FRANCE MÉDECINE GÉNOMIQUE 2025

aviesan

French Genomic Medicine Plan 2025

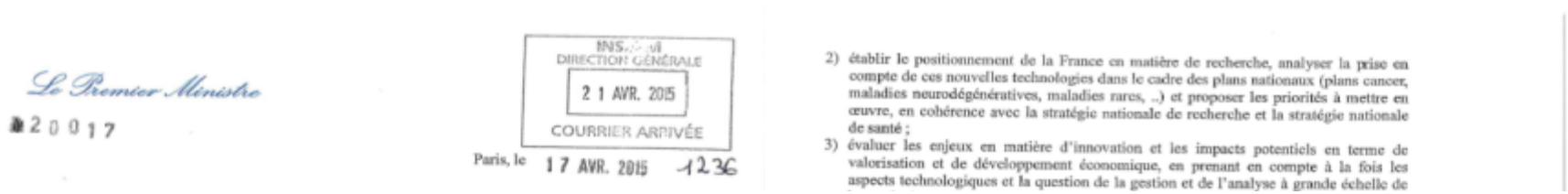
Franck Lethimonnier

May 27, 2019

Berlin

All started with :

Terms of Engagment letter from the Prime Minister



Le Premier Ministre

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DIRECTION GÉNÉRALE
21 AVR. 2015
COURRIER ARRIVÉE

Paris, le 17 AVR. 2015 1236

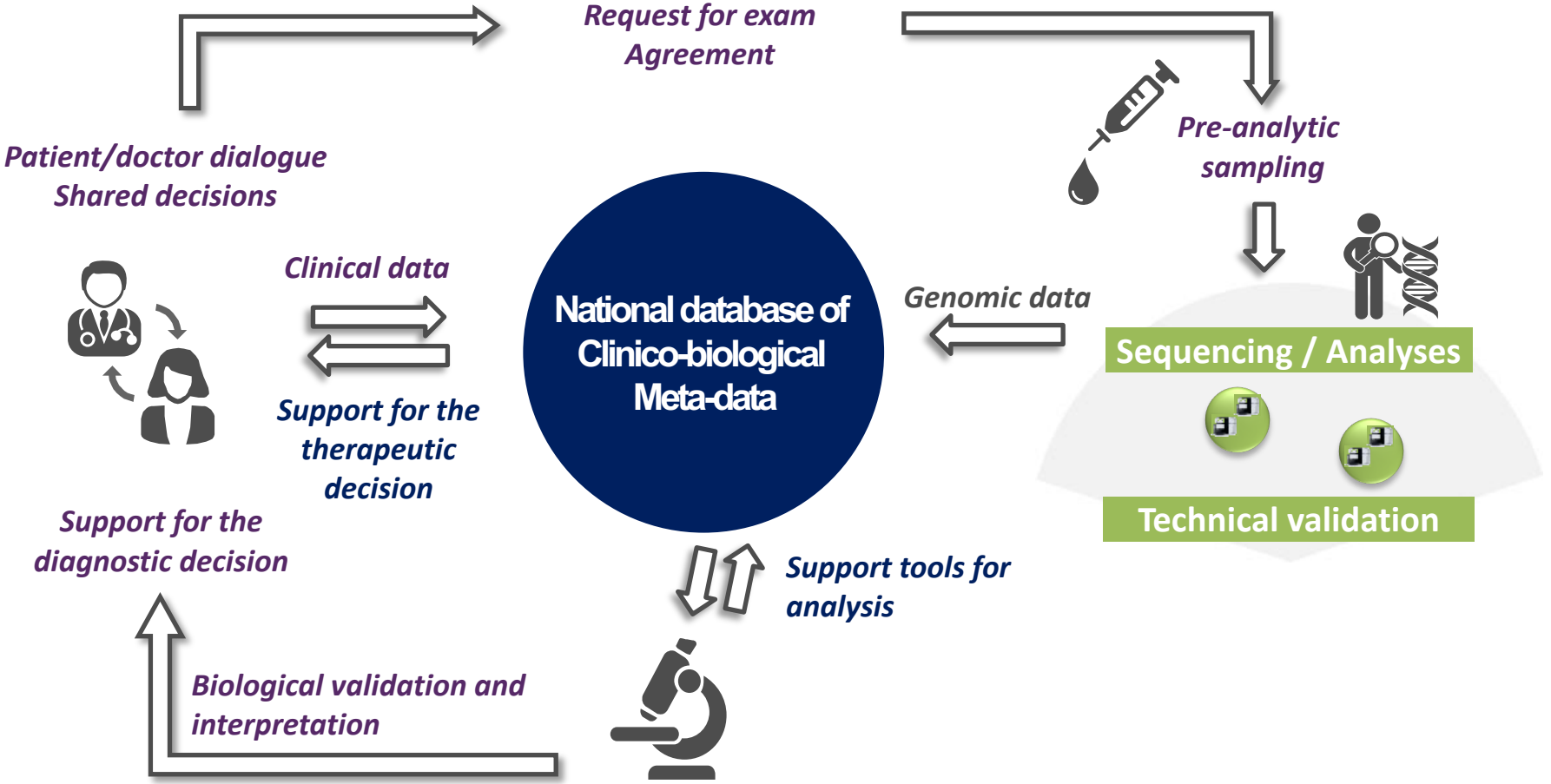
2) établir le positionnement de la France en matière de recherche, analyser la prise en compte de ces nouvelles technologies dans le cadre des plans nationaux (plans cancer, maladies neurodégénératives, maladies rares, ..) et proposer les priorités à mettre en œuvre, en cohérence avec la stratégie nationale de recherche et la stratégie nationale de santé ;
3) évaluer les enjeux en matière d'innovation et les impacts potentiels en terme de valorisation et de développement économique, en prenant en compte à la fois les aspects technologiques et la question de la gestion et de l'analyse à grande échelle de

The Prime Minister entrusted Aviesan with the task of examining the current landscape for incorporating genome sequencing in the context of the healthcare pathway by touching on the following four points in his mission statement:

1. Defining the presence and importance of genomic sequencing in current medical practices as well as expected future developments in the coming 10 years.
2. Evaluating France's positioning in the field of genomic research and its role in current health plans and priorities to be implemented in line with national strategies for health and research
3. Evaluating the issues related to innovation and technology transfer and economic growth, taking into account technological aspects, management of large data sets and ethical implications.
4. Proposing a long-term medico-economic model integrating coverage by medical insurance and the establishment of an industrial sector to support such an initiative.

Ambition of the French initiative

- Integrate sequencing into a generic healthcare pathway
- Develop a national genomic medicine sector



FRANCE MÉDECINE GÉNOMIQUE 2025 aviesan

A CO-CONSTRUCTED 10-YEAR NATIONAL PLAN

I- SET UP THE TOOLS FOR A GENOMIC HEALTHCARE PATHWAY:

Action ① Creation of a network of **12 sequencing platforms** → AURA GEN AUvergne Rhône-Alpes GÉNomique / SeqOIA LA PLATEFORME GÉNOMIQUE DE PARIS RÉGION

Action ② Creation of a **Central Analyser of Data (CAD)** to process and use the volume of data generated

Action ③ Allow the integration and use of patient data in the healthcare pathway

II- ENSURE THESE DEVELOPMENTS IN A SAFE TECHNICAL & ETHICAL FRAMEWORK:

Action ④ Set up a **Center of REFerence, Innovation, eXpertise and transfer** : **CReflX**

Action ⑤ Overcome barriers encountered along the pathway: 4 pilots (cancer, ID, diabetis, population)

Action ⑥ Set up an evaluation and validation system of **new indications for access to genomic diagnosis**

Action ⑦ Foster new skills and personnel capable of of analyzing and interpreting the data

Action ⑧ Integrate **ethical aspects** related to the processing of clinical & genomic data

III - IMPLEMENT MONITORING AND MANAGEMENT TOOLS:

Action ⑨ Mobilize industry stakeholders around the project : create a specialised **industry sector**

Action ⑩ Guide sector activities to address industry issues in the genomic healthcare pathway

Action ⑪ Monitor the developments at the **international level**

Action ⑫ Implement a program dedicated to **health economic** aspects

Action ⑬ Organize information, consultation, and involvement of concerned **stakeholders in society**

Action ⑭ Governance of the Plan

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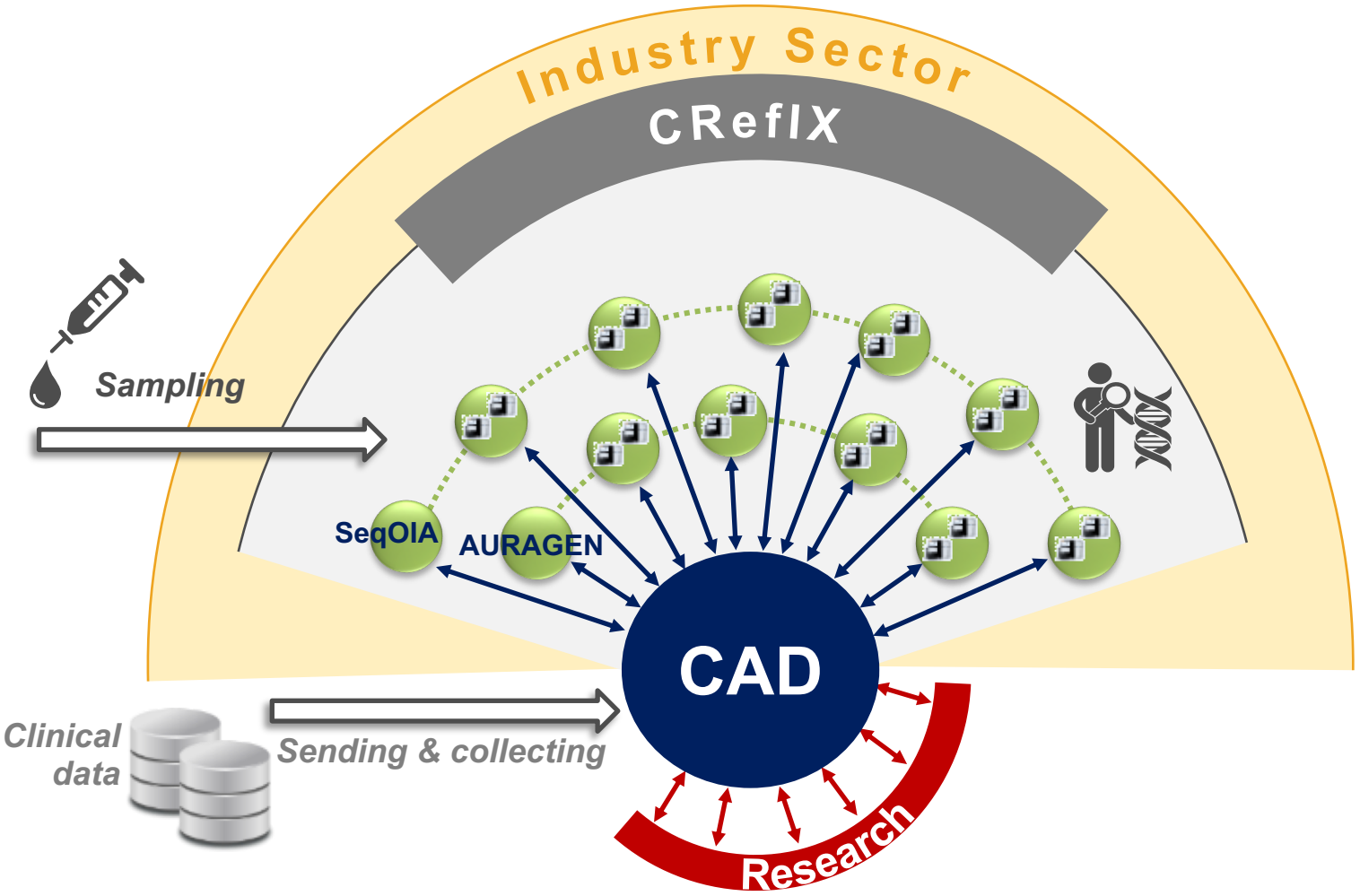
RÉPUBLIQUE FRANÇAISE
Premier ministre

Global vision of the implemented tools

Central Analyzer of Data (CAD)

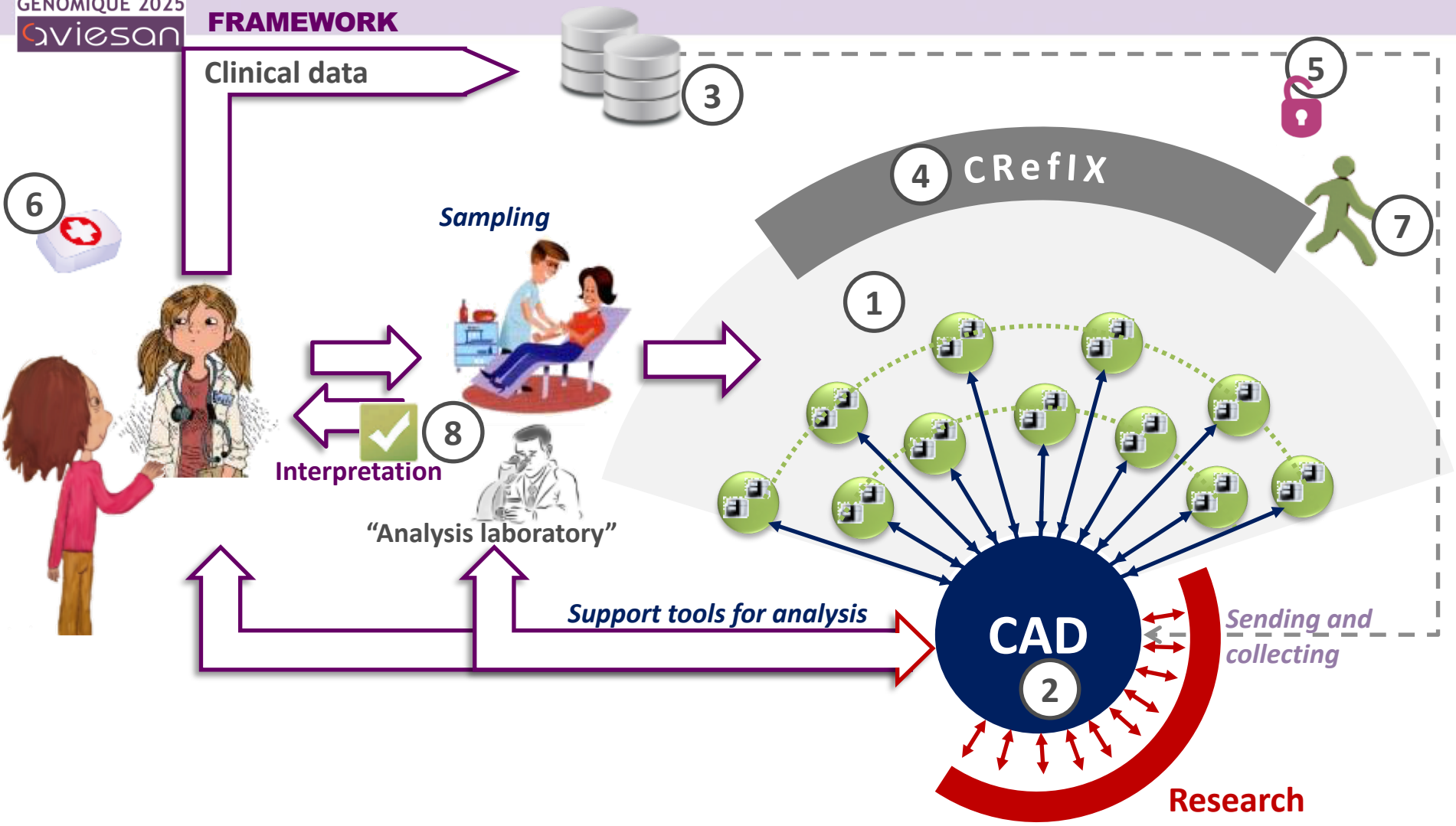
Network of sequencing platforms

Center of reference, innovation, expertise and transfer (CRefiX)



200,000 genomes sequenced per year from 2025

Objective II : Ensure these developments in a safe technical & ethical framework



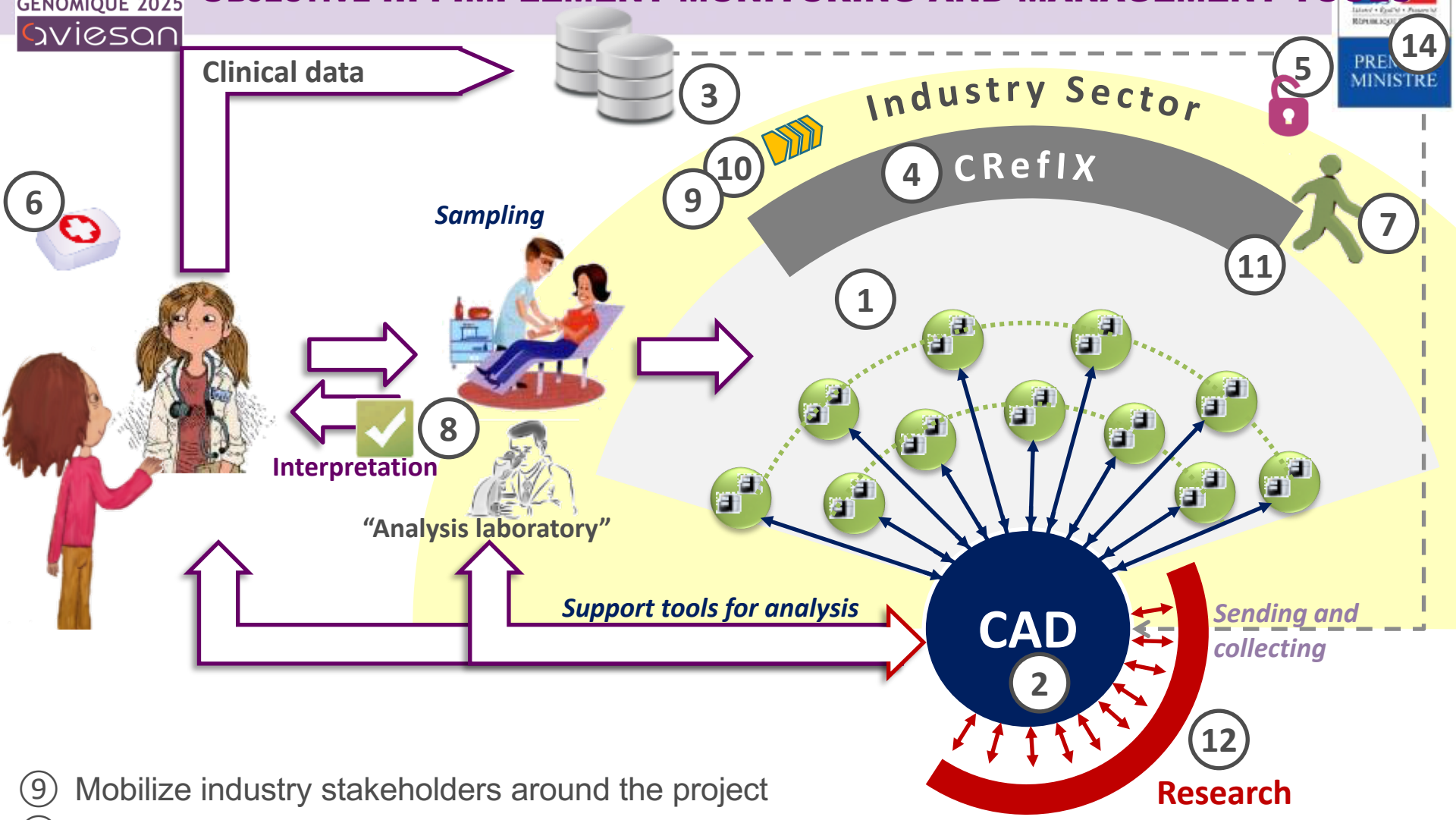
⑤ Overcome technological, clinical and regulatory barriers encountered along the pathway

⑥ Set up an evaluation and validation system of new indications for access to genomic diagnosis

⑦ Foster new skills and personnel capable of meeting the challenge of analyzing and interpreting the data

⑧ Integrate ethical aspects related to the processing of clinical & genomic data

OBJECTIVE III : IMPLEMENT MONITORING AND MANAGEMENT TOOLS



⑨ Mobilize industry stakeholders around the project
⑩ Guide sector activities to address industry issues in the genomic healthcare pathway
⑪ Monitor the developments at the international level
⑫ Implement a program dedicated to health economic aspects
⑬ Organize information, consultation, and involvement of concerned stakeholders
⑭ Governance of the Plan

GOUVERNANCE AND ORGANIZATION

- **A national organization set up since summer 2016.**

Interministerial steering committee

Once or twice a year

Composition : Prime Minister Office, Ministers' Offices (Research, Health, Industry), Directors of the central administrations of the Ministries involved, Director of the National Insurance Fund Salaried Workers (CNAMTS), President of the French National Authority for Health (HAS), President of Aviesan, Patient Associations, Health industries representatives.

Monitoring committee

Once per trimester

Composition : the pilots of each action, the institutions and agencies involved.

Operational committee

Monthly

Composition : the pilots of each action.

- **WG « Platforms »** (Ministry of Health / Inserm)
- **WG « Industry »** (Genopole Evry)
- **WG « Trainning »** CPU
- **WG « CAD »** (Inserm/CEA/Inria)
- **WG « ethics, regulatory aspects and society »** (Ministry of Health / Inserm)
- **WG « Commu-nication »** (Inserm)
- **WG « CRefiX »** (CEA/Inria)
- **WG « Clinical indications »** (High Authority of Health)
- **WG « Medico-economic »** (CNAM)
- **WG «Pilot projects »** (Inserm)
  - WG « Multipli » (cancer)
  - WG « DefiDiag » (Rares diseases)
  - WG « Glucogene » (Diabetes)
  - WG « PopGen » (General population)

- **More than 300 people mobilized in 14 Working Groups (WGs) under Aviesan presidency.**

Progress status of the French initiative

The 14 action mesures are currently active:

- The first 2 sequencing platforms are in the start-up phase
- The first 14 clinical indications have been defined
- A technical scenario has been defined for the CAD
- The CRefiX recruites & accompanies the future clinical preindications in order to overcome several technological obstacles
- Two Pilot projetcs entered the launch phase
- A mid-term report has been delivered concerning the training action mesure
- WG « ethics, regulatory aspects and society » accompanies the sequencing platforms on the patient consents
- The pharmaceutical industry sector is mobilizing to support this initiavie
- Concerted communication actions have been implemented
- Medico-economic assessments have been launch

THE FIRST 2 SEQUENCING PLATFORMS

June 2019

SeqOIA
LA PLATEFORME GÉNOMIQUE DE PARIS RÉGION

AURA GEN
AUvergne **R**hône **A**lpes **GEN**omique

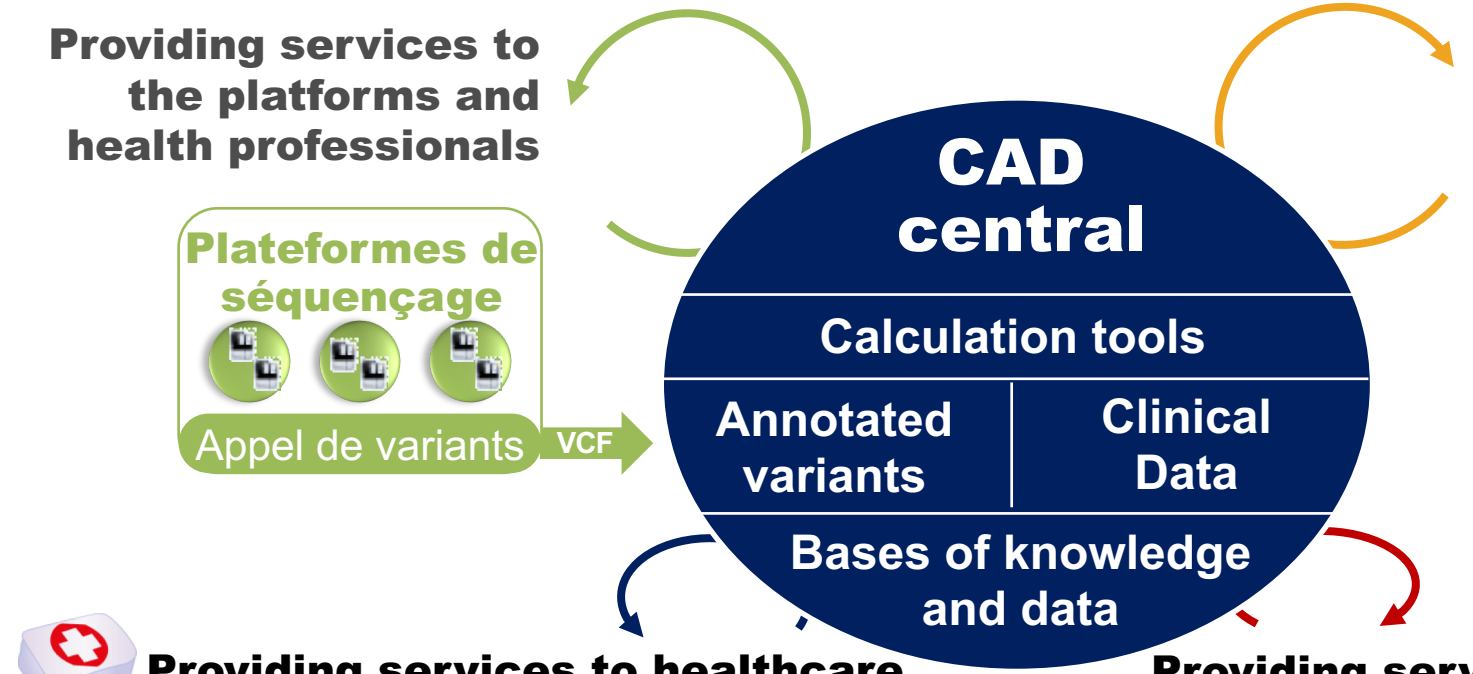
Sampling → Sample transfer → **Sequencing platforms** ← Standardized procedures & processes ← **Reference center (CRefIX)**

Sequencing platforms ↔ Variant Call File (VCF) transfer ↔ **CAD**

FIRST 14 CLINICAL INDICATIONS SELECTED FOR THE SEQUENCING PLATFORMS

indications	Number/year
Constitutional bone diseases	600
Mitochondrial diseases of particular gravity	360
Severe abnormalities of sex differentiation of gonadal and hypothalamic-pituitary origin	60
Primitive ovarian insufficiency	90
Hereditary diseases of the metabolism with atypical biochemical profile	900
Chronic nephropathy of undetermined origin	300
Inflammatory and monogenic autoimmune diseases	150
Familial dilated cardiomyopathy	300
Leukodystrophies	150
Child or teenager bearing a solid malignant tumor, a malignant hemopathy or a brain tumor that fails treatment curators	500
Cancer patients in the context of a particularly severe family history suggestive of predisposition and for whom diagnostic gene panel analysis is normal	50
Patients with "extreme" familial isolated tumor phenotypes and for whom diagnostic gene panel analysis is normal	50
Patients with relapsed acute leukemia, eligible for curative treatment	250
Young patients (< 40) with a solid tumor with treatment failure	2000

CAD : A SERVICE PROVIDER INFRASTRUCTURE



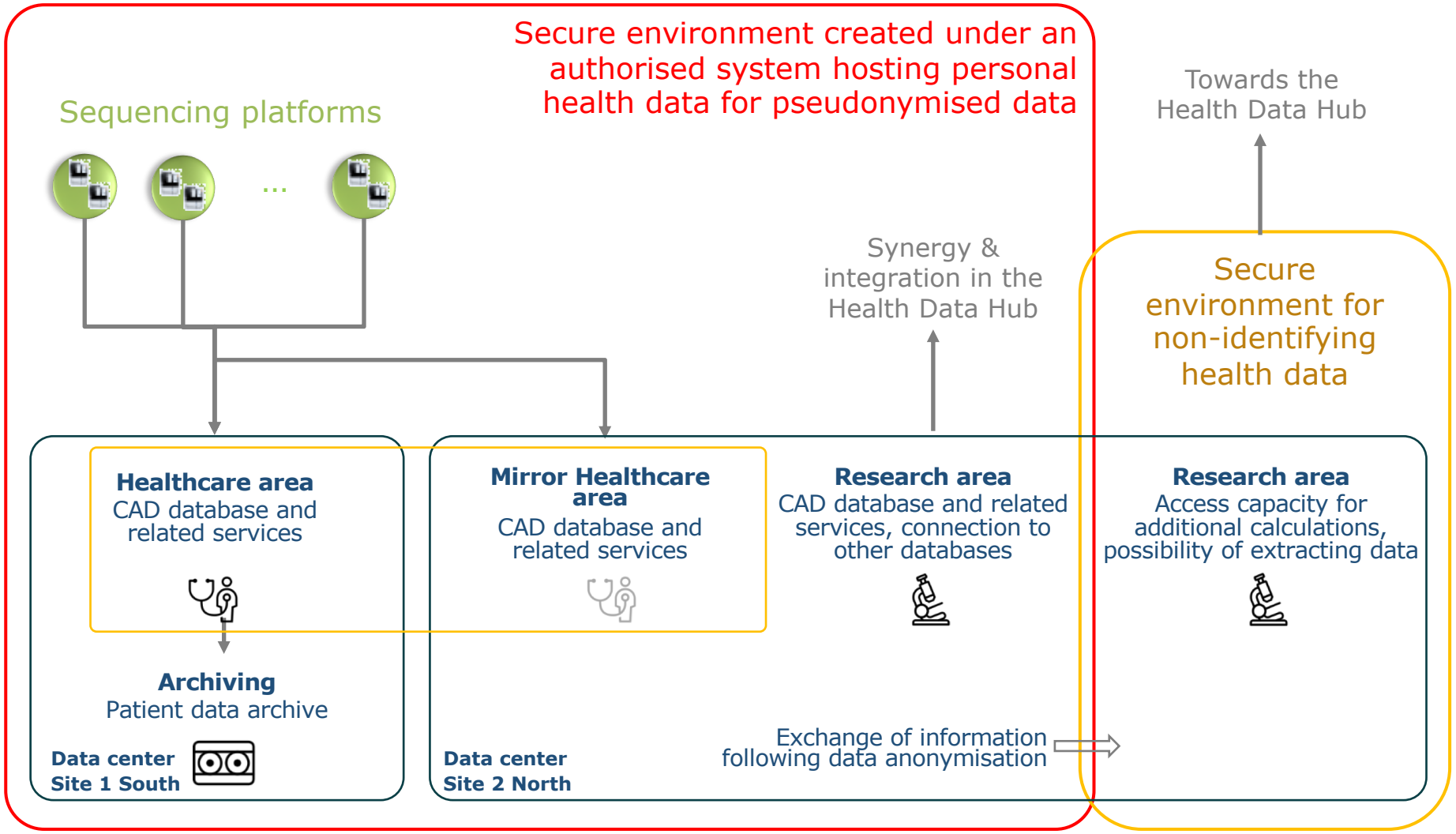
Providing services to healthcare

- Patient Data Access Service
- Access service to databases for the analysis steps
- Access service to analytical tools
- Access service to genome visualization and comparison tools
- Access service to decision support tools
- Data reanalysis service
- Secure web service for interaction between healthcare professionals using the CAD
- Version Management Service

Providing services to Research

- Reception service for research project submissions
- Help desk and project design consultancy
- Access service to data catalogs and datasets
- Service Access to Software Tool Libraries
- Access service to virtual machines
- Re-analysis service for research
- CAD researchers interaction web service
- Monitoring and methodological consulting service

CAD : A SERVICE PROVIDER INFRASTRUCTURE



ROLE OF THE CREFIX

- **C**entre de **R**é**F**érence de la médecine génomique:
  Reference Centre for Genomic Medicine
  - To know the national and international state of the art
  - To establish and disseminate SOPs, standards and recommendations
- **I**nnovation:
  - To implement and/or develop new solutions
  - To respond to problems and predict the future
- e**X**pertise:
  - To develop a network of expertise (expert platform)
  - To serve as a β test site
- Technology **T**ransfer:
  - Dissemination and exploitation of results (publications, patents, spin-offs, licensing…)

4 Clinical Pilot Projects

Rare Disease: DEFIDIAG
Intellectual Disability

- Compare the percentage of causal diagnosis of Intelectual Disability.
- Establish a reference strategy versus a "sequential analysis" of the whole genome (NGS) in trio.

Cancer : MULTIPLI
Sarcoma (Multisarc trial) or metastatic Colorectal Cancers (Acompli trial)

- Evaluate the feasibility and benefits of genomic medicine in cancer
- Evaluate the feasibility of genomic sequencing (NGS).
- To evaluate whether NGS-guided treatments improve patient survival.

Common disease: GLUCOGENE
Atypical forms of Diabetes

- Evaluate the contribution of the sequencing of the whole genome and of a coordinated multidisciplinary patient management on the diagnosis and management of atypical forms of diabetes.

General Population: POPGEN

- To meet the needs of "filtering" the exomes and genomes of patients to eliminate common genetic variants in the general population.
- Provide a reference on the frequencies of genetic variants in a panel of individuals representative of the population.

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Clinical Pilot Projects

Four pilot projects have been initiated

Methodology and statistics | **Regulatory aspects** | **Initiation of clinical study**

Goal
Investigators identification
Inclusion criteria
WES / WGS Sequencing
Number of patients to be included.
Record of clinical data modalities
Data transfers (in & out) and analysis
Biological specifications : samples taking, labelling and transfer
Clinical reports modalities
Information modalities and informed consent
Quality (Study monitoring, storage, archiving, anonymization and safeguarding data
Regulatory file submission

Soft-tissue sarcomas and advanced colorectal cancer	**Multipli => Cancer**
Intellectual disability	**DefiDiag => Rare disease**
Atypical type 2 Diabetes	**Glucogene => Commun disease**
	PopGen => General population

ETHICS, REGULATORY ASPECTS AND SOCIETY

Patient information and consent

- **Methodology**
  - Hearing of national and international stakeholders
  - Collecting different clinical care/research frameworks (information and consent, including incidental findings)
  - Exchanges/confrontations with pilot projects
- **Working group:** Researchers (included human and social sciences), Ministries (Health, Justice), Patient/user associations, Different institutional levels (Health insurance, Health Agencies), Professional and scientific genetic societies

Data protection : storage and processing modalities of personal data resulting from sequencing

Human and Social Sciences researches

THANK YOU FOR YOUR ATTENTION