



Hub PASREL 15th of March 2022

BMK TOOLS

Bridging biomarkers from the lab to the patient

Funded by the
European Union



Agenda

1. A bit of context: Aviesan
2. What is actually a value chain ?
3. The biomarker value chain
4. The BMK TOOLS platform

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The National alliances

5 alliances

- Improve the coordination of players within the same research field
- Build a prospective thinking
- Increase performance, visibility and international influence
- Highlight French research

Energy



Human and
social sciences



Environment



Digital
technologies



Life sciences
and health



Aviesan

The project started within the Alliance **Aviesan** (National French Alliance for life sciences and health)

aviesan

alliance nationale
pour les sciences de la vie et de la santé

Associated members



Founders



Aviesan main objectives

- Scientific coordination
- Operational coordination

- More visibility and reactivity
- To share priorities on structuring projects



CVT-Aviesan: A think tank to smooth knowledge transfer

The CVT « thematical valorization consortium » gathered the technology transfer offices of the Aviesan members with these aims:

- Understand the value chains of innovation: current and future
- Identify the barriers and opportunities
- Bet on the complementarity of the different players
- **Design and test tools among the ecosystem**



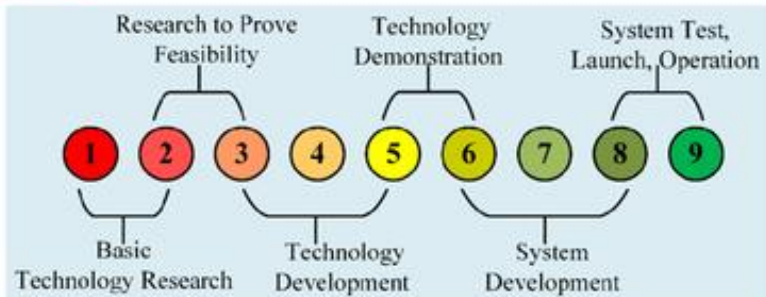
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Beyond the « Technology readiness level »

Technology Readiness Levels (TRL)

- 1 Basic Concept:** Basic principles observed and reported
- 2 Conceptual Design:** Technology concepts and/or applications formulated
- 3 Preliminary Design:** Analytical and experimental critical function and/or characteristic proof-of-concept
- 4 Detailed Design:** Component and/or breadboard validation in laboratory environment
- 5 Bench/Lab Testing:** Component and/or breadboard validation in relevant environment
- 6 Prototype:** System/subsystem model or prototype demonstration in a relevant environment
- 7 Field Test:** System prototype demonstration in operational environment
- 8 Pre-Production:** Actual system completed and flight-qualified through test and demonstration
- 9 Commercialized:** Actual system proven through successful mission operation



- Technology readiness level (TRL) is a system used to estimate technology maturity
- The use of TRLs enables consistent, uniform discussions of technical maturity across different types of technology

→ Who are the key players involved ?

→ Ecosystem definition / value chain understanding

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What about biomarker ?

Definition:

A biomarker is a **biological characteristic** that can be **measured objectively** and that reflects a biological process (normal or pathological) or a biological response after a therapeutic intervention

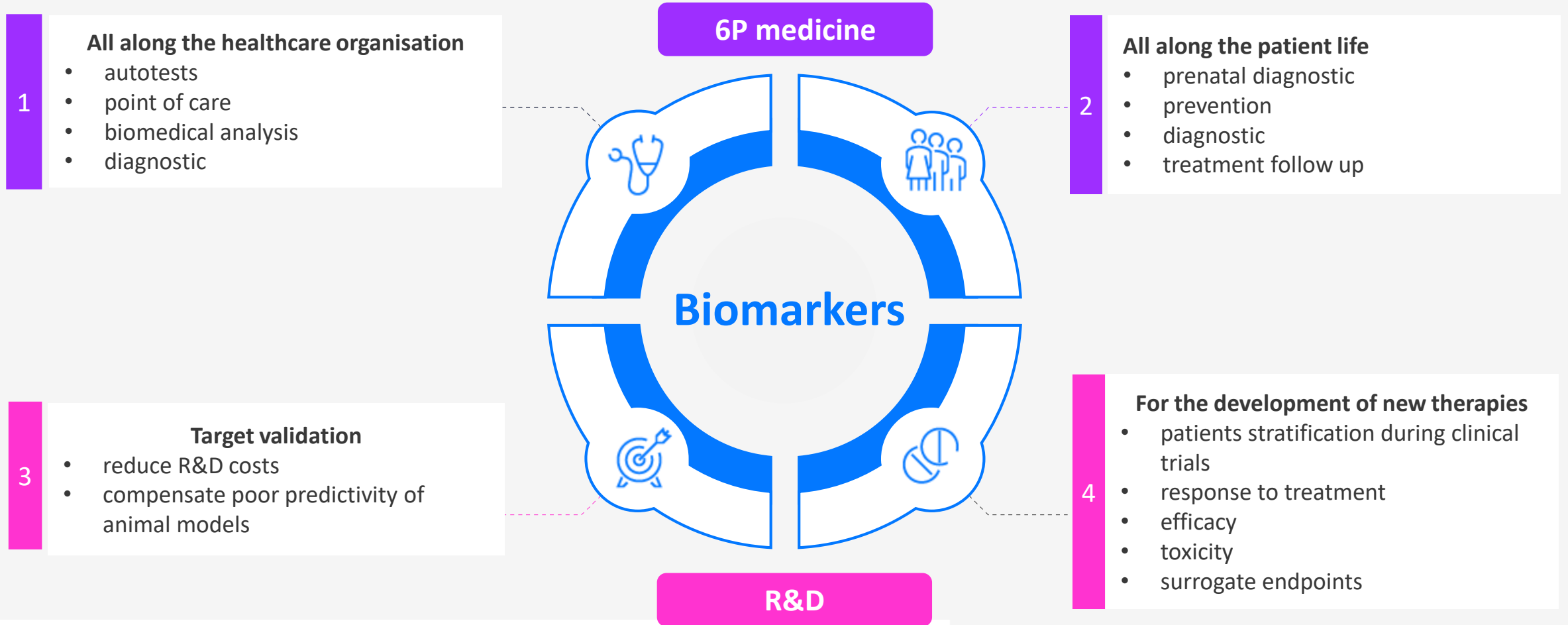
The majority of medical decisions relies on biomarker and diagnostic tools

Increasing need to discover and develop new biomarker for a better care of the patients:

- Risk evaluation (genetic tests)
- Prevention
- Early diagnostic
- More accurate diagnostic
- Targeted therapies

➔ **Biomarkers are the best allies for the precision medicine !**

The central role of biomarkers



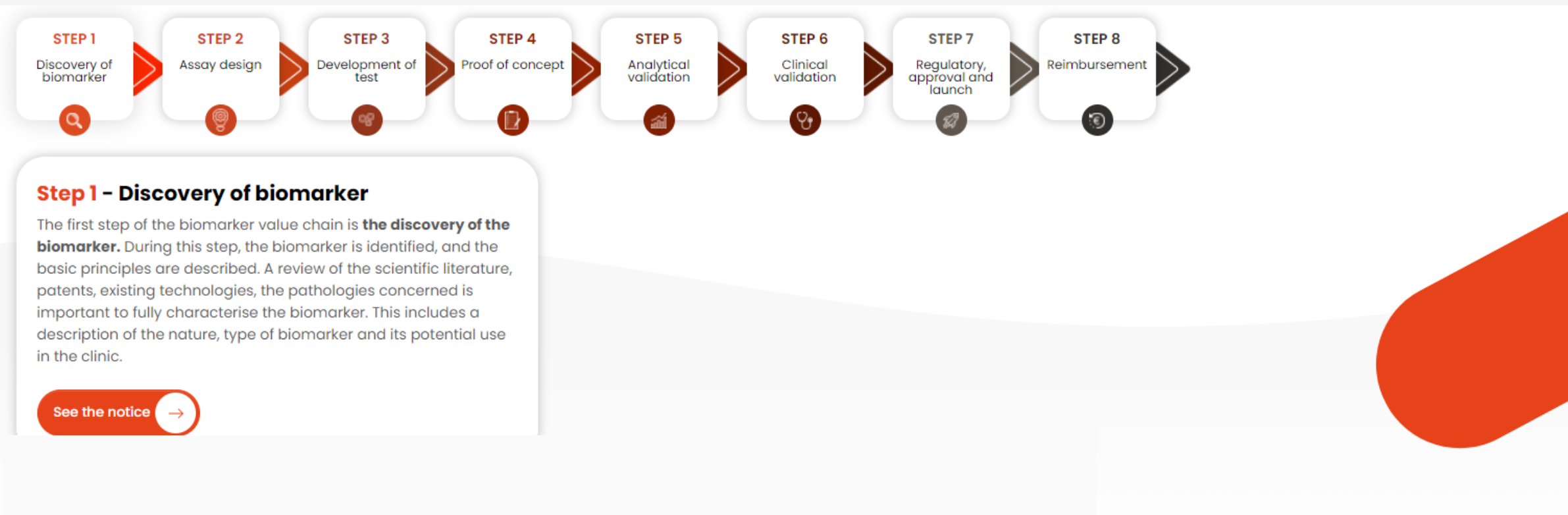
The biomarker value chain: the steps

> THE BIOMARKER VALUE CHAIN

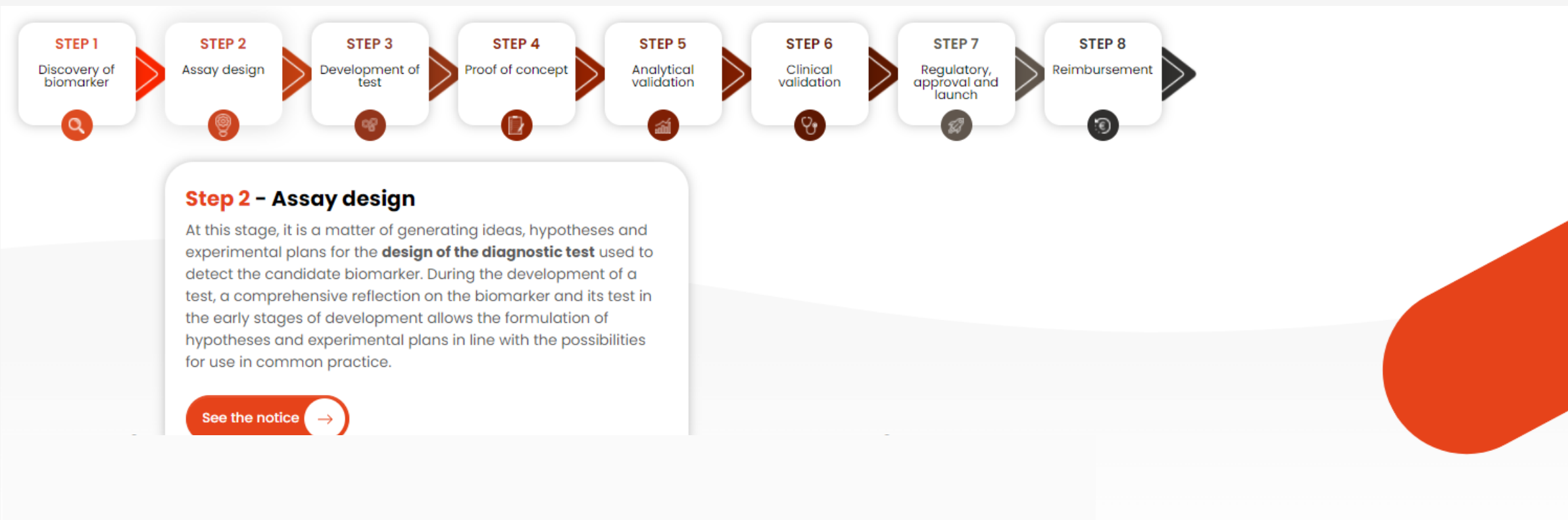
Development stages of a biomarker



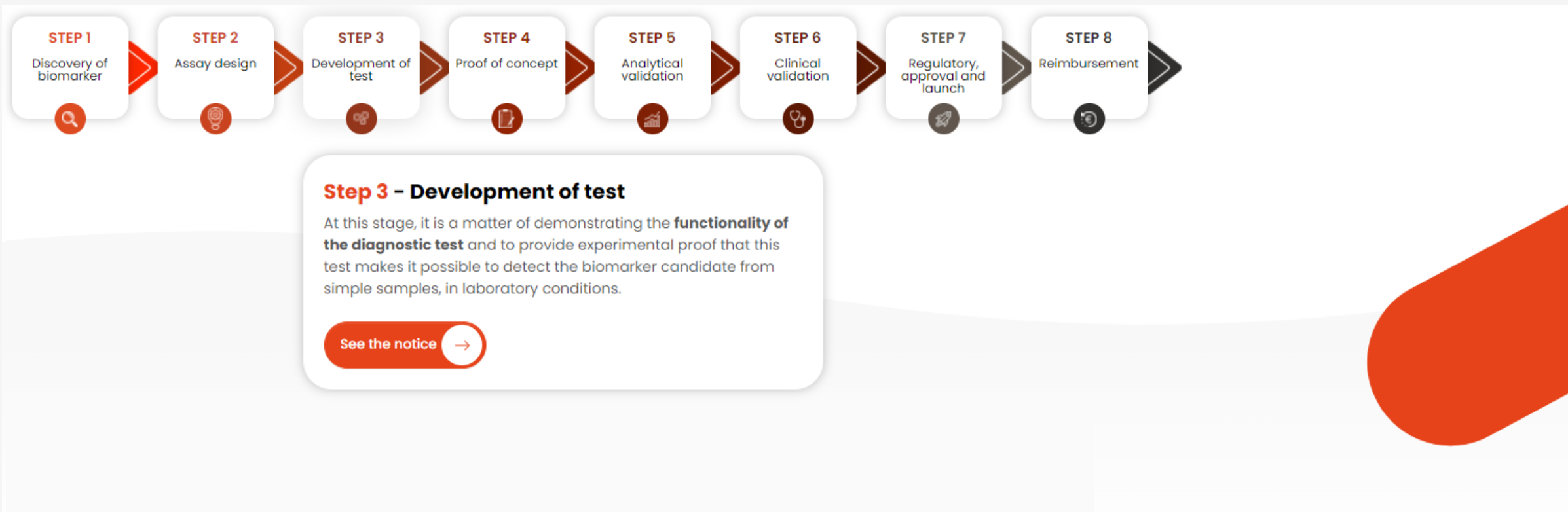
The biomarker value chain: the steps



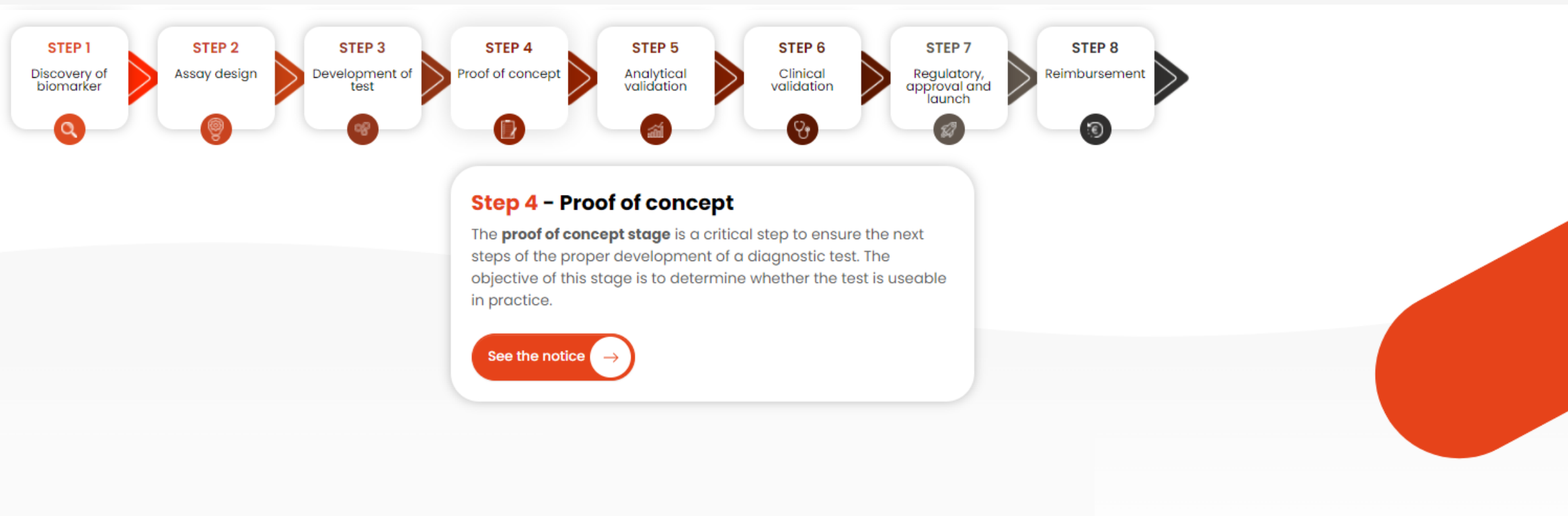
The biomarker value chain: the steps



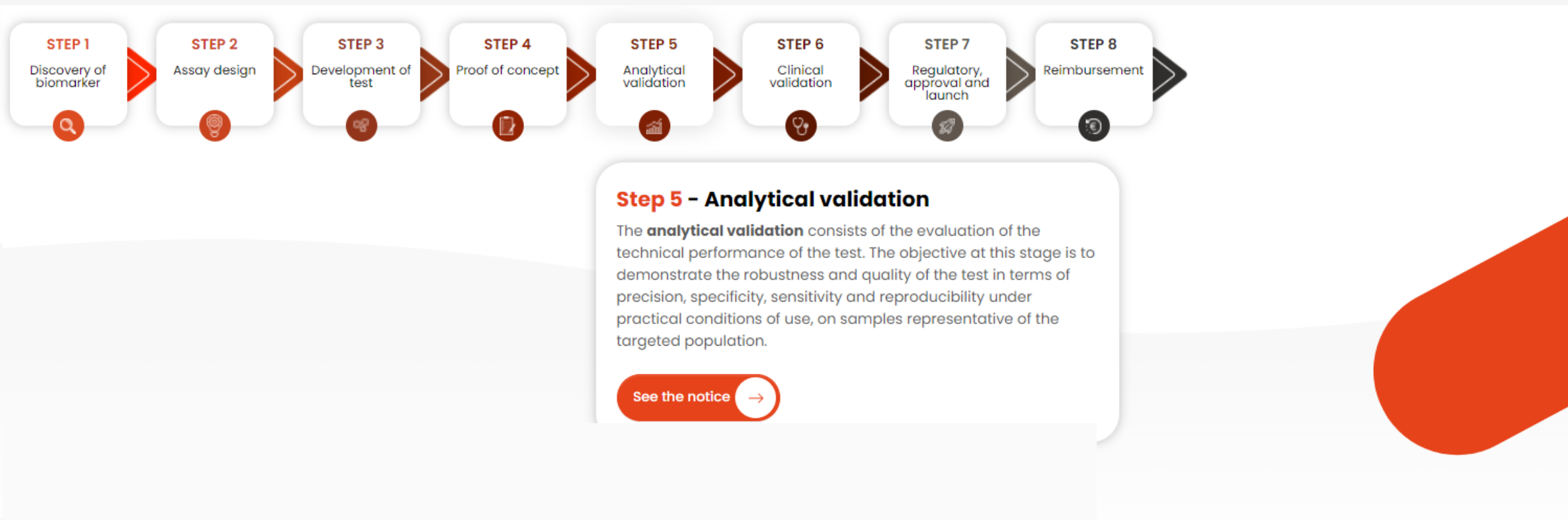
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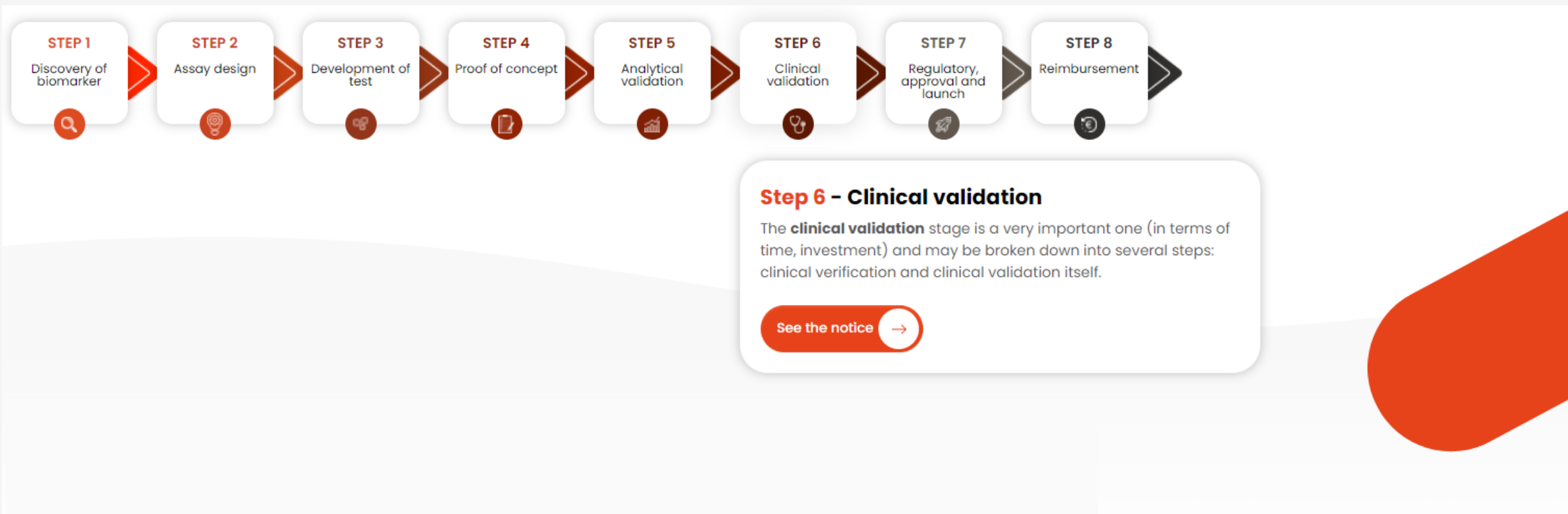
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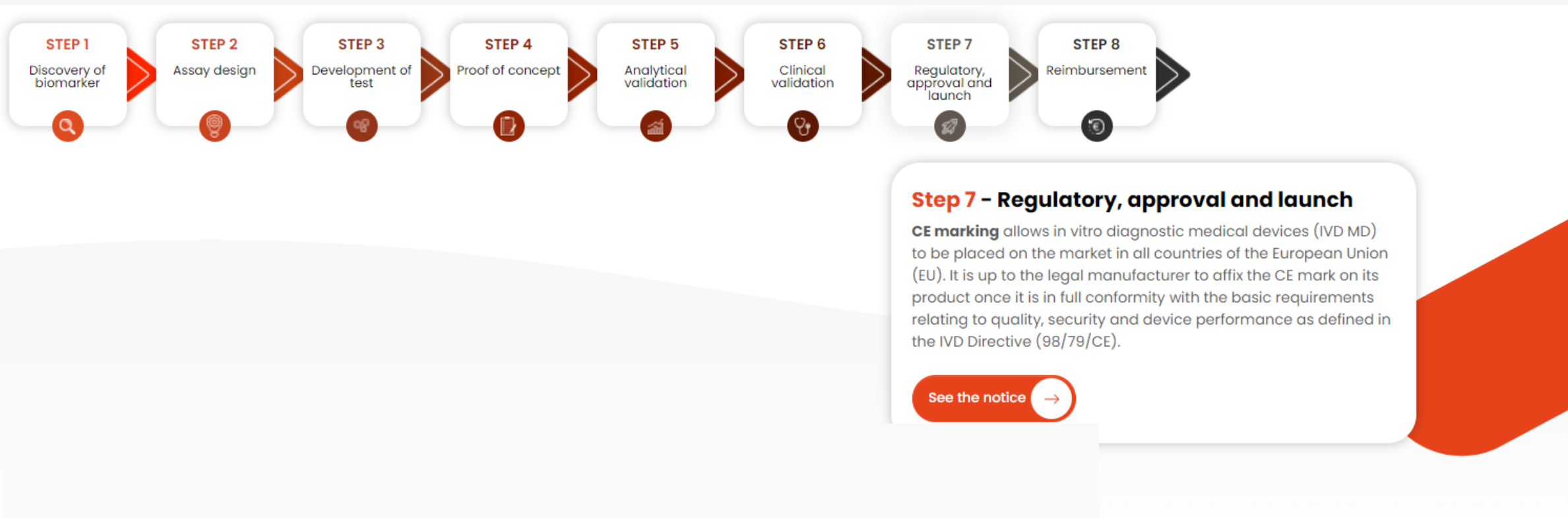
The biomarker value chain: the steps



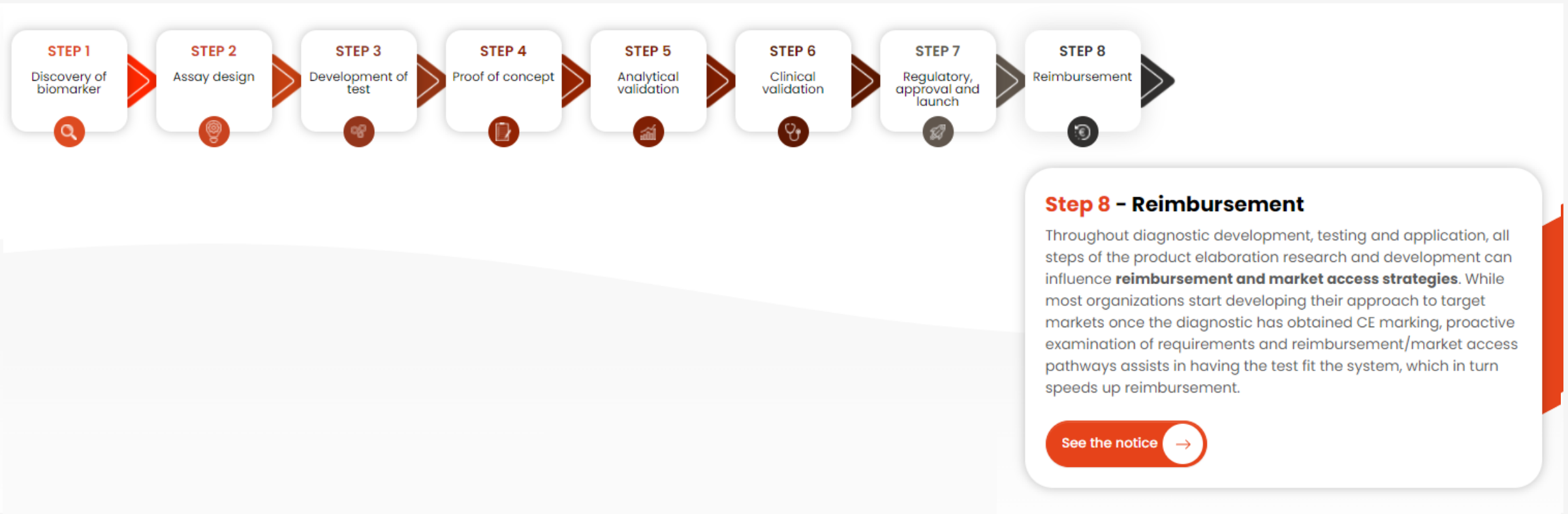
The biomarker value chain: the steps



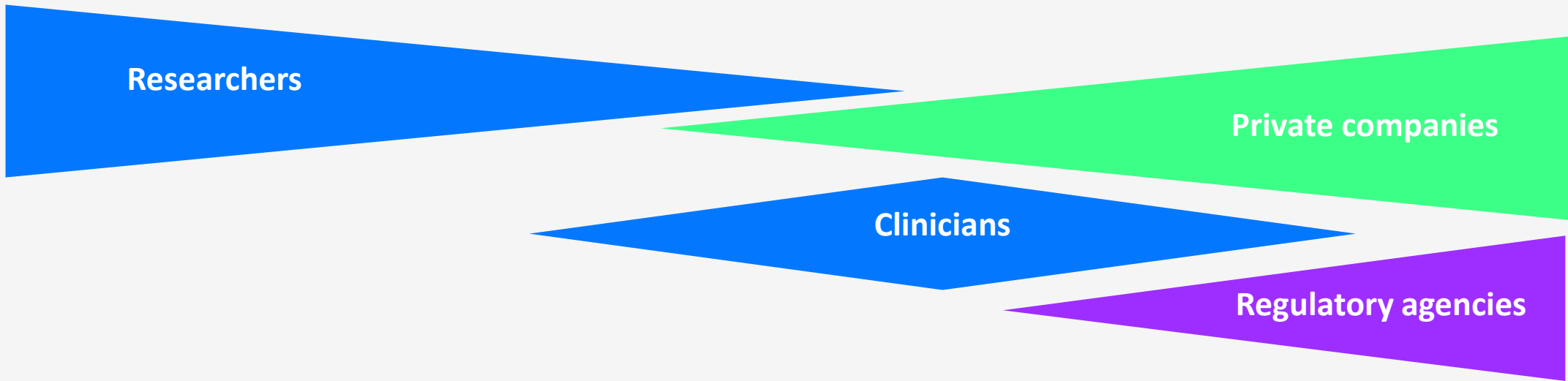
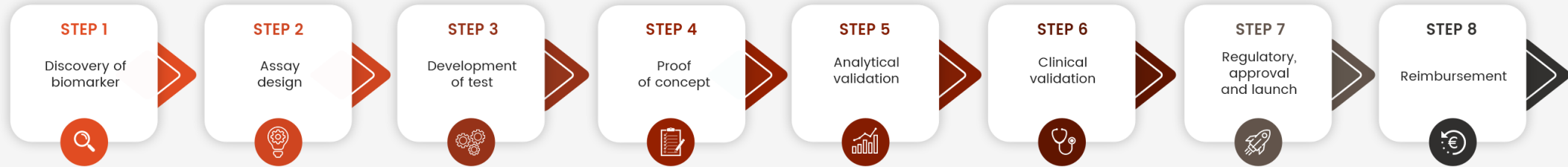
The biomarker value chain: the steps



The biomarker value chain: the steps



The biomarker value chain: the key players



Multiple steps and actors implying different goals, requirements and languages

The biomarker value chain: the gap

There is a « translational » gap

- Despite the profusion of publications and patents, only a few (less than 1%) biomarkers are really used in clinical practices
- Market is difficult to address because of the diversity of the sectors: Pharma, IVD, Biotech, Medtech...



Need of coordination between the stakeholders



Importance of the public / private partnerships



**Design a tool to bridge biomarkers
from the lab to the patient**



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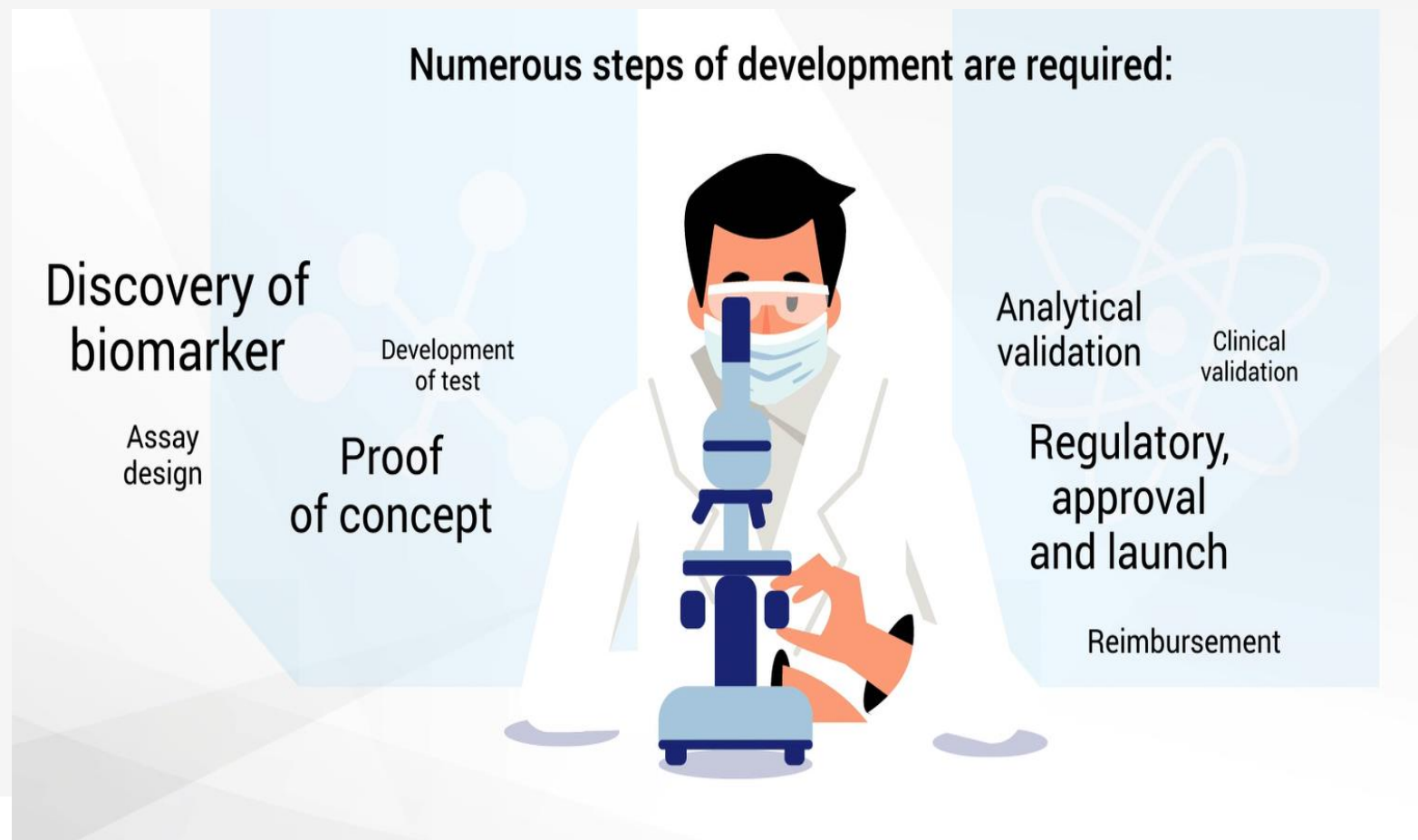
The BMK TOOLS platform



Get informed: all the steps of the value chain

Position a project on the value chain

Align the players of the ecosystem



Align the players of the ecosystem

A long way to come, involving many partners and expertises



The « education » module



Explanation sheet



- Step description
- Questions to investigate
- Definitions
- Links
- ...

The « education » module

BMK TOOLS booklet



BMK TOOLS
Faciliter le passage des Biomarqueurs du Laboratoire au Patient

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Scientific identification and evaluation of biomarkers
TRL1 "Review of scientific basis"

The first step of the biomarker value chain is the discovery of the biomarker. During this step, the biomarker is identified, and the basic principles are described. A review of the scientific literature, patents, existing technologies, the pathologies concerned is important to fully characterise the biomarker. This includes a description of the nature, type of biomarker and its potential use in the clinic. A summary of the different stakeholders involved in biomarker development may also be made. Indeed, the partners (public, private), valorisation organisations, and clinicians essential to development need to be identified. At this stage, a targeted market study may also help to build a strategy for the next steps.

Objectives	Tasks	Sample questions
Characterisation of biomarker	- identify nature of biomarker	Is the measured parameter anatomical, morphological, biological...?
	- describe type of biomarker	Is the biomarker a circulating protein, a genetic mutation...?
Measurement of biomarker	- identify therapeutic area and pathology concerned	Is it a biomarker of predisposition for a disease, a biomarker for toxicity...?
	- list techniques to measure biomarkers	Is the biomarker specific to a type of cancer, is it associated with a therapy, a medication...?
Role of biomarker	- describe current practices and define needs	Does it exist in different forms (glycosylation, isoforms, cleavage...)?
	- define target population	Commonly, what reference technique is used (PCR, an ELISA, a scanner...) to detect the biomarker?
Contribution of biomarker	- describe how biomarker meets clinical need	At what time does the biomarker intervene in patient management?
	- assess implementation of biomarker in clinical practice	How will the use of a biomarker change current clinical practice?
Protection and valorisation of biomarker	- identify scope of biomarker	Is the biomarker specific to pathology, different pathologies, a patient sub-group (treatment-resistant, particular stage...)?
	- review intellectual property around biomarker	How will the biomarker influence the therapeutic decision?
Stakeholders	- assess implementation of biomarker in clinical practice	Will the biomarker save time, money, personnel?
	- identify scope of biomarker	Is the targeted market to use the biomarker France, Europe, the USA...?
Stakeholders	- review intellectual property around biomarker	Is it necessary to make a declaration of innovation, to file a patent when a biomarker is discovered?
	- list different partners and their involvement in discovery of biomarker	Have you published a scientific paper?
		On which valorisation organisation do you depend?
		Who are your academic, industrial partners...?
		Have you identified potential partners (collaboration academic, clinicians, startups...)?

3

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Validation of test in real conditions
TRL5 "Advanced characterisation of product"

Biomarker detection will have to meet important validation requirements since they are in vivo. The tests should complete the analytical and clinical validation stages in order to demonstrate the robustness and quality of the test in terms of precision, reproducibility under practical conditions of use, on samples representative of the target population. The goal is to define whether the test measures the identified biomarker with sufficient accuracy and to define the optimal conditions of use to ensure reliable results. This includes a pre-analytical and post-analytical part. Pre-analytical validation concerns issues of collection, preparation, and storage need to be specifically described and strictly followed. Post-analytical validation concerns issues of data analysis and interpretation (e.g., flow cytometry, positivity threshold, immunohistochemistry scoring...).

Definition:

- Ability of test to detect all positive cases or give a positive result when the condition is present.
- Ability of test to distinguish the biomarker in presence of other components usually present (impurities, other products, matrix products...)
- Ability to obtain measurement results directly proportional to the concentration of the substance of the sample tested, within a certain range.
- Ability to obtain the same results for repeated measurements.
- Ability to demonstrate agreement between the value obtained during the test and the reference value or medical true value.
- Ability to obtain measurements made under different conditions.
- Ability of test to provide only slight changes in results when it is submitted to controlled modifications of the conditions of application (room temperature, atmospheric pressure, humidity, reagents, appliances...)

Tests

Sample questions

- What are the analytical specificity and sensitivity of the test?
- What are the steps for sample handling?
- How many samples have been tested?
- What quality control mechanisms have been set up?
- Is the test robust, reproducible?
- How is the test positioned compared to existing methods?
- What are the analysis biases (possible interferences)?

1

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Reimbursement
TRL6 "Market access and reimbursement"

Reimbursement mechanism for the commercialization of your device in France may be the National Commission for the Evaluation of Medical Health Technology (CNEDIMTS), the National Union of Health Insurance Funds (UNAF), the Economic Committee for Health Products (CEPS). Steps should be designed with the main decision maker's perspective in mind and models should be created from the point of view of the main decision maker.

Reimbursement pathways for new reimbursement mechanisms in mind can be slow in the device field and it can take years to achieve optimal coverage. Companion diagnostics do not necessarily have clear reimbursement pathways; they may even include two distinct pathways with different requirements and timelines. Steps and requirements for interim funding that are available in several European countries should be created from the point of view of the main decision maker.

Reimbursement scheme is broken down into 3 main steps (Fig. 1):

1. **Market Access:** This step involves the submission of a dossier to the ANSM (French Healthcare Safety Product Agency) for evaluation. The ANSM ensures that new medical devices are in accordance with European standards and the CE mark.
2. **Reimbursement:** This step involves the submission of a dossier to the CNEDIMTS (National Commission for the Evaluation of Medical Health Technology) for evaluation. The CNEDIMTS will evaluate the clinical value and how it will be reimbursed (of the device into the French market by the ANSM, the CNEDIMTS will evaluate the clinical value and how it will be reimbursed).
3. **Market Access:** This step involves the submission of a dossier to the UNAF (National Union of Health Insurance Funds) for evaluation. The UNAF will evaluate the economic impact of the device and determine the appropriate reimbursement pathway.

Figure 1. Reimbursement scheme is broken down into 3 main steps

2



The « education » module



- **Facilitate the understanding of the different steps of the biomarker development**
- **Allow the different communities to rely on the same language**
- **Accelerate public / private partnerships**

Position a project: the questionnaire



Personnal account:

A secure space

A dynamic questionnaire to position projects

A possibility to ask for support

Position a project: the questionnaire

The dynamic questionnaire to position the research projects

1/ Fill a new form

Formulaire



Bienvenue sur votre compte BMK Tools

Depuis votre compte, remplissez de nouveaux formulaires et modifiez-les à tout moment. Une fois soumis vous pouvez les télécharger aux formats excel ou pdf.

Pour vous préparer à remplir un formulaire, vous pouvez télécharger le formulaire et prendre connaissance des différentes informations dont vous avez besoin. Des fiches explicatives sont également disponibles.

- [Remplir un nouveau formulaire](#)
- [Formulaire téléchargeable](#)
- [Fiches explicatives](#)

Mes formulaires

Date	Titre	État	Action
Aucun formulaire de trouvé.			



BMK TOOLS
Faciliter le passage des Biomarqueurs
du laboratoire vers le patient

Contact

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75019 Paris



Ministère de la Santé



LE SERVICE PUBLIC
DE LA SANTÉ

BMK TOOLS® a été créé pour faciliter la maîtrise et la complémentarité, par choice, des différentes étapes de développement d'un biomarqueur.

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2/ Answer the questions



Confidentialité des données

Pour mémoire, le CVI d'Avisson est une entité publique qui s'engage à recevoir et traiter votre projet de biomarqueur en toute confidentialité.

Saisies des informations

Vous pouvez sélectionner plusieurs réponses lorsque des cases à cocher sont proposées.

1. Découverte du biomarqueur

1.1. Caractérisation du biomarqueur

[Voir la fiche](#)

Indiquez la(es) Aire(s) thérapeutique(s) ciblée(s) et précisez la(es) pathologie(s) visée(s)

- Allergologie
- Dermatologie et cosmétique
- Gynécologie et reproduction
- Hématologie
- Immunologie et inflammation
- Infectiologie
- Maladies cardiovasculaires
- Maladies hépatites
- Maladies métaboliques
- Maladies rares
- Maladies respiratoires
- Neurologie et psychiatrie
- Oncologie
- Ophtalmologie
- Os et cartilage
- Toxicologie
- Transplantation et greffes
- Urologie et néphrologie
- Autres

Indiquez la nature du/des paramètre(s) mesuré(s) :

- Anatomique
- Biochimique

3/ Ask for expertise



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Saisies des informations

Vous pouvez sélectionner plusieurs réponses lorsque des cases à cocher sont proposées.

6. Validation clinique

[Voir la fiche](#)

Note: Les validations préclinique et clinique d'un biomarqueur impliquent la réalisation d'études cliniques sur des cohortes de patients indépendants de celles ayant été utilisées dans les étapes précédentes. De ce fait, cette étape requiert un investissement très important et plusieurs années pour être jugée suffisante. L'implication des Industriels dans la phase de validation clinique est donc indispensable - Industriels pharmaceutiques pour les biomarqueurs compagnons et les Industriels du diagnostic pour les autres types de biomarqueurs.

*Réflexion prospective autour des biomarqueurs, PIPAME, Décembre 2009.

Décrivez le protocole préclinique et/ou clinique défini et les résultats préliminaires obtenus (le cas échéant). Comment envisagez-vous la suite de l'étude (type d'essai, sur quelle population...)?

1 page maximum (3200 caractères max)

Afin de conserver vos réponses,
pensez à bien les enregistrer à chaque fin de question.

[← RETOUR](#)

[ENREGISTRER](#)

[TRANSMETTRE LE FORMULAIRE A BMK TOOLS](#)

[SOLICITER UNE EXPERTISE](#)

[BESOIN D'AIDE](#)



Position a project: the questionnaire



- Bridges between stakeholders
- Share expertise
- Connect the different communities

→ Help projects to move forward !

The support of experts

1

Online projects filing



2

Autonomous use

or

Help

or

Advisory committee



Advisory committee

What ?
Who ?
When ?

→ All the projects
→ Independent of the BMK Tools® team
→ Throughout the year

→ Early projects
→ Questions addressed by the BMK Tools® team
→ Throughout the year

→ Mature projects / specific needs
→ Advisory committee
→ 2 or 3 committees per year

3

Researchers / Industrial meeting

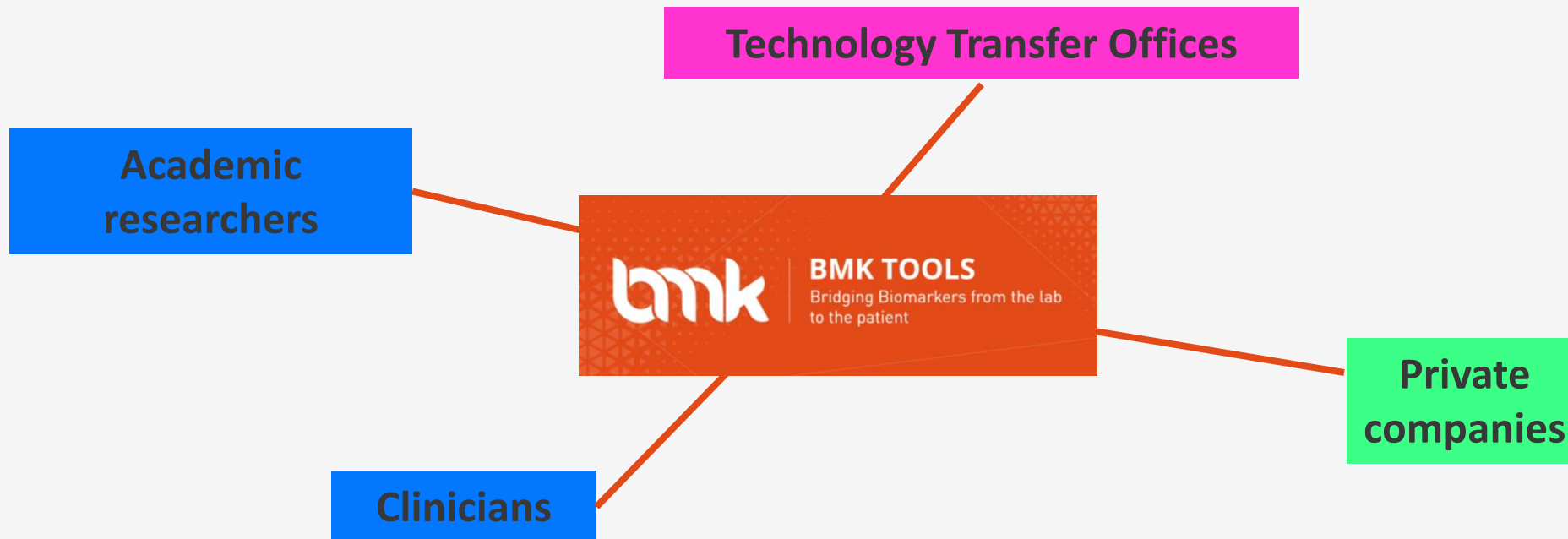


4

Public / Private partnership

- Alain Horvais : Kurma Life Sciences
- Catherine Larue : EATRIS
- Christophe Cans : Sanofi
- Daniel Laune : KYomedINNOV
- Jérôme Sallette : Cerba Healthcare
- John De Vos : CHU Montpellier
- Karine Kaiser : Biomérieux
- Patrick Rossignol : CHU de Nancy
- ...

Connecting the dots...



Connecting the dots by creating a unique place to gather all the key players

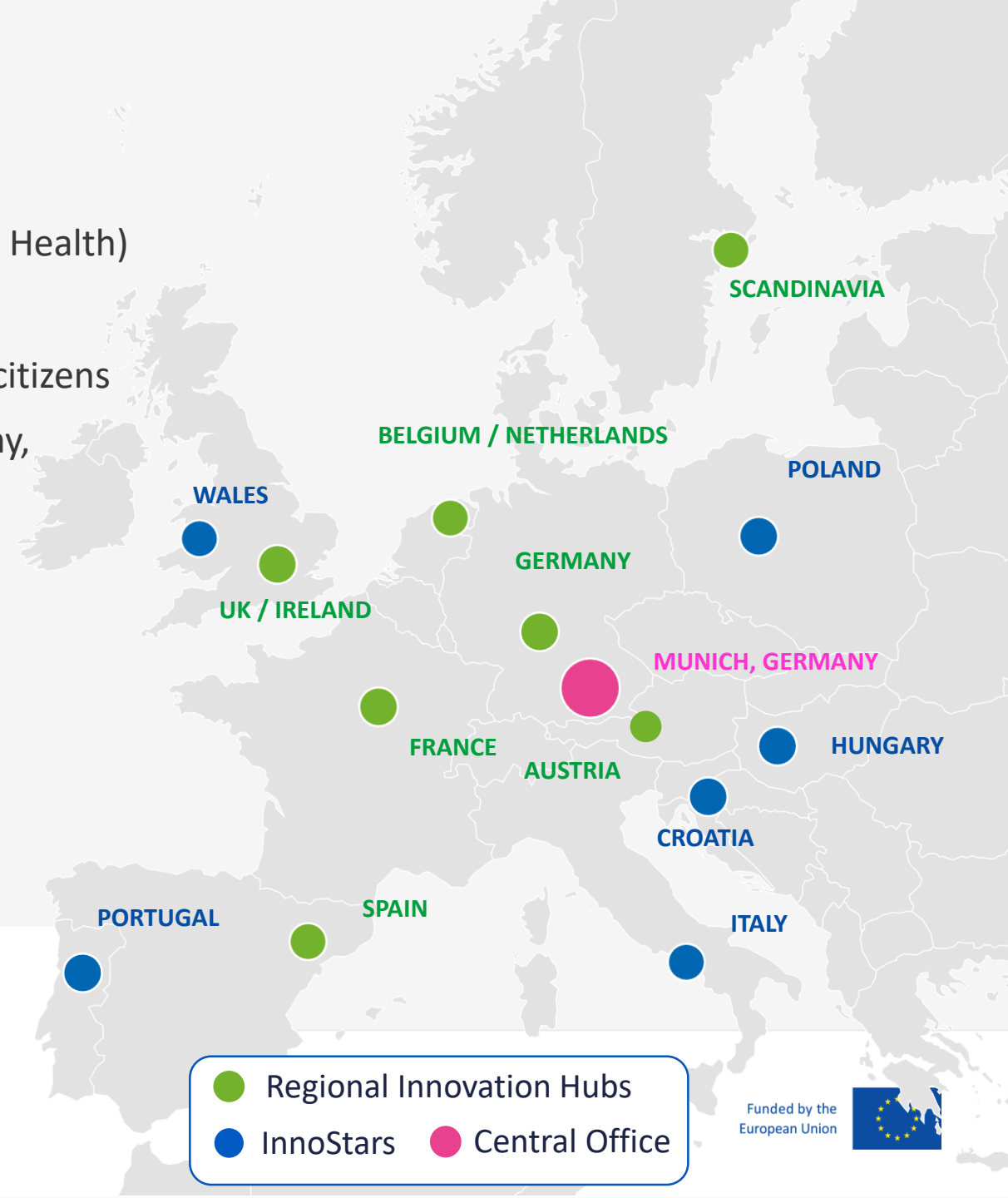
EIT Health involvement

EIT Health (European Institute of Innovation and Technology in Health)

- A network of public and private partners
- Programmes to support students, startups, research teams, citizens
- Develop and implement digital tools (WorkInHealth, Academy, RABBIT...)

Investments in the BMK TOOLS project

- Fundings
- Technological skills
- Partner network
- Experts all over Europe



Bridging biomarkers from **the lab to the patient**



<https://biomarqueurs.aviesan.fr>



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