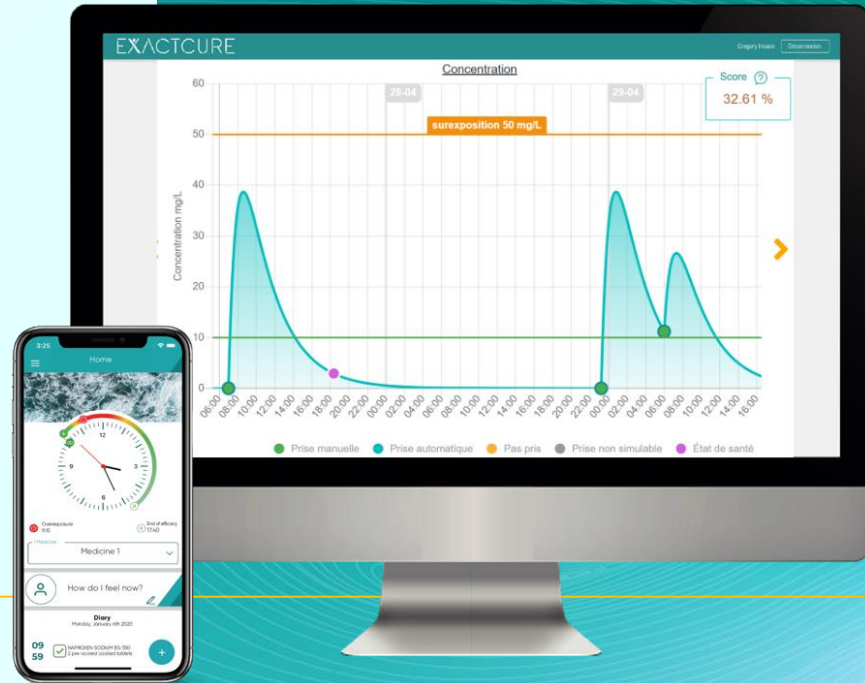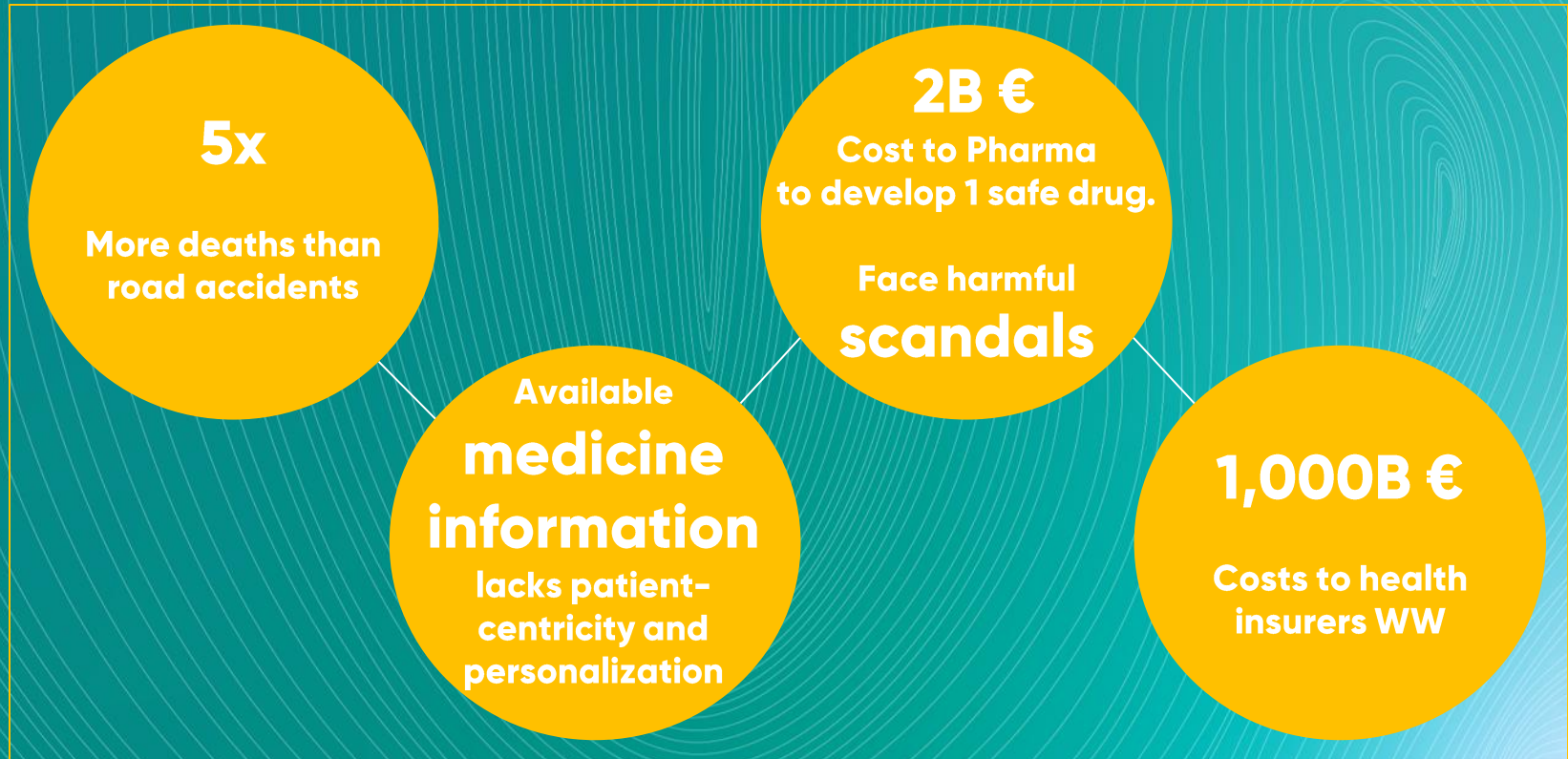# EXACTCURE

Your Digital Twin for a Personalized Medication

Company Purpose

ExactCure develops a solution to **personalize medications** and **properly use drugs**
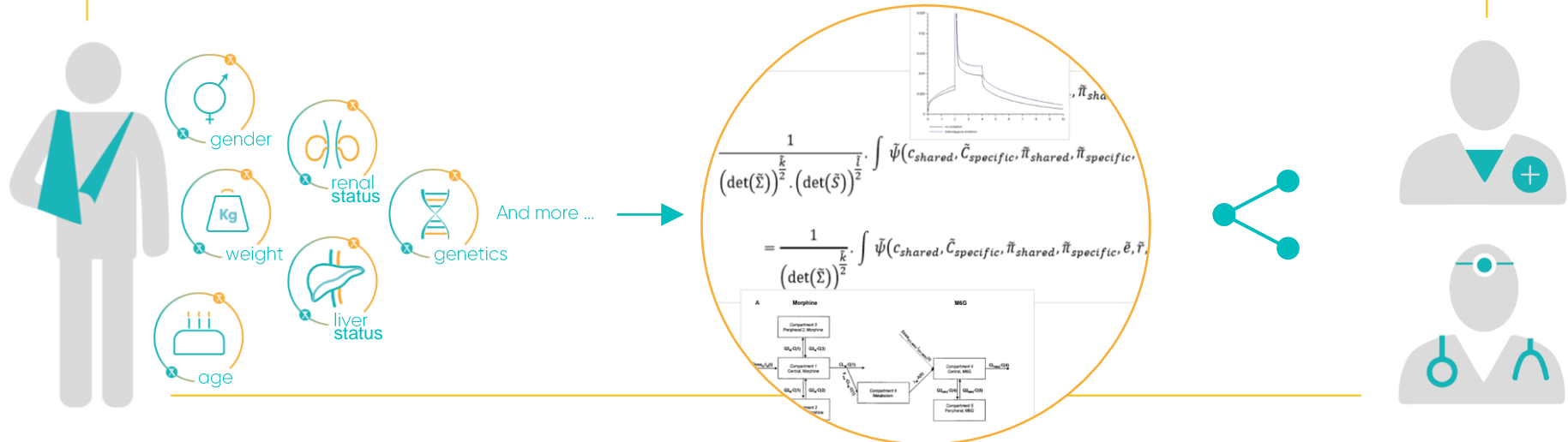
Problem: Medication Errors

5x

More deaths than road accidents

Available medicine information lacks patient-centricity and personalization

2B €

Cost to Pharma to develop 1 safe drug.

Face harmful **scandals**

1,000B €

Costs to health insurers WW

A **lack of personalization** is involved in **36% of medication errors**

Solution : Personalized *in silico* drug modeling

A *Digital Twin* to simulate the **concentration of medicines** in the blood of patients, and their **effects**, **based on personal characteristics** (weight, renal status, DNA...)
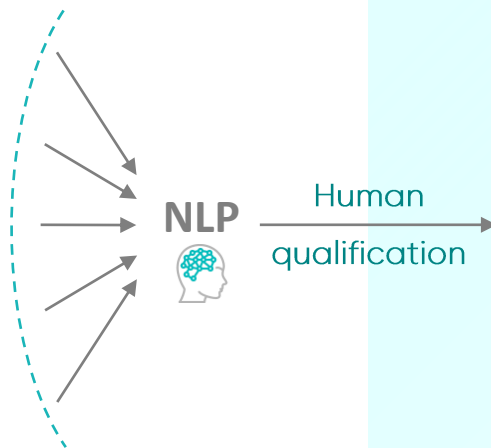
gender

renal status

weight

genetics

liver status

age

And more ...

$$\frac{1}{\left(\det(\tilde{\Sigma})\right)^{\frac{k}{2}} \cdot \left(\det(\tilde{S})\right)^{\frac{l}{2}}} \cdot \int \tilde{\psi}\left(c_{shared}, \tilde{C}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific},\right.$$

$$= \frac{1}{\left(\det(\tilde{\Sigma})\right)^{\frac{k}{2}}} \cdot \int \tilde{\psi}\left(c_{shared}, \tilde{C}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific}, \tilde{e}, \tilde{r},\right.$$

Pharmacokinetic / Pharmacodynamic
Personalized PK/PD simulations

How? Proven Disruptive Technology

1

Proprietary **NLP** to mine the literature

2

Mathematically **aggregate** qualified models

NLP

Human qualification

Best model in the world
by EXACTCURE.

PAGE
2 posters

GMP
Speaker

THERAPEUTIC DRUG MONITORING
1 article published

Value Proposition

Personalized Drug Simulations as a Service

CE

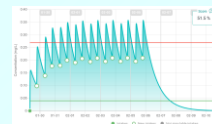**Call our API to integrate simulations into your platform**

API

- Medicine Information Providers
- Pharmaceutical companies
- Health insurance companies

Healthcare Professionals

Patients

Provide Personalized Drug Simulations

✓ **Enrich drug information quality**
✓ **Reduce costs**
✓ **Improve image**
✓ **Gain market share**
✓ **Get Real World Evidence**
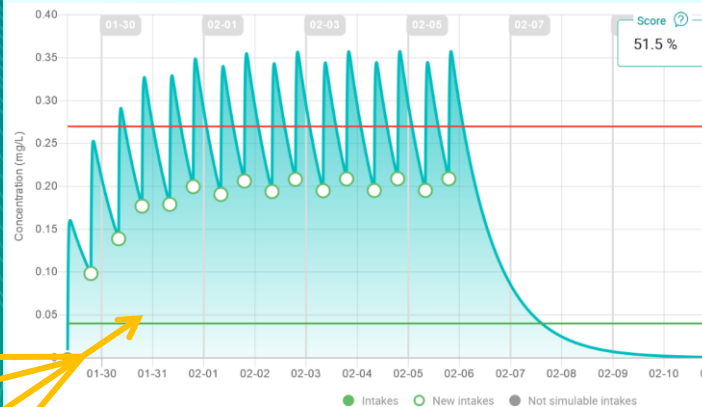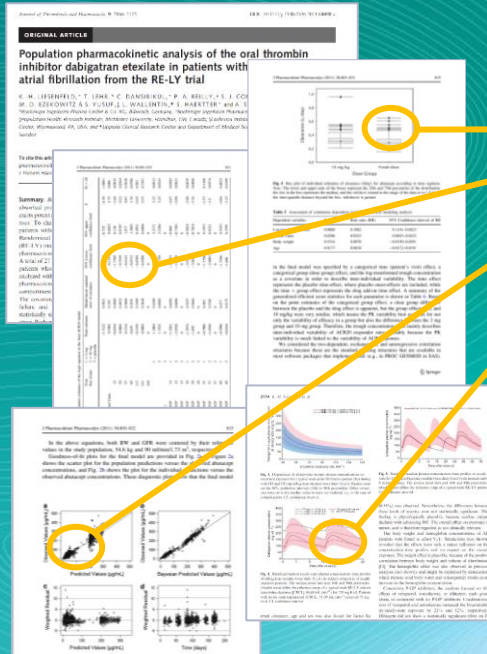
Run personalized drug simulations on demand to adapt posology, avoid under-doses, overdoses and drug-drug interactions, and **reduce medication errors.**

ExactCure

ExactCure's customers

End users

7

For Healthcare Professionals

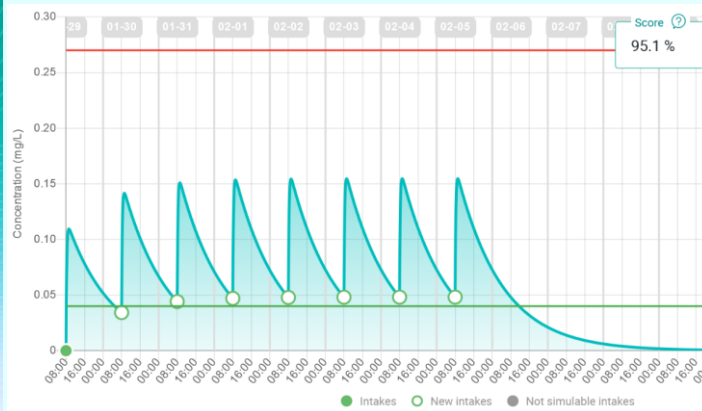## Example: dabigatran

Used to treat cardio-vascular diseases

- Woman
- 55 years old
- 45 kg
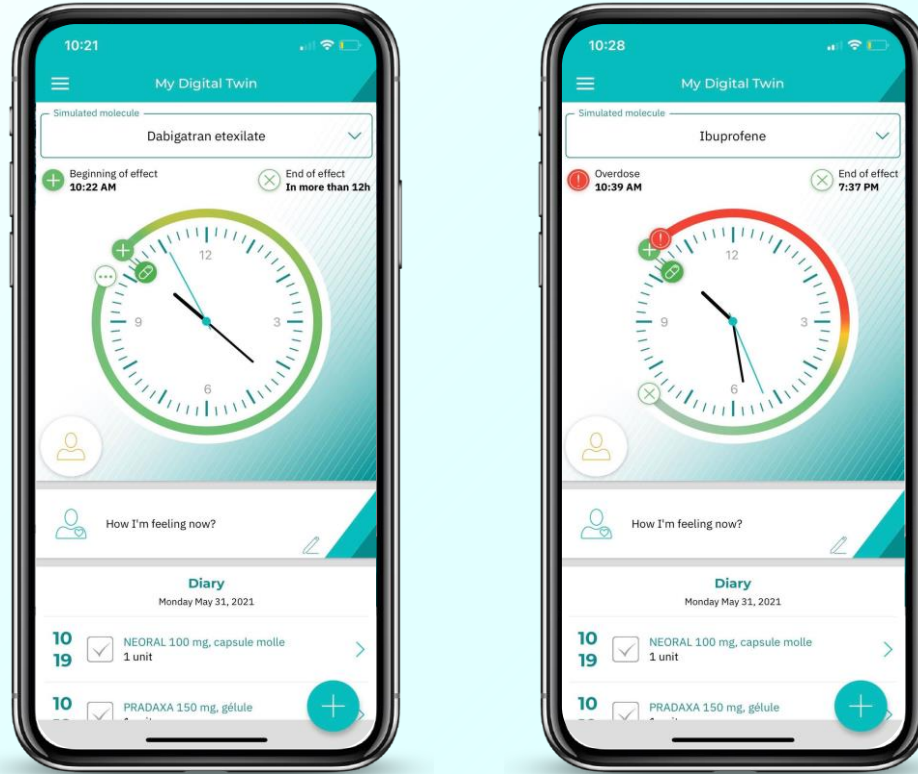- Strong renal impairment
- Normal genotype

150 mg 2/day

75 mg 1/day

Adapt posology to each individual patient

For Pharma's or Insurance's End Users

Avoid medication errors

✓ **Avoid under-doses, overdoses and drug-drug interactions**

✓ **History** of reported effects **correlated** to drug concentrations

✓ **Keep track** of treatments

✓ Improve **adherence**

✓ **Share** with Healthcare Professional

✓ Improve **health outcomes**

✓ Any additional service proposed by the third-party developing the app ● ● ●

11

Market Size

Personalized Medication
is an emerging market

Total Available Market
60 bn€

Charging
100€/month/patient

for 50M
most expensive patients
(3% of chronic patients,
<1% of WW population)

Served Available Market
15 bn€

Developed countries

Target Market
1.5 bn€

10% of the SAM

Market Segments – Pricing model: €/user/month

Medicine Information Providers
Go-to-Market: Integration

Examples in Pipeline:

ViDAL · BCB · TabulaRasa HealthCare®
ELSEVIER · Dedalus · CGM CompuGroup Medical

1€/bed/month
10€/HCP/month

Pharmaceutical companies
Go-to-Market: Direct

100€/patient/month
for a chronic patient

Health insurance companies
Go-to-Market: Direct
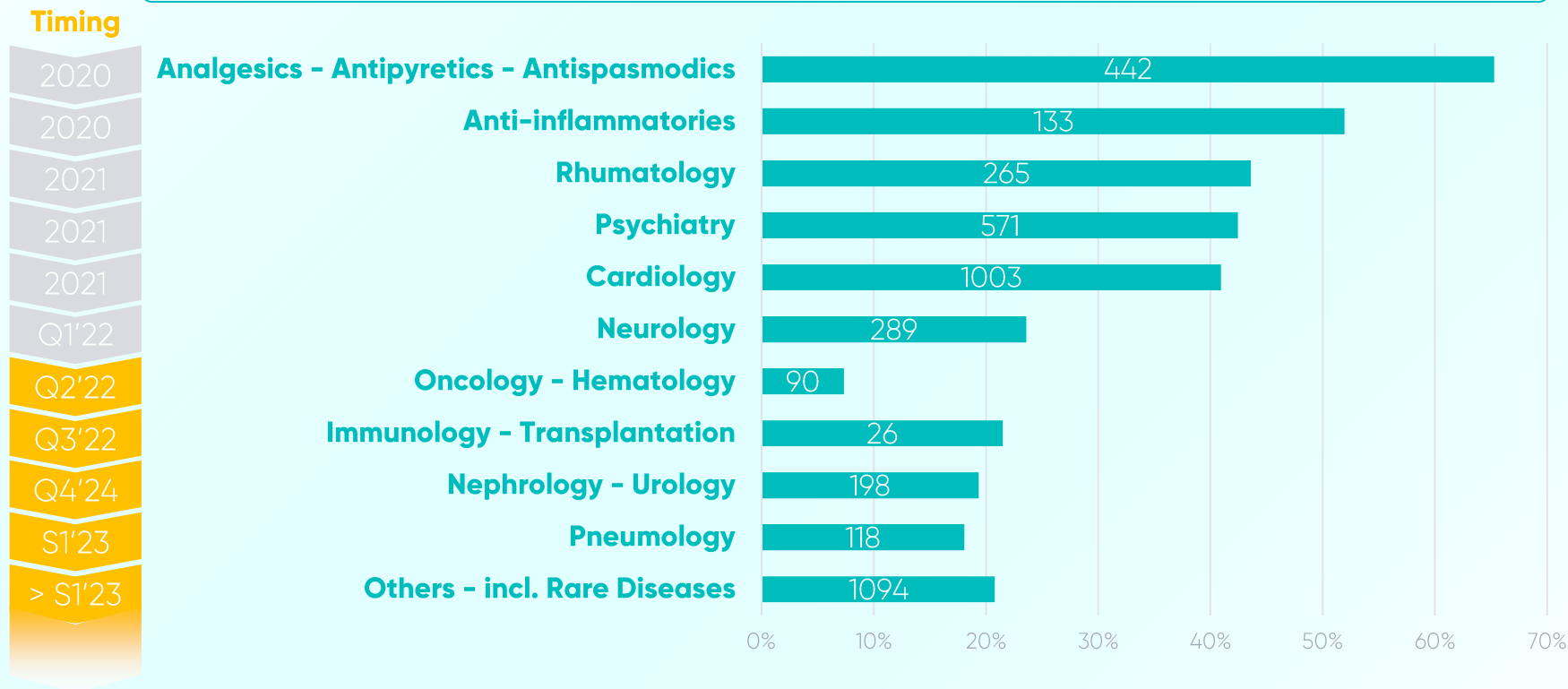
100€/patient/month
for a chronic patient

2022 | 2023 | 2024

Drugs Prioritization : most expensive & narrow therapeutic windows

3,700 drugs currently simulated. % vs total existing # of drugs*:

Timing

Timing	Therapeutic Area	Value
2020	Analgesics - Antipyretics - Antispasmodics	442
2020	Anti-inflammatories	133
2021	Rhumatology	265
2021	Psychiatry	571
2021	Cardiology	1003
Q1'22	Neurology	289
Q2'22	Oncology - Hematology	90
Q3'22	Immunology - Transplantation	26
Q4'24	Nephrology - Urology	198
S1'23	Pneumology	118
> S1'23	Others - incl. Rare Diseases	1094

0% 10% 20% 30% 40% 50% 60% 70%

* around 10% of drugs are counted in two or more therapeutic areas.
As of Q2'22 ExactCure simulates 33% of drugs in Top 10 therapeutic areas and 28% of all existing drugs.

Roadmap

Paying B2C app?

Animals Health?

Pay-per-API call?

CE

Class IIa

Patient Metabolism

Patient Feedback

Multi-Drugs Interactions

Class I MD. CE
API.
White-labelled
mobile app
& HCP simulator.

FDA

| S1'2022 | S2'2022 | S1'2023 | S2'2023 | S1'2024 | S2'2024 |

Track Record

Awarded disruptive technology
based on fundamental research
+
Customers
Med&Moi app +1000 users/week

2022
TRHC,
France 2030

2021
UPSA,
EU project

2020
Elsevier,
Dômes
Pharma

2019
Vidal
Partnership

2019
Seed Round
i-Lab

2018
EU Seal of
Excellence

2018
Established,
Accelerated

Fundamental
Research

16

Revenue and pipeline

102%
Q1'22 revenue vs FY2021

+50%
revenue growth 2021 vs 2020

(no revenue in 2019)

Revenue (k€)
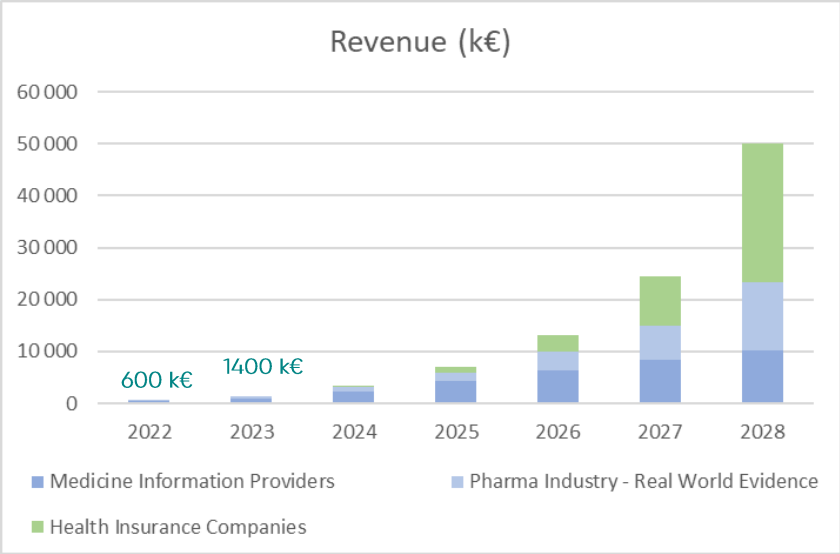
	Prospect	Expected € / year	Year 1	Probability
Medicine Information Providers	Tabula Rasa HC	100k€	2022	90%
		500k€	2023	75%
	Elsevier	250K€	2022	50%
		500k€	2023	50%
	Vidal	100k€	2022	75%
	BCB	100k€	2022	50%
	IQVIA	500k€	2022	25%
Pharma Companies	UPSA v2	100k€	2022	75%
	Angelini	200k€	2023	33%
	Orphalan	100k€	2022	33%
	Abbvie	100k€	2023	25%

17

France 2030 laureate

1,37M€ awarded

820k€ subsidy + 550k€ grant

Corresponds to 45% of the submitted project

PREMIER MINISTRE

Liberté
Égalité
Fraternité

Secrétariat général
pour l'investissement

Le Secrétaire général

Dossier suivi par Jean-Christophe DANTONEL
jean-christophe.dantonel@pm.gouv.fr
Réf : BB/JCD/n°53

Paris, le 29 MARS 2022

Monsieur le Président,

J'ai le plaisir de vous annoncer que le Premier ministre a décidé d'attribuer une participation de France 2030, à hauteur de 1 375 823 € à votre société dans le cadre du projet OncoTwin. Ce projet s'inscrit en effet pleinement à l'appel à manifestation d'intérêt de la stratégie France 2030 « Santé Numérique ».

Bpifrance, opérateur de l'Etat pour ce programme, prendra prochainement contact avec vos équipes afin de permettre, dans les meilleurs délais, la contractualisation du financement apporté par l'Etat à ce projet.

J'appelle votre attention sur le fait que la décision du Premier ministre est assortie d'une clause de caducité et que cette contractualisation doit intervenir sous six mois, faute de quoi cette décision ne serait alors plus valide.

Je vous prie de recevoir, Monsieur le Président, l'expression de ma considération distinguée.

Bruno BONNELL

Competition : less personalization, fewer drugs

	EXACTCURE Your Digital Twin for a Personalized Medication	DoseMeRx / PrecisePK / Insight RX / MW PHARM ++
Personalized PK simulations	✓	✓
Personalized PD simulations	✓	✗
Number of covariables in the models (age, weight...)	Aggregation of several models into 1 meta-model per drug -> more covariables	Only 1 ref. model per drug -> less covariables
Number of drug models	3,000 (aim 10,000)	20~50
Solution for Healthcare Professionals	✓	✓
Solution for patients	✓	✗
Leverage Patient Feedback to improve models	✓	✗
Integrate mutli-drugs interactions	✓	✗
Provide access to simulations as a service via an API	✓	✗

Barriers to Entry

Regulatory since May 2021
We have 3-year derogation to sell Class I
But competitors will have to be Class II

C E

Trade secret
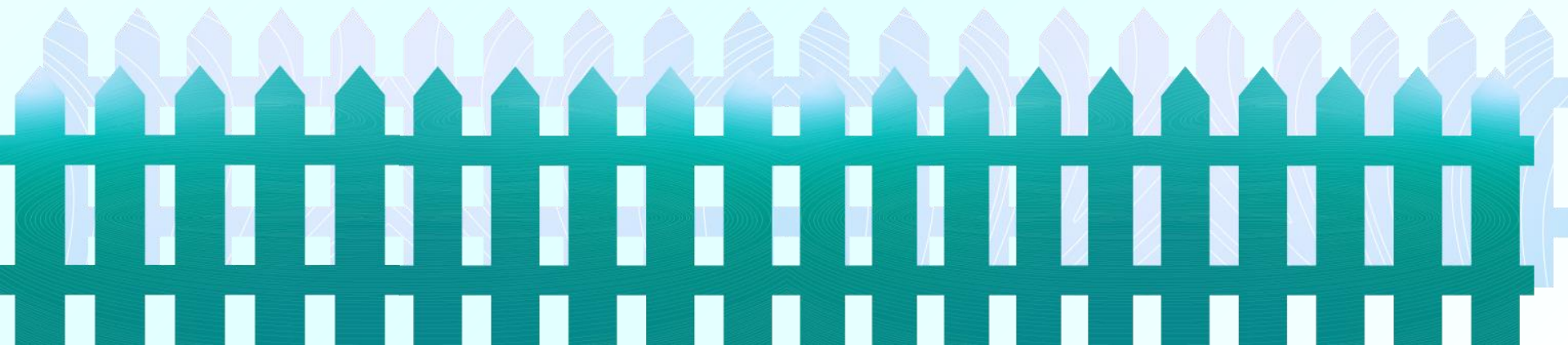Disruptive approach of pharmacology

First Mover Advantage
« Powered by ExactCure® »

High **Switching Costs**

Team: 25 people incl. 6 PhD and 4 PharmD

Pharmacists, mathematicians, data scientists, front & back end, biz dev.

Frédéric Dayan
Chief Executive Officer

Engineer, **Pharmacist**, PhD in biology

University, Sobios, Dassault Systèmes

International R&D Management

Sylvain Benito
Chief Scientist Officer

PhD in **Mathematics**

ING, Sobios, Dassault Systèmes

Complex bio-modeling

Fabien Astic
Chief Business Dev Officer

Engineer, **INSEAD MBA**

Nokia, Technicolor, EIT Digital

International Market Development

Dr. Marc Salomon
Medical Director
Cardiologist. Founded
Clairval private hospital
and LeFigaroSante.fr

Sophie Deret
Senior Product Manager
20 years in drug
development & IT

21

Strategic Advisory Board

Dr. Anne Baille

Professor in Strategy.
GM in **Pharma industry**:
Allergan, Teva, J&J.

Jacques Turgeon

CSO, Tabula Rasa HealthCare.
Chief Executive Officer of the
University of **Montreal Hospital**.

Pr. Dr. P. Beaune

Highly cited researcher in
personalized medicine.
APHP, **Inserm** Unit Dir.

Pr. Dr. Pierre Marquet

**Professor of medical
pharmacology** at the
University of Limoges.

Eric Marée

CEO of Virbac for 18 years.
Former CEO of Roche-
Nicholas France.

Yasmina Fechkeur

Owner at LF Laboratory.
Board Member at RedMed.
Pharmacist and Biologist.

Main Awards, Prizes and Recognition

"eHealth" grant decided by the French Prime Minister

Analyzed in article by INSEAD Strategy Professor

EU Seal of Excellence.
H2020 RIA Project (5% success rate)

Speaker at MIT's
"AI for Healthcare" summit

From the French Ministry of Research in person

Cited in same article as Elsevier and Certara

"Most successful INNOLABS SME" (119 EU candidates)

Featured in same broadcast as Astra Zeneca

1st prize from the French Society of Digital Health

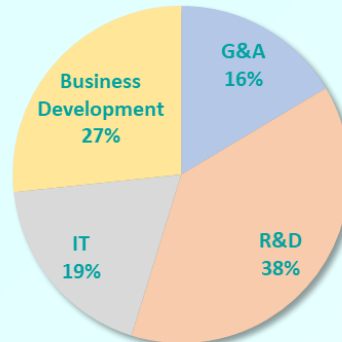Laureate of several EIT Health EU programs

Use of our Next Financing Round

ExactCure raised 700k€ in equity with **oneRagtime**,
who is committed to 1M€ and will co-lead our 2nd round.

We target to raise **5M€** by Q4 2022. We are looking for a lead investor.

Sales Development

- ✓ Build Sales team
- ✓ Strengthen French market
- ✓ Expand internationally
  - ✓ DACH
  - ✓ US
  - ✓ Gulf Countries
  - ✓ Japan, China

Industrialization

- ✓ Clinical trial to reach class IIa
- ✓ Integrate Multi-Drugs Interactions
- ✓ Develop Patient Feedback
- ✓ Down to 2 hrs/new drug model
- ✓ Cover 10 000 drugs

Pie chart:
- G&A 16%
- R&D 38%
- IT 19%
- Business Development 27%

Thank-you

Our ambition: become the worldwide reference

in personalized medication simulations

f.astic@exactcure.com
+33 6 73 18 25 72

s.benito@exactcure.com

f.dayan@exactcure.com

Backup

Our Unique Approach to Properly Use Drugs

1

Disruptive Usage
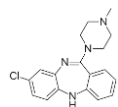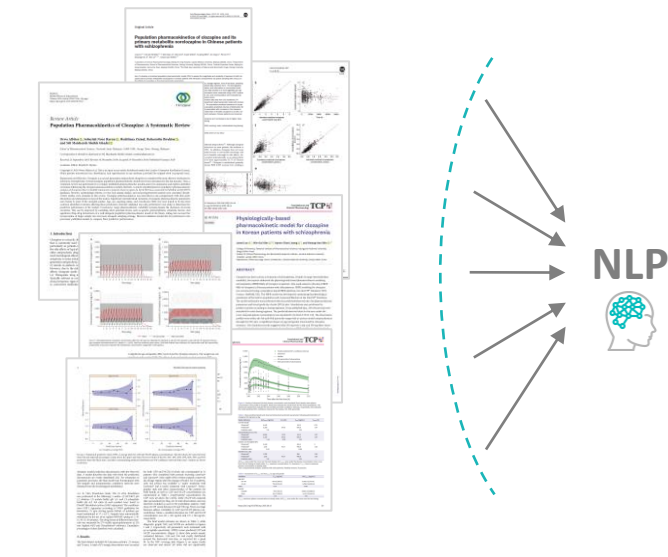
Monitor drug concentration

2

Meta–modeling

Integrating state-of-the-art literature

3

Patient Feedback
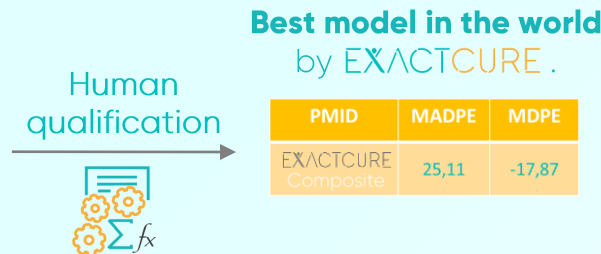
AI to fine-tune models in real time

How? Proven Disruptive Technology

NLP

Clozapine (psychiatry)

PMID	MADPE	MDPE
22820910	34,54	19,23
24342896	31,18	15,93
21422906	35,82	11,91
30956977	32,52	11,68
12188102	31,32	4,47
9384461	29,39	-18,96
19349931	43,9	38,5

7 best models from literature.
Tested on
53 patients (external evaluation)

Human qualification

Best model in the world by EXACTCURE .

PMID	MADPE	MDPE
EXACTCURE Composite	25,11	-17,87

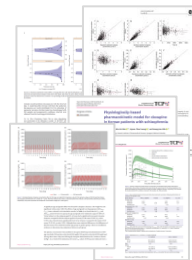**PAGE**   **GMP**   THERAPEUTIC DRUG MONITORING

2 posters   Speaker   1 article accepted

① Proprietary NLP to mine the literature

② Mathematically aggregate selected models

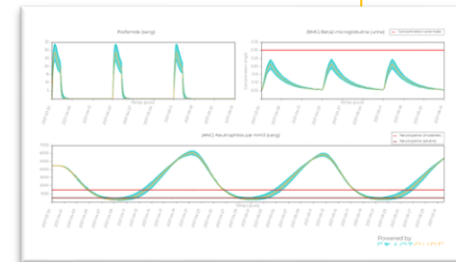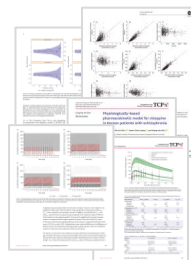**Ifosfamide (kidney cancer)**

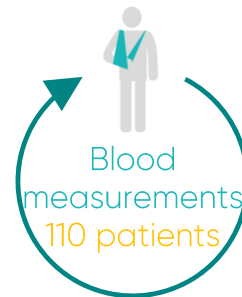NLP → PKPD model **With probabilistic layer** by ExactCure

Pazopanib (kidney cancer)

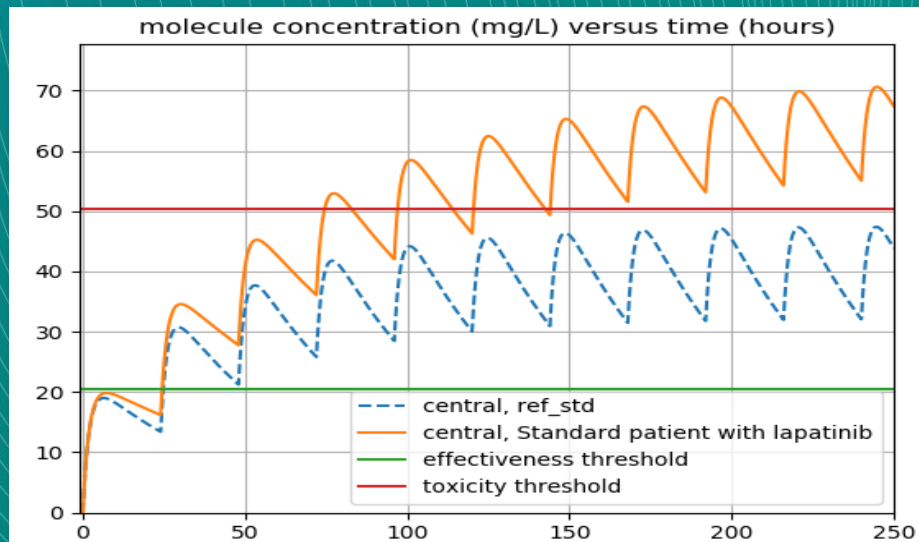NLP → **PK model** by ExactCure + Blood measurements 110 patients = MADPE improved by **33%**
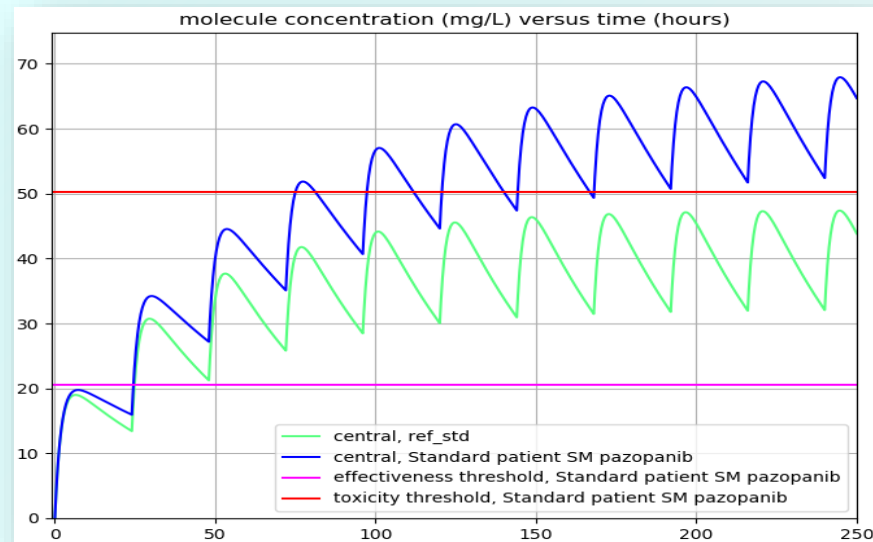
MDPE improved by **64%**

For Healthcare Professionals

Example of pazopanib (kidney cancer)

Influence of lapatinib (Drug-Drug Interaction)

Influence of CYP3A4 mutation (Genotype)

molecule concentration (mg/L) versus time (hours)

- central, ref_std
- central, Standard patient with lapatinib
- effectiveness threshold
- toxicity threshold

molecule concentration (mg/L) versus time (hours)

- central, ref_std
- central, Standard patient SM pazopanib
- effectiveness threshold, Standard patient SM pazopanib
- toxicity threshold, Standard patient SM pazopanib

Existing Class I Medical Device (Simulation Engine)

Psychiatry
(proven for clozapine on 53 patients)

2 world-class symposiums in pharmacology

2 posters   Speaker   1 article accepted

Kidney cancer
Convinced them to run a clinical trial

molecule concentration (mg/L) versus time (hours)

- central, ref_std
- central, Standard patient with lapatinib
- effectiveness threshold
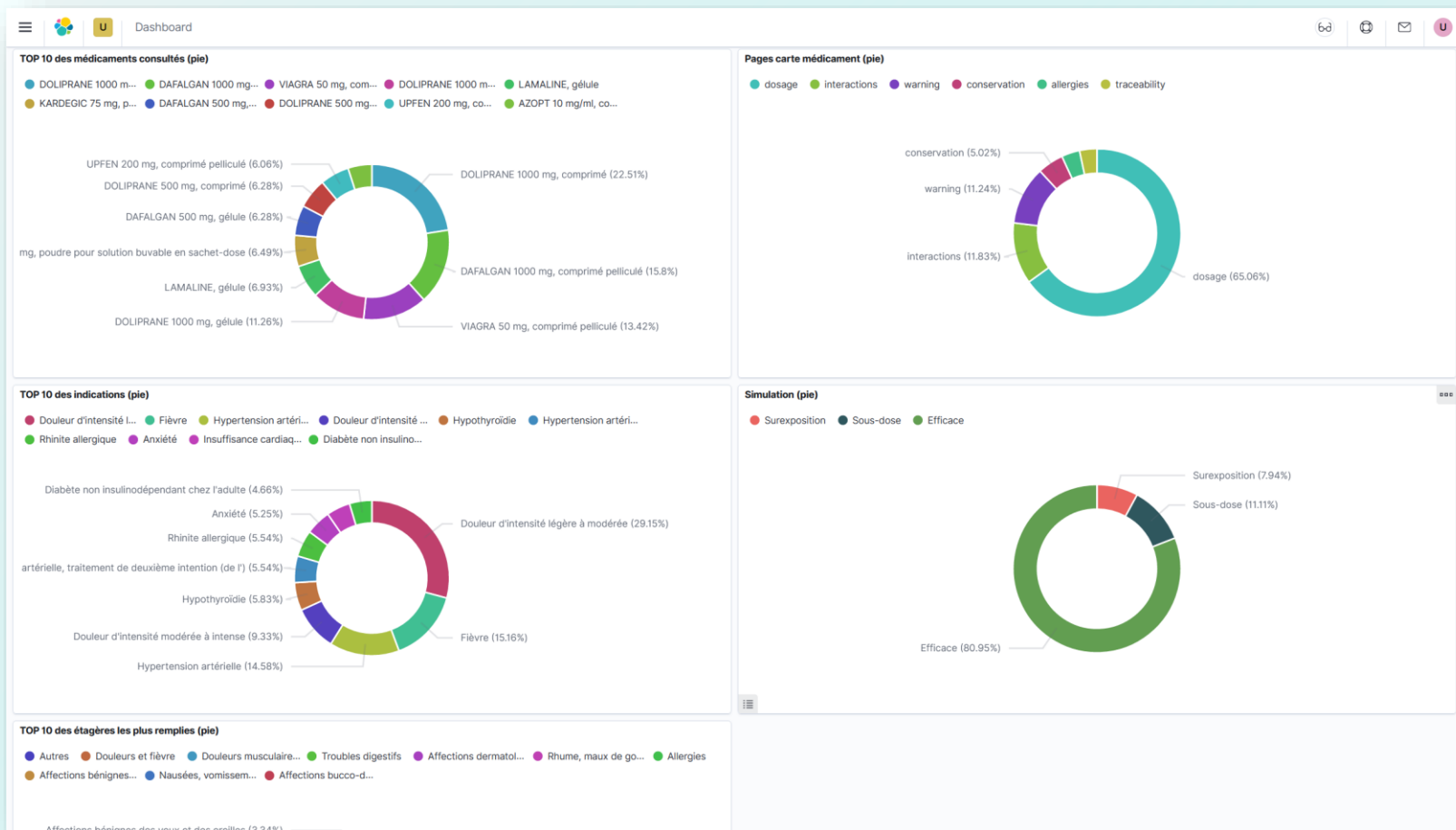- toxicity threshold
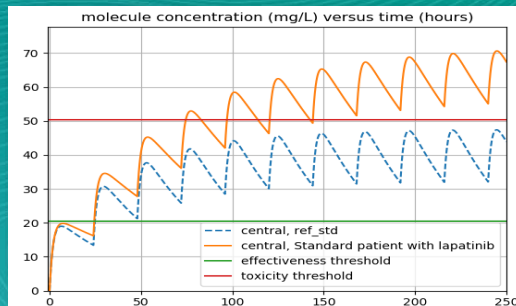
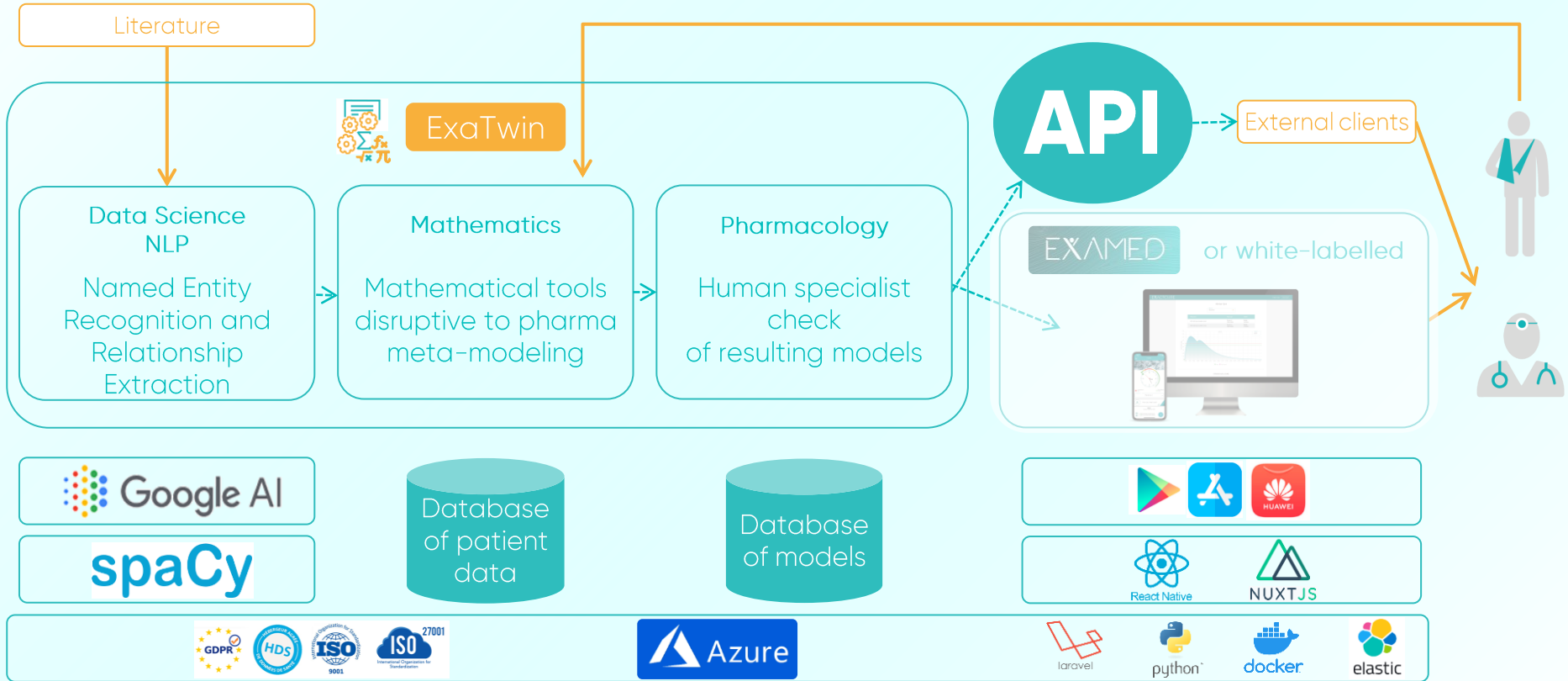## Immunosuppression
Co-direct a PhD thesis

Starting project to build a PD model of Mycophenolate mofetil, to monitor neutropenia after an injection of this immuno modulator.

And other promising discussions in cardio-vascular diseases, epilepsy, nephro-oncology, anaesthesia.

# For Pharma: Dashboard – Real World Evidence

Technology

Based on Fundamental Research with Inria

$$= \int \tilde{\phi}\big(c_{shared}, \tilde{C}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific}, \tilde{e}, u\big) \, \mathrm{d}\mathbb{P}_{c_{shared}}(c_{shared}) \cdot \mathrm{d}\mathbb{P}_{\tilde{e}}(\tilde{e}).$$

Il est naturel d'exprimer que $\tilde{\psi}_m$ doit dépendre explicitement de la matrice de covariance $\tilde{\Sigma}$ mais pas de $\tilde{S}$. $\tilde{E} \sim \mathcal{N}\big(0, \tilde{\Sigma}\big)$ et $\tilde{R} \sim \mathcal{N}\big(0, \tilde{S}\big)$ nous avons

$$\tilde{\psi}_m\big(\tilde{C}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific}, \tilde{\Sigma}, u\big)$$

$$= \frac{1}{\big(\det(\tilde{\Sigma})\big)^{\frac{\tilde{k}}{2}} \cdot \big(\det(\tilde{S})\big)^{\frac{\tilde{l}}{2}}} \cdot \int \tilde{\psi}\big(c_{shared}, \tilde{C}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific}, \tilde{e}, \tilde{r}, u\big) \cdot \exp\left(-\frac{\tilde{e}^t . \tilde{\Sigma}^{-1} . \tilde{e} + r^t . \tilde{S}^{-1} . \tilde{r}}{2}\right)$$
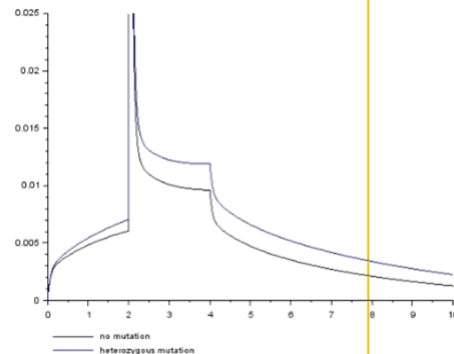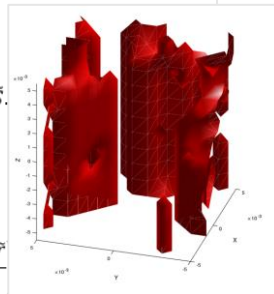
$$= \frac{1}{\big(\det(\tilde{\Sigma})\big)^{\frac{\tilde{k}}{2}}} \cdot \int \tilde{\psi}\big(c_s$$

Cette réponse peut être compar

$$C_{specific}:$$

$$= \mathbb{E}\big(\hat{\psi}\big(C_{share}$$

$$J\left(\hat{c}^{(i)}_{specific,unknown}, \hat{\Sigma}^{(i)}_{specific,unknown}\right)$$
$$= \left(\hat{\psi}^{(i)}_m\left(c^{(i)}_{shared}, c^{(i)}_{specific}, \tilde{c}^{(i)}_{specific}, \pi, \pi_{specific}, \hat{\pi}^{(i)}_{specific,unknown}, \hat{\Sigma}^{(i)}_{specific,unknown}, u\right) \dots\right.$$
$$\left. - \tilde{\psi}^{(i)}_m\left(c^{(i)}_{shared}, \tilde{c}^{(i)}_{specific}, \tilde{\pi}_{shared}, \tilde{\pi}_{specific}, \tilde{\Sigma}, u\right)\right)^2.$$

où les paramètres $\pi_{shared}, \pi_{specific}, S, \tilde{\pi}_{shared}, \tilde{\pi}_{specific} \tilde{\Sigma}$ et $\tilde{S}$ ont déjà été appris.

Pour conclure il suffit d'estimer les paramètres $\hat{\pi}^{(i)}_{specific,unknown}, \hat{\Sigma}^{(i)}_{specific,unknown}$. Cela passe par la minimisation de la distance J :

$$\left(\hat{\pi}^{(i)}_{specific,unknown}, \hat{\Sigma}^{(i)}_{specific,unknown}\right) = \arg\min(J).$$

35
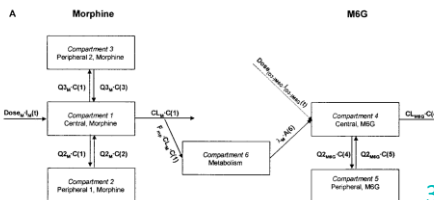
Market Access Channels to end-users via our customers
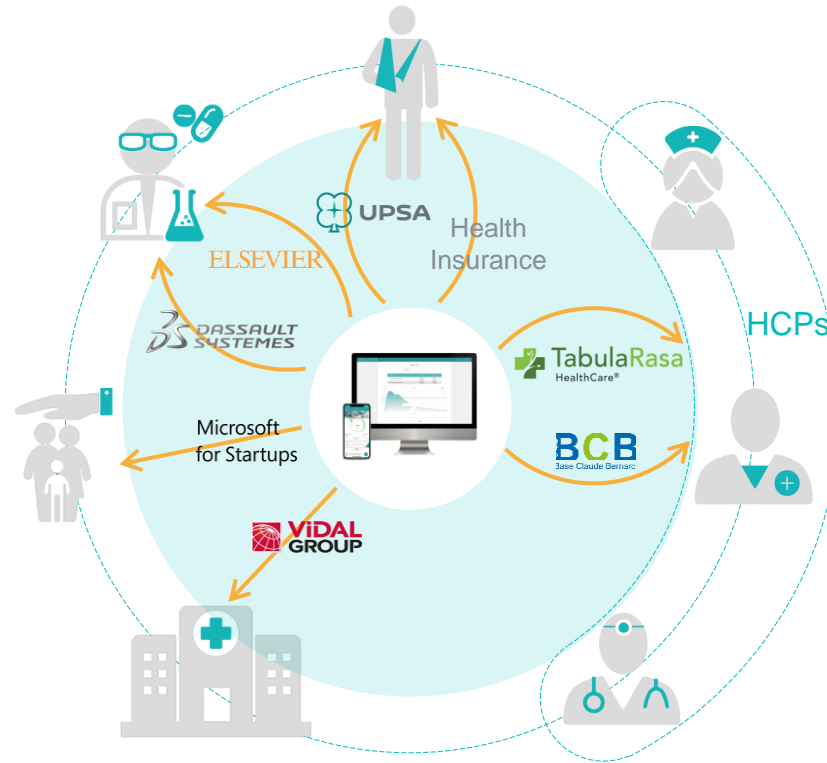
Competition : less drugs, less personalization
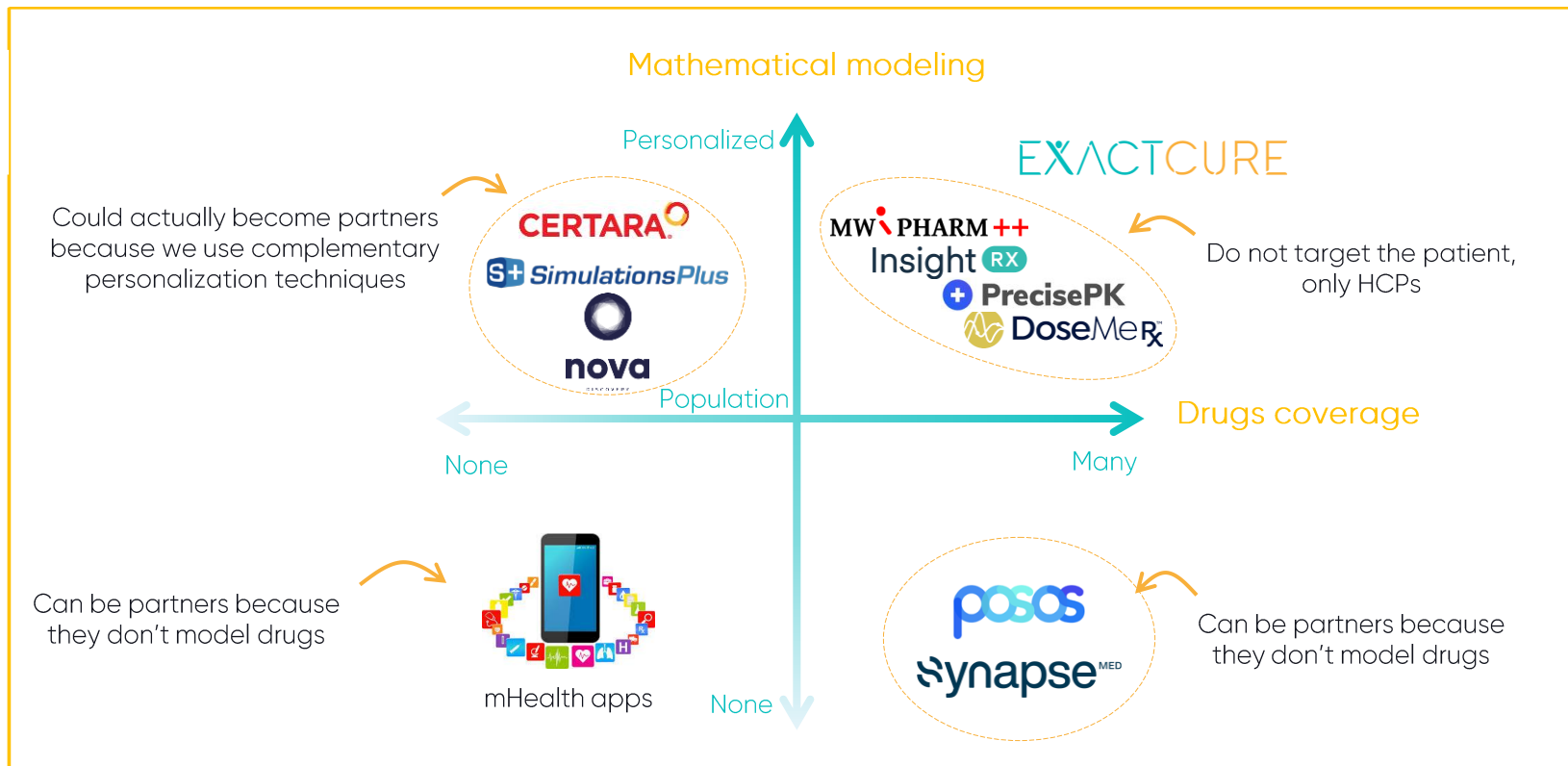

Mathematical modeling

Personalized

EXACTCURE

Could actually become partners because we use complementary personalization techniques

CERTARA

S+ SimulationsPlus

nova

MW PHARM ++

Insight RX

PrecisePK

DoseMeRx

Do not target the patient, only HCPs

Population

Drugs coverage

None

Many

Can be partners because they don't model drugs

mHealth apps

None

posos

Synapse MED

Can be partners because they don't model drugs

US Market Segmentation + Priorization

Ability to Compete and Size of Market
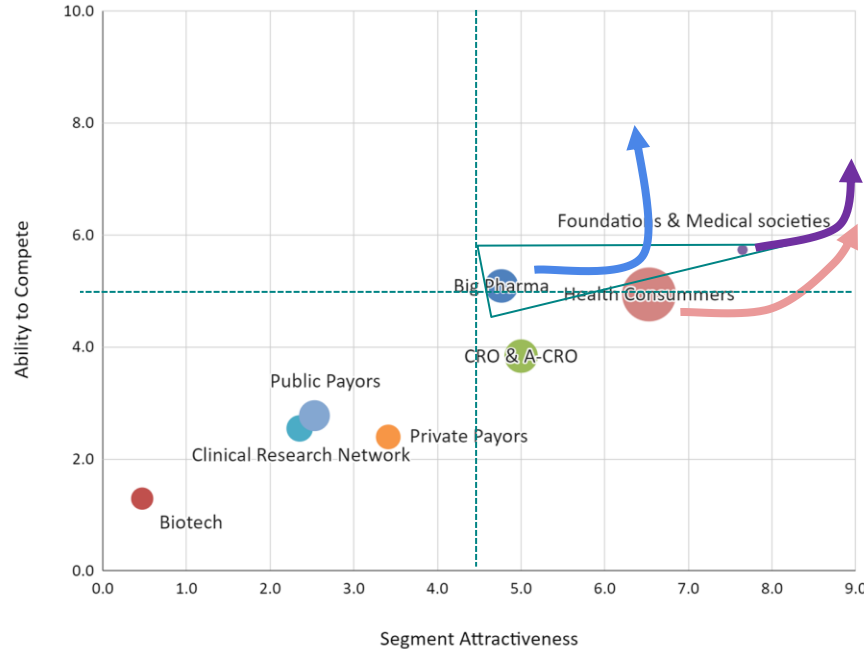
#1: Big Pharma
+ **Extend reach & scope based on their needs (R&D; Commercial or safety)**
+ **Build credible presence in the U.S. (team & board)**

Explore MDDS model to minimize regulatory burdens

#2: Foundations & Medical societies
+ **Market research to identify the ones that fit the most with your track record**
+ **Build database conditions based on their needs (what matters to them)**

#3: Health consumers
+ **Clarify & accelerate the dedicated product roadmap (readiness)**
+ **Raise tons of funding**
+ **Be a specialist, partner & recommended by pharmacist (CVS > additional services ?)**

MEDICATION ERRORS:
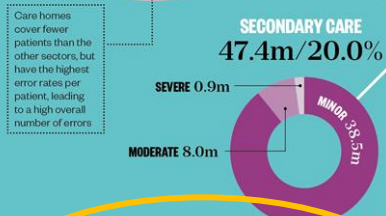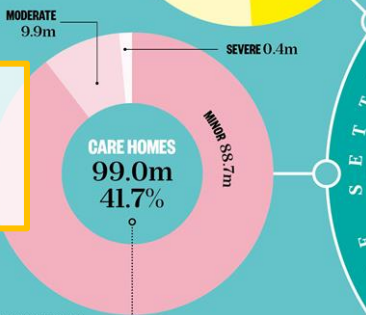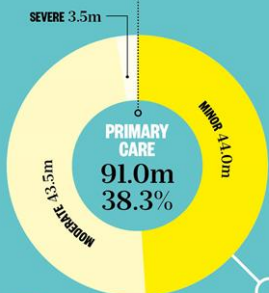## WHERE DO THEY HAPPEN?

MEDICINES SAFETY *special*

Reducing medicines-related harm requires a clear understanding of where and when errors occur. This visual summary shows the latest estimates in England per year.
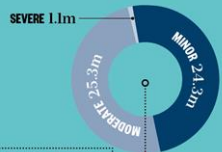
DAWN CONNELLY & MARTIN COTTERELL

Error rates per patient are lowest in primary care but more medicines are used, so the overall number of errors is second highest

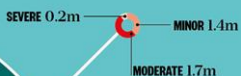**PRESCRIBING**
50.7m/21.3%

SEVERE 1.1m
MODERATE 25.3m
MINOR 24.3m

Deaths owing to definitely avoidable adverse drug reactions per year:
712

NHS costs of definitely avoidable adverse drug reactions per year:
£98.5m

SEVERE 3.5m

PRIMARY CARE
91.0m
38.3%
MINOR 44.0m
MODERATE 43.5m
SEVERE 0.4m

Prescribing errors are most likely to cause moderate harm (41.2% of moderate errors)

TRANSITIONING
3.3m/1.4%
SEVERE 0.2m
MINOR 1.4m
MODERATE 1.7m

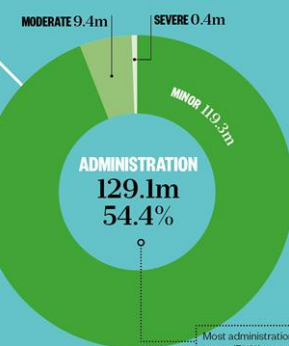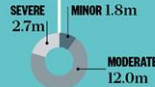## TYPES OF ERROR

Around 20,000 medicines-related incidents were reported...

> **>36% related to lack of personalization**

MODERATE 9.9m

CARE HOMES
99.0m
41.7%
MINOR 88.7m
SEVERE 0.4m

STAGE OF MEDICINE
CARE SETTING
STAGE OF MEDICINE USE

TOTAL ERRORS
237.4 million

DISPENSING
37.8m/15.9%
SEVERE 0.4m
MINOR 24.5m
MODERATE 12.9m

Dispensing errors account for 17.5% of errors that have the potential to cause moderate or severe harm in primary care

Care homes cover fewer patients than the other sectors, but have the highest error rates per patient, leading to a high overall number of errors

MODERATE 9.4m
SEVERE 0.4m

SECONDARY CARE
47.4m/20.0%
SEVERE 0.9m
MINOR 38.5m
MODERATE 8.0m

ADMINISTRATION
129.1m
54.4%
MINOR 119.3m

SEVERE 2.7m
MINOR 1.8m
MODERATE 12.0m

MONITORING
16.5m/7.0%

Most administration errors (71.1%) occur in care homes

MINOR: Error with little or no potential to cause harm
MODERATE: Error with potential to cause moderate harm
SEVERE: Error with potential to cause severe harm

The World Health Organization wants to reduce severe avoidable medication-related harm globally by 50% by 2022

POTENTIAL SOLUTIONS

Several strategies can be employed to reduce medicines-related harm.

- Roll out and optimise electronic prescribing and medicines administration systems
- Roll out proven interventions, such as PINCER, where pharmacists identify patients who are at risk from hazardous prescribing (see page 95)
- Improve the information available to patients to promote joint decision-making
- Use patient-friendly packaging and labelling
- Improve shared care across different settings
- Embed adequate training in safe and effective medicines use in undergraduate training and continuing professional development
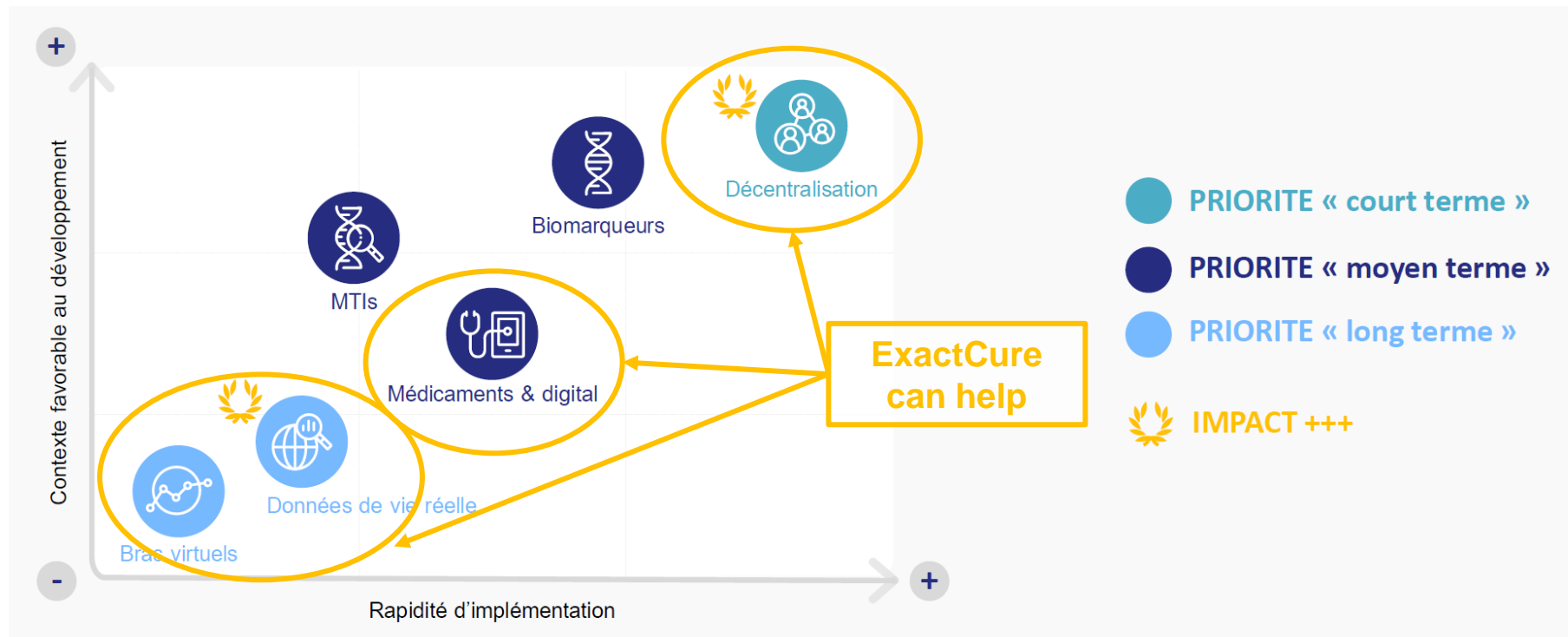- Encourage reporting of medication errors (see page 120)
- Reduce inappropriate polypharmacy

Source: Department of Health and Social Care.

Types of error percentages:
22.8% Other
21.3% Omitted medicine/ingredient
11.5% Wrong/unclear dose or strength
8.0% Wrong frequency
5.5% Wrong drug
3.9% Wrong quantity
2.8% Mismatch between patient and medicine
2.7% Wrong method of preparation/supply
2.4% Contraindication
1.9% Wrong formulation
1.8% Unknown
1.8% Wrong/omitted/passed expiry date
1.5% Patient allergic to treatment
1.5% Wrong route
1.4% Adverse drug reaction (when used as intended)
1.2% Wrong/transposed/omitted medicine label
0.5% Wrong/omitted verbal patient directions
0.1% Wrong/omitted patient information leaflet

La décentralisation des essais cliniques = évolution prioritaire

Verbatim

"Your application is very pleasant and very complete, I will tell those around me!"

Siegfried D., chronic patient

"You bring PKPD to the masses. Your tool can be very useful for healthcare professionals."

Emre I., Head of Drug Metabolism and Pharmacokinetics at a big pharma

"Your solution is clearly disruptive. This is real-time drug monitoring on an app, this is crazy!"

Taher H., BU Head Neurology & Immunology at a big pharma

"A clinician cannot dream of anything better than a reliable tool allowing him/her to adapt dosages according to the most relevant parameters."

Prof. Dr. Jacques M., Scientific Director of a French CRO, former advisor to Minister of Health

"Personalized is the future of medicine"

Master Yoda, Jedi