy Board
- NIH collaboration within metastatic castrate-resistant prostate cancer – *first validation*
- Oxford University/Churchill Hospital – melanoma study - *second validation*
- Early results suggest that the existing preclinical model architecture may be appropriate for making clinical predictions
- Advanced discussion with large pharma to start clinical collaborations



Copyright Physiomics PLC
Private and Confidential

Case Study - Translational Validation
Predicting Clinical Efficacy Using Preclinical Data

ADVANCE:	Validation of the translational capability of the Virtual Tumour
OBJECTIVE:	To determine whether our technology could accurately predict the mean change in tumour size over time in a phase II clinical study of Docetaxel vs. Docetaxel/Selumetinib in BRAF WT metastatic melanoma
PARTNER:	Mark Middleton, Oxford ECMC
START POINT:	Single drug xenograft dose-response data, preclinical and clinical PK
DURATION:	6 weeks
OUTCOMES:	Correctly predicted mean change in tumour size over time in both arms of the study and provided schedule options to ameliorate toxicities

Copyright Physiomics PLC
Private and Confidential

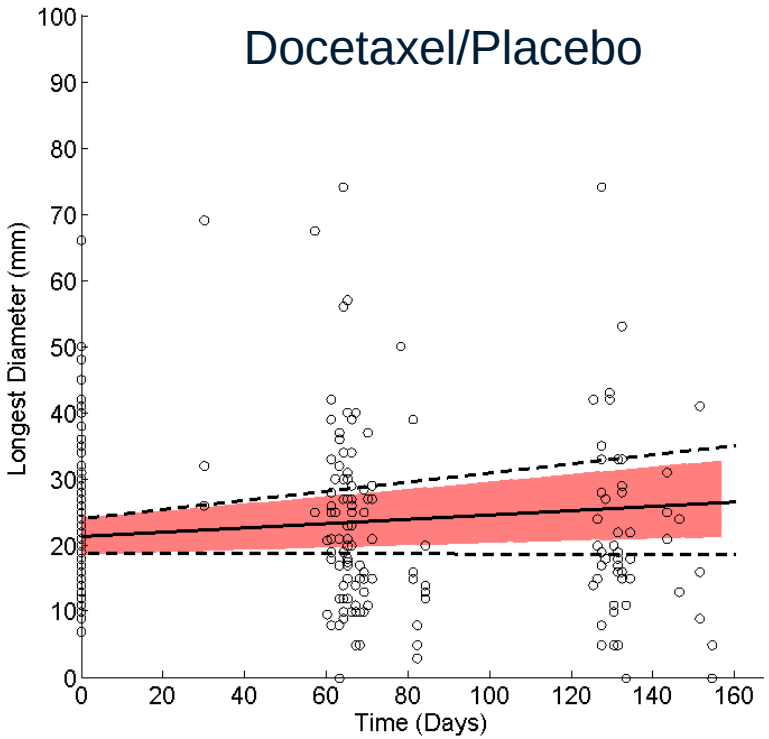
Case Study – Translational Validation: Modelling Plan

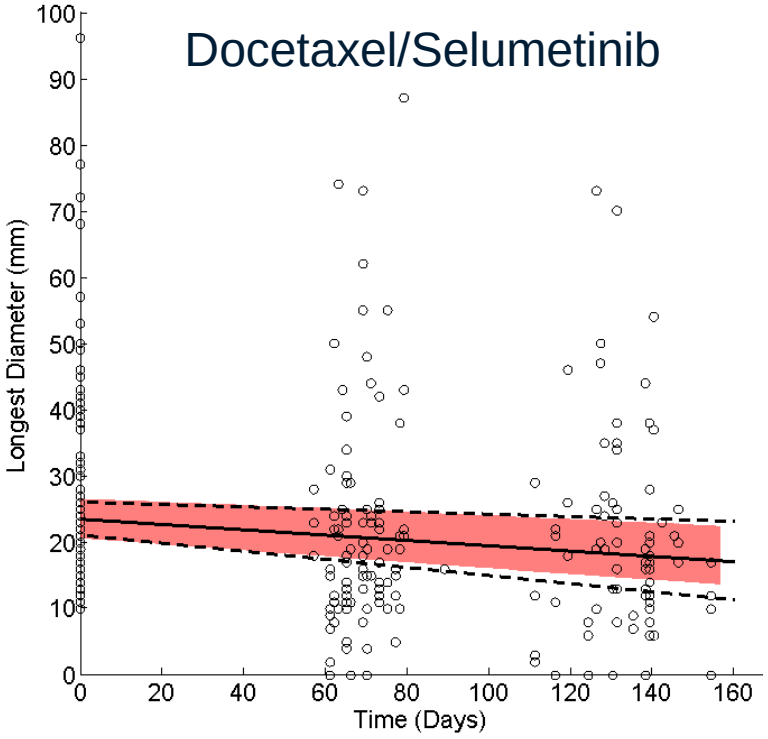
- **Step 1:** Calibrate Virtual Tumour to preclinical data for each agent
  - PK and xenograft data sourced from literature
- **Step 2:** Switch preclinical growth settings for clinical growth settings
- **Step 3:** Predict the two-arm phase II trial
  - Clinical PK models sourced from literature
- **Step 4:** Population analysis of the clinical study
- **Step 5:** Compare prediction with actual result

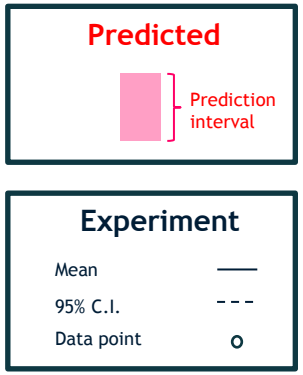
Copyright Physiomics PLC
Private and Confidential

Case Study – Translational Validation: Steps 4 and 5: Validation

- **Perform a population analysis of the clinical data and overlay the results**
- **Accurate predictions for both arms of the study**







Copyright Physiomics PLC
Private and Confidential

Summary

- **Successfully predicted the mean change in lesion size for each arm of the phase II trial, using monotherapy preclinical efficacy data and clinical PK data**
  - Performed further predictions for Oxford ECMC, exploring different dosing regimens and changing docetaxel for paclitaxel
- **Virtual Tumour Clinical can provide significant cost-savings**
  - accurate translation of preclinical efficacy reduces the number of clinical studies required to find optimal doses and schedules
- **Virtual Tumour Clinical could reduce attrition rates**
  - Optimised regimens can enhance efficacy, increasing the chance of clinical trial success.
- **Fee-for service and licensing options available**

Copyright Physiomics PLC
Private and Confidential