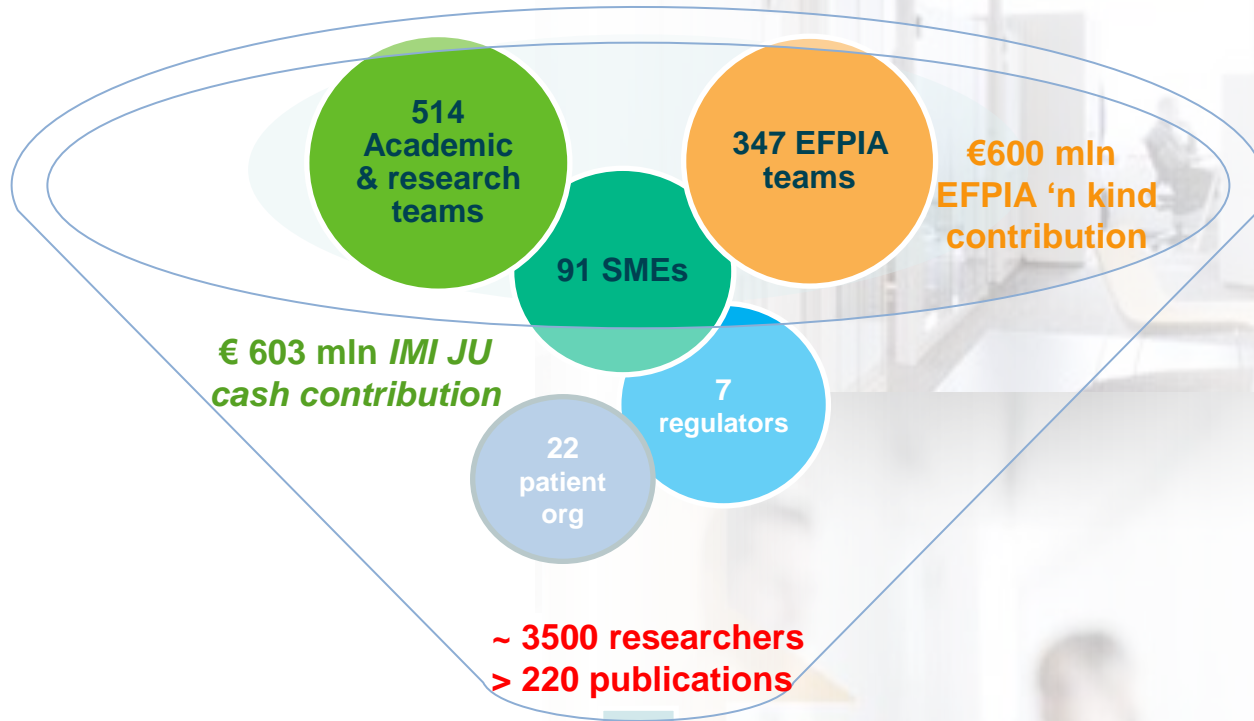


IMI- Putting Ideas Into Practice





Key Figures of 37 on-going Projects



**R&D Productivity
Improvements**

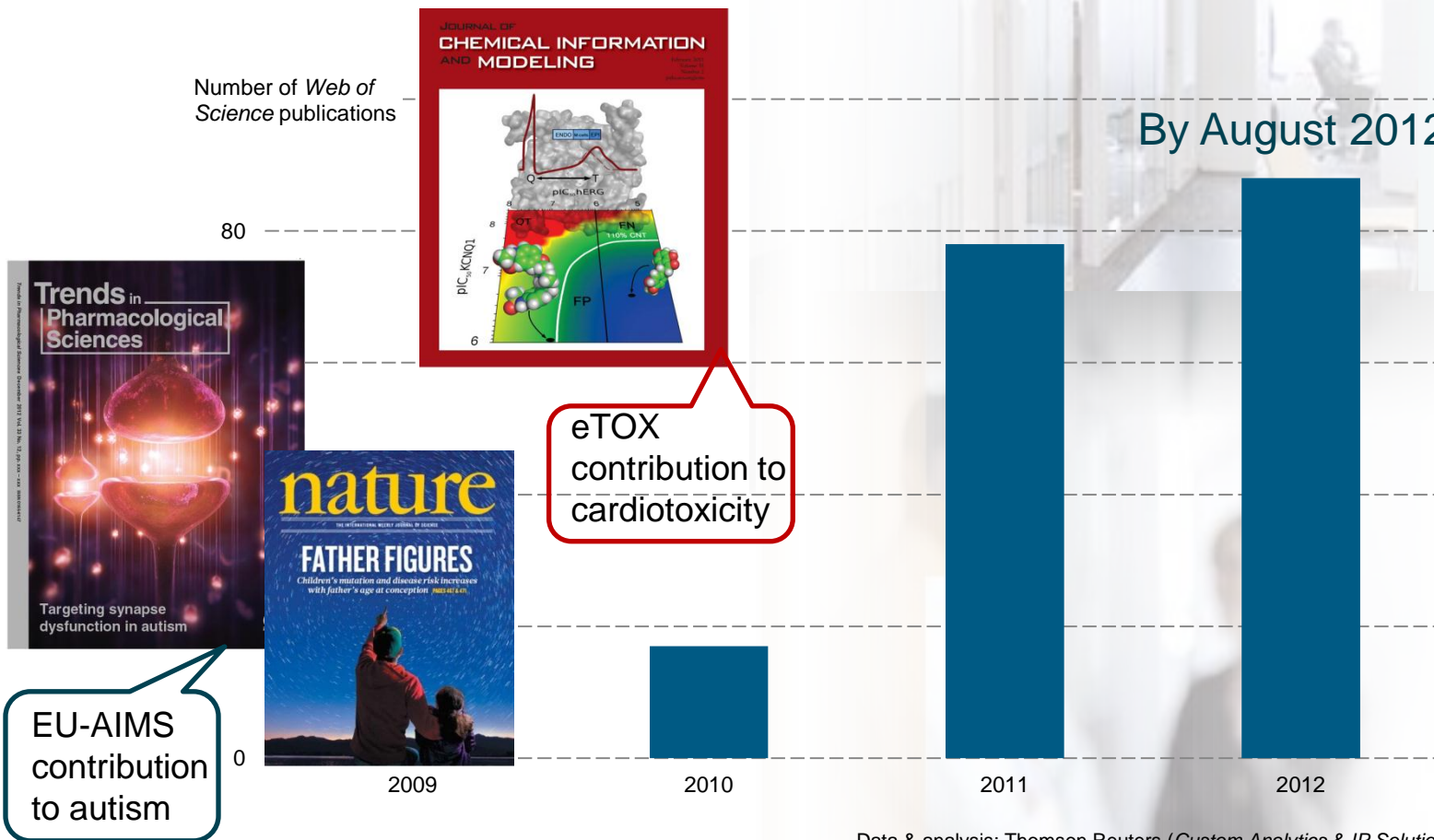




Bibliometric Output so Far

Number of Web of Science publications

By August 2012



Data & analysis: Thomson Reuters (Custom Analytics & IP Solutions)





On-going Projects - Calls

- 1
- 2
- 3
- 4



MARCAR (safety)					MARCAR (safety)
PREDECT (cancer)		ONCOTRACK (cancer)		CHEM21 (manufacturing)	
ONCOTRACK (cancer)	SUMMIT (diabetes)				
StemBANCC (IPS)	DIRECT (diabetes)				
SAFE-T (safety)	NEWMEDS (schizophrenia, depression)				
EU-AIMS (autism)					
K4DD (drug binding)	PHARMACOG (Alzheimer's disease)				K4DD (drug binding)
U-BIOPRED (asthma)					
IMIDIA (diabetes)					
PREDICT-TB (tuberculosis)					
MIP-DILI (safety)		QUICKCONCEPT (cancer)		PROTECT (safety)	
ABRISK (biopharmaceuticals)		StemBANCC (IPS)		MIP-DILI (safety)	
DDMORE (KM)		BIOVACSAFE (vaccines)		StemBANCC (IPS)	
OPENPHACTS (KM)				DDMORE (KM)	
EUROPAIN (chronic pain)					
BTCURE (RA)		BTCURE (RA)		EMIF (KM)	
COMPACT (biopharmaceuticals)		RAPP-ID (infectious disease)		EH4CR (KM)	
ORBITO (oral drug delivery)		SAFE-T (safety)		COMPACT (biopharmaceuticals)	
		PROactive (COPD)		ORBITO (oral drug delivery)	
				SAFE-T (safety)	



IMI improving R&D productivity (1)

Establishment of robust validated models for drug development

Alzheimer's Disease	translatable sleep deprivation model developed characterized multiple Tg mice models
Chronic Pain	sleep deprivation model validation on-going menthol model validation on-going UVB irradiation model validation on-going
Schizophrenia Depression	new animal models developed, multiple models evaluated translatable imaging methodology develop
Autism	developed animal model that mimics nonsyndromathic autism
Diabetes	developed new animal models that mimic T1 and T2 diabetes, multiple models evaluated Tg mice developed developed human B cell line
Asthma	2 new animal models developed FCA/HDM and CT & MRI imaging of chronic HDM model evaluated and harmonized multiple animal models



Science

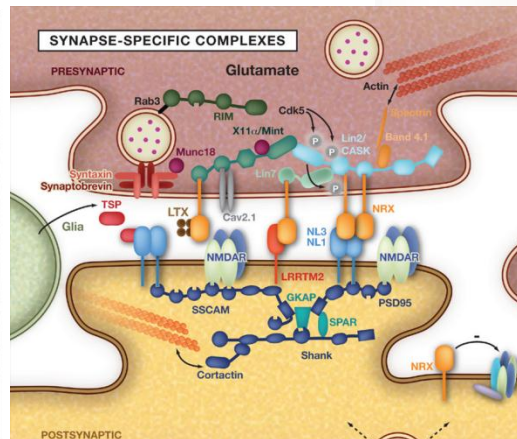
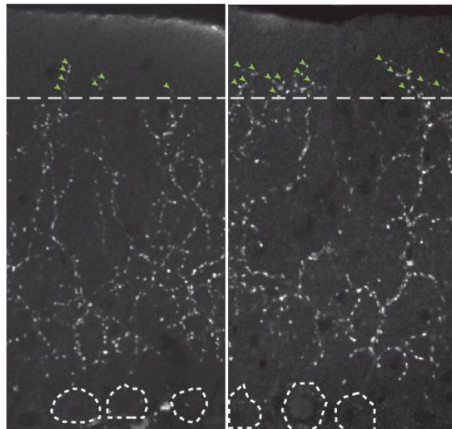
Shared Synaptic Pathophysiology in Syndromic and Nonsyndromic Rodent Models of Autism

October 5th 2012

Stéphane J. Baudouin,¹ Julien Gaudias,¹ Stefan Gerharz,^{1*} Laetitia Hatstatt,¹ Kuikui Zhou,² Pradeep Punnakkal,¹ Kenji F. Tanaka,^{3,4} Will Spooren,⁵ Rene Hen,³ Chris I. De Zeeuw,^{2,6} Kaspar Vogt,¹ Peter Scheiffele^{1†}

wild-type

Nlgn3^{KO}



The consortium has developed an animal model replicating a nonsyndromic autism and demonstrated that the condition can be reversed with specific therapy

This new development is be of great importance for clinical development of new treatments for autism



IMI improving R&D productivity (2)

Development of novel biomarkers for drug development

Alzheimer's Disease	novel biomarkers that follow disease progression in Tg mice
Chronic Pain	translatable imaging biomarkers of brain activation related to chronic pain
Schizophrenia Depression	clinical imaging biomarkers clinical and molecular biomarker candidates for antidepressant response surrogate proteomic biomarkers for efficacy prediction
Diabetes	candidate lipodomic and metabolomic biomarkers novel genetic markers identified
Asthma	genetic, proteomic, metabolomic, breathomic biomarker candidates – validation on-going
Safety	novel early non genotoxic carcinogen biomarkers identified potential biomarkers of drug induced injury of liver, kidney and vascular system





SAFE-T

OPEN ACCESS Freely available online

PLOS ONE

Real Time Identification of Drug-Induced Liver Injury (DILI) through Daily Screening of ALT Results: A Prospective Pilot Cohort Study

Development of liver injury alert algorithm for real time patient assessment and comparison with the efficacy of the routine examination

The new strategy was much more efficient in identifying potential liver injury incidents, **12x more** cases were identified than with the standard strategy

The cases identified with the centralized strategy were much milder allowing for timely intervention

This new approach presents a significant improvement in timely identification of DILI cases and will allow faster intervention to prevent from more serious events such as liver failure





IMI improving R&D productivity (3)

Exploitation of pooled data from multiple sources

Schizophrenia Depression	<p>combined data analysis of 23,401 schizophrenia patients</p> <hr/> <p>combined genetic data analysis on 2146 DNA samples</p>
Autism	<p>sequenced 78 Icelandic parent–offspring trios, a total of 219 distinct individuals (44 autistic, 21 schizophrenic offspring) and identified 4933 <i>de novo</i> mutations</p>
Chronic Pain	<p>pooled data from 43 past trials to understand the pain medicines mechanism of action and factors important in placebo response</p>
Safety	<p>building a toxicology information database utilising toxicology legacy reports to develop better in silico tools for toxicology prediction of new chemical entities (1274 reports extracted so far, 2092 were cleared, 3564 are planned in total)</p> <hr/> <p>exploited EFPIA in vivo mouse and rat toxicology studies, tissue archives and molecular profiling data for >30 reference compounds to study NGC, genotoxic carcinogens and non-hepatocarcinogen controls</p>





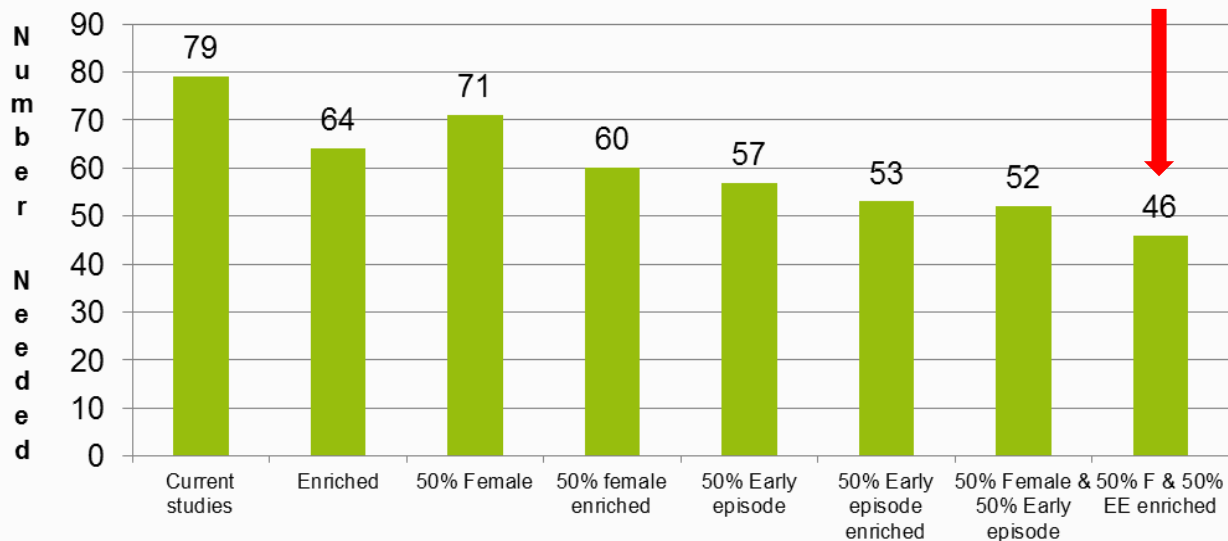
schizophrenia trials results

Average cost savings € 2,8 million

Samples can be reduced from 79 to 46 patients per arm by targeting trials

In addition the trial duration can be reduced from 6 to 4 weeks

6 Weeks



Current mix =70% female; 20% early episode; 40% enriched

Enriched=prominent positive and negative symptoms

Early episode=under 3 with 4 or more years of illness

Note: Per patient cost 6wk study \$70,000-\$100,000





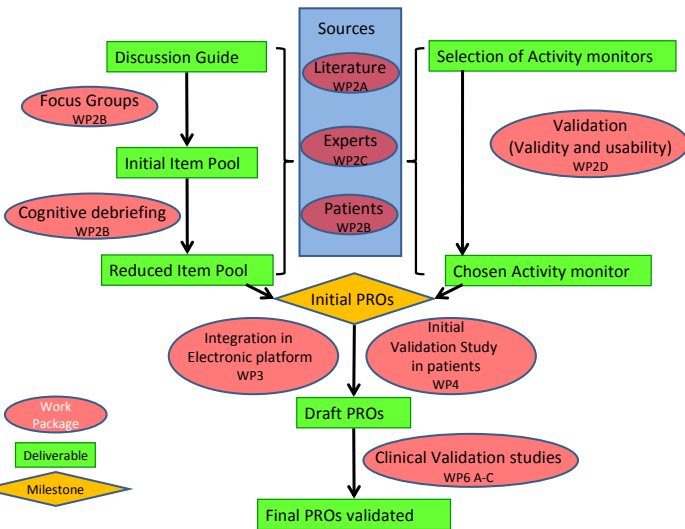
IMI improving R&D productivity (4)

Agreeing development and regulatory submission of key standards for drug development

Asthma	diagnostic criteria on severe asthma
Schizophrenia Depression	clinical biomarker meaningfulness calculator for predicting biomarker candidate utility in predicting antidepressant response identified phenotypes associated with schizophrenia CNVs
Diabetes	developed non-invasive carotid histology for diabetic macroangiopathy generated phenotype definitions for diabetic complications
COPD	derived a conceptual model for physical activity developed patient reported outcome tools – validation on-going
Safety	established generic qualification strategy for translational biomarkers building ontology for preclinical pathology, 3917 terms and 2535 synonyms have been mapped



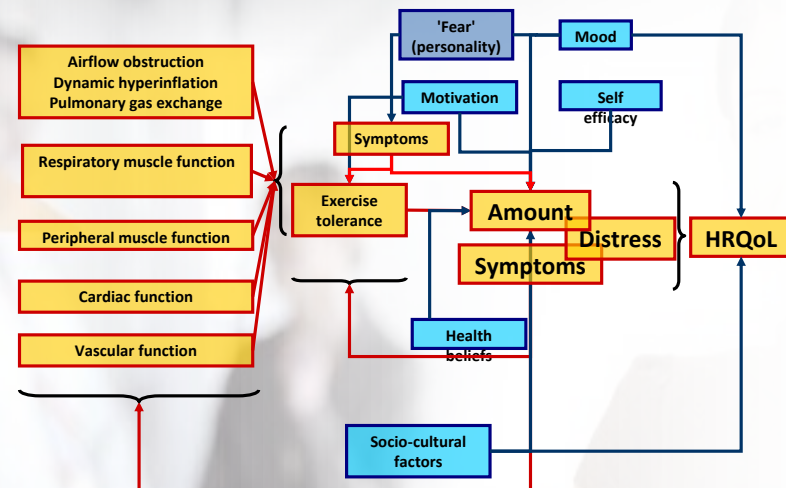
Item pool generation for PROactive



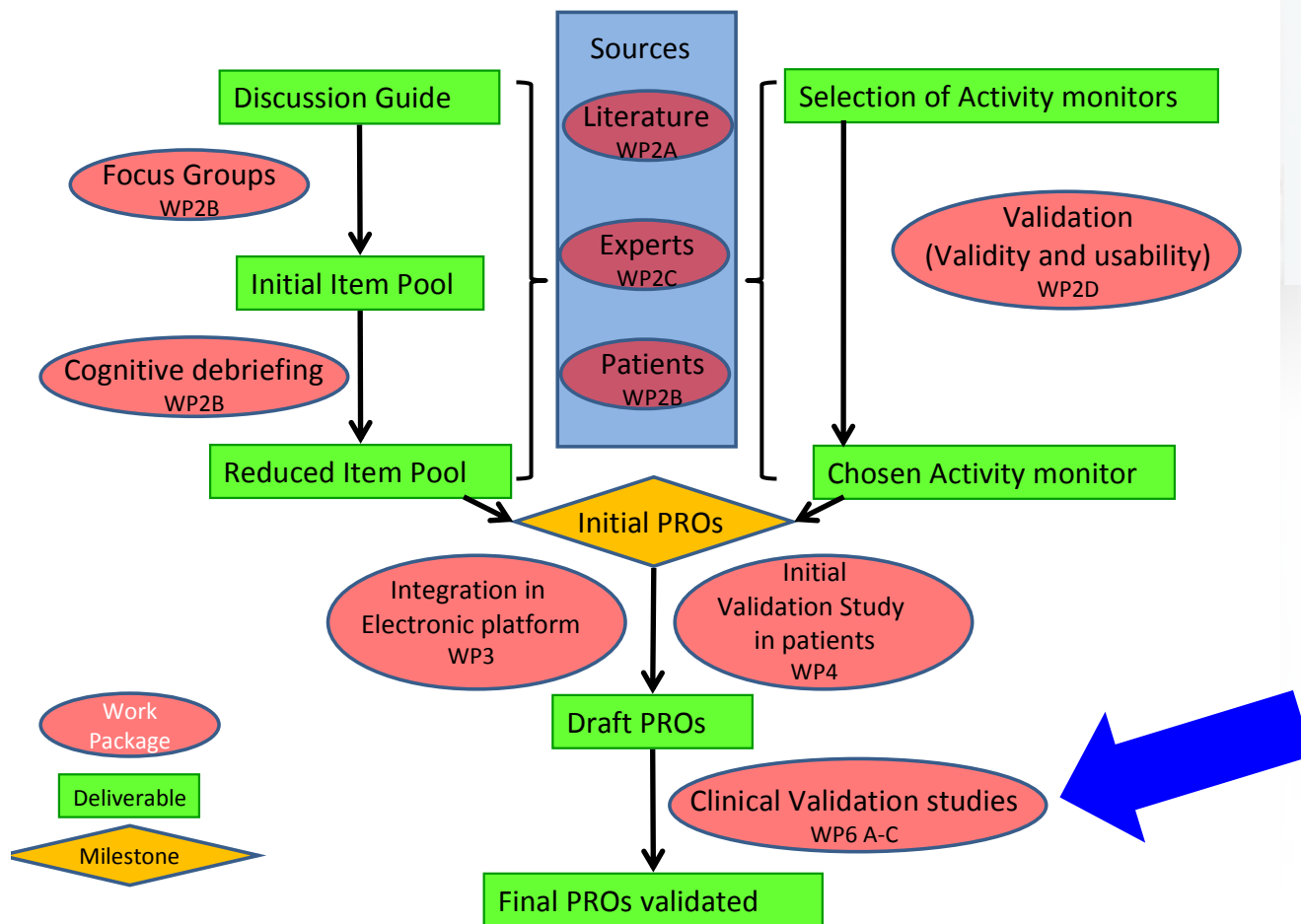
Activity monitor(s) selection



Summary of existing conceptual frameworks and development of the conceptual model



Development of Patient Reported Outcome tools





IMI improving R&D productivity (5)

Optimizing clinical trials

**Antibiotics
Autism**

creation of pan-European clinical investigator networks

**Asthma
COPD**

involving patients in clinical trials and beyond
established network of excellence in bronchoscopy in severe asthma
generated central registry of patients with severe asthma

**Schizophrenia
Depression**

proposed reduction in duration of schizophrenia trials
developing new approach of combining medication with therapy

**Alzheimer's
Disease**

new clinical study designs

Tuberculosis

aims to improve the development of new more effective treatment combinations for TB

**Knowledge
Management**

identification of clinical sites through EHR



THANK YOU

