Clinical Development of Cell and Gene Therapy (CAGT) Products in Japan

Accelerated approval system for regenerative medical products

- The MHLW* introduced an updated approval system that rewards developers with **accelerated approvals to encourage clinical development of CAGT products in Japan.**
  * MHLW : Ministry of Health, Labor and Welfare
- Previously, clinical trials that evaluated the efficacy and safety were required for approval but **under the new system sponsors can obtain approval if efficacy is predicted and safety is demonstrated.**

Conventional regulatory approval process

Faster patient access to new and improved therapies

Regulatory system that facilitates early practical application of cellular or tissue-based products

Cell, gene and tissue therapies which treat severe diseases are typically eligible to this system.

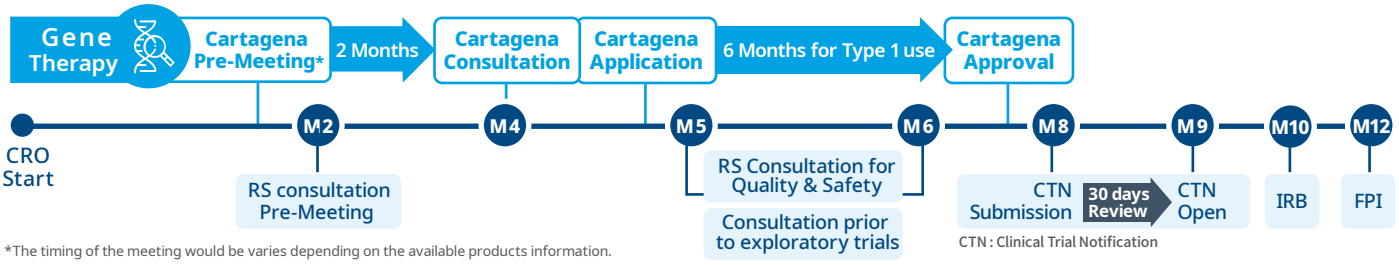
Path to FPI

Required Meetings and Rough Timelines Leading to Clinical Development

Important points to consider for CAGT development in Japan

The PMDA requires sponsors to conduct the following consultations:

1. Regulatory Science (RS) Consultation for Quality (e.g. Process, Specification, Testing method, Biological materials standard)
2. RS Consultation for Safety (e.g. Tumorigenicity test)
3. Cartagena Consultation (e.g. Satisfaction and appropriateness of submission documents for gene therapy)
4. Consultation prior to starting exploratory clinical trials (e.g. Protocol design, Clinical study package)



*The timing of the meeting would be varies depending on the available products information.

CTN : Clinical Trial Notification

IQVIA, the leading CRO in Japan

Supporting CAGT products from pre-clinical to post marketing

Regulatory Affairs team with the **capability** and experience to support **specific Japanese regulatory requirements** for **CAGT** products.

IQVIA' s **Core Data coverage** supports identifying **limited patient populations** for any CAGT products targeting rare diseases.

Global footprint provides sponsors the option to **include Japan** as part of a **Multi-Regional Development Plan for CAGT** investigational products.

IQVIA's end-to-end support for CAGT products in Japan

CONSULTING	CLINICAL		NDA (New Drug Application)		POST- MARKETING
GCTP (Good Gene, Cellular, and Tissue-based Products Manufacturing Practic	Regulatory	Data management	CTD (Common Technical Document	APPROVAL	Post-Marketing Surveillance
Gap analysis	Monitoring	Biostatistics	Post-Marketing Surveillance		Medical Science Liaison
Development strategy	Investigational product management	Audit			
Regulatory strategy	Medical monitoring	Medical writing	Conformity audit		Sales (MR)
Pre-IND (Pre- Investigation New Drug	Safety	ICCC (In-Country Clinical Caretaker			

ICCC:

In-Country Caretaker for Clinical trials. This is mandatory for biopharmaceutical companies based outside of Japan who are intending to perform clinical studies in Japan. The ICCC is the representative of the company who sponsors the clinical trial and ensures that procedures are followed as per regulations. IQVIA has a perfect **compliance record with no major observations** while acting as the ICCC on behalf of our partners in Japan.

SPONSOR Outside Japan

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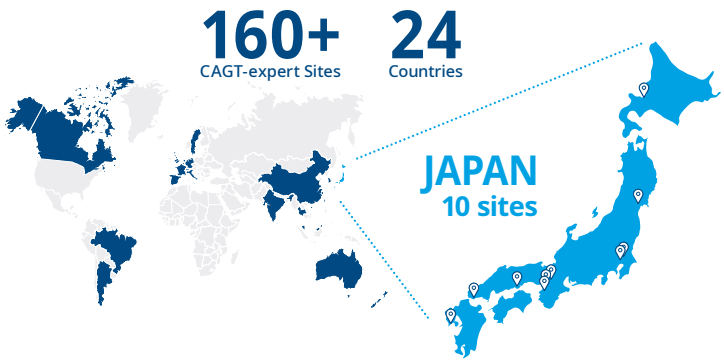
IQVIA ICCC Inside Japan

SITES	IMPORT	PMDA*6
-Contracting	-Management of importation	-CTN preparation
-IRB*1 documents	-Compliance with GMP*4 & GCP*5	-CTN submission
-ADR*2 reporting	-Storage	-Follow-up meetings
-IMP*3 & Lab kit delivery	-Distribution	-ADR reporting

*1 IRB : Institutional Review Board
*2 ADR : Adverse Drug Reactions
*3 IMP : Investigational Medicinal Product
*4 GMP : Good Manufacturing Practice
*5 GCP : Good Clinical Practice
*6 PMDA : Pharmaceuticals and Medical Devices Agency

Dedicated Global CAGT Site Network



- IQVIA's multi-disciplinary **CAGT expert sites** can be leveraged for many types of studies
- Strong relationship with KOLs in the CAGT Site Network to provide **real-time updates** and **solutions for potential challenges** based on their **feedback and insights**
- Active local CAGT networking activities
  - **CAR-T trials focused Round Table with KOLs in Japan CAGT Site Network** on December 21, 2022
  - Topic : Efficient operation of CAR-T trials

Sharing intelligence and collaborating with our other global site networks

Prime & Partner Site Network

Early Phase Oncology Site Network

Pediatric & Rare Disease Site Network

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