ENSEMBLExJ Project

BIO2026 in San Diego

ENSEMBLE

Empowered National Synergy
for Medical Biotech Landscape Expansion across Japan

Head Office: National Cancer Center Japan

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Deputy Director, Research Institute /

Deputy Director, Strategic Planning Bureau

National Cancer Center Japan

Real Value to Come to Japan Market

I know Japan well because I used to work for a Japanese Pharma!

(20 years ago …)

JAPAN is

- Everything is **complicated**!
- Regulation is completely **different** from FDA/EMA.
- Can you conduct global clinical trials? I don't think so.
- Maybe some sites can do it, but **slow and extremely expensive**, I heard.
- Very **limited market**.
- **Low drug price**,
- **… maybe.**

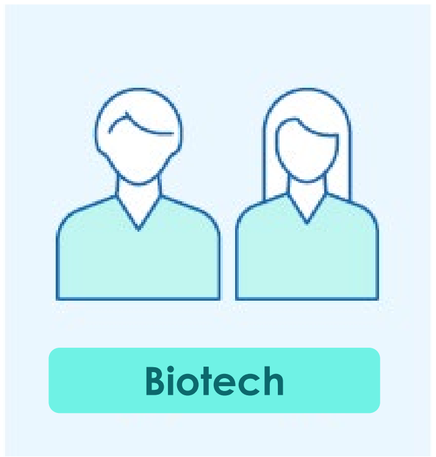
That's no longer correct!

Things have changed.

Be updated and don't miss a business opportunity!

Missing Opportunities Due to Lack of Awareness Is a Loss

Do you have enough resource to identify the information you need for a strategic consideration?



KOL pool	**Development Strategy** (e.g. appropriate path/timing to involve JP)
Medical advisor pool for PI mgt	**Development Operation** (e.g. clinical trial excellence)
Commercial/ Marketing	**Business Opportunity** (e.g. market size, unmet medical needs)
Regulatory/ Market access	**Regulatory Excellence** (e.g. fast track strategy)
Company matching	**Business Operation** (e.g. Post-launch activity in Japan)

NCCJ National Cancer Center Japan

MHLW-funded One-Stop Service Platform for Global Biotech Companies

“ENSEMBLE cross J” serves like your Japan team

ENSEMBLE
Empowered National Synergy
for Medical Biotech Landscape Expansion across Japan

- All Japan Initiative
- Funded by Ministry of Health, Labour and Welfare (MHLW)
- Supports global biotech companies without a local presence in Japan in entering the Japanese market.
- Managed by 6 National Centers covering all disease areas (Head office: National Cancer Center Japan)
- Collaborated with PMDA, a regulatory authority in Japan
- Provides Expert insights for your go/no go decision on an entering Japan market
- Manages matching with appropriate your partner from our partner consortium (Clinical Sites (KOLs), CRO, Pharma, Venture Capital)
- Free of charge for any service by ENSEMBLExJ

NCCJ
National Cancer Center Japan

All Japan platform with Government-Academia-Industry Partnerships

ENSEMBLE×J

MHLW
(owner)

Biotech

ENSEMBLE×J
w/ 6 National Centers

PMDA
Tight Engagement

KOL pool — **Development Strategy** (e.g. appropriate path/timing to involve JP)

Medical advisor pool for PI mgt — **Development Operation** (e.g. clinical trial excellence)

Commercial/ Marketing — **Business Opportunity** (e.g. market size, unmet medical needs)

Regulatory/ Market access — **Regulatory Excellence** (e.g. fast track strategy)

Company matching — **Business Operation** (e.g. Post-launch activity in Japan)

Partner Clinical Sites

CRO/ Pharma/ VC Partner Consortium

NCCJ
National Cancer Center Japan

ENSEMBLExJ Operational Scheme: Stage 1 Screening Phase

Biotech

(1) Registration & Request Form

ENSEMBLE×J

ExJ Secretariat @ NCC

ExJ-ONC Project Lead

(2) Assignment of ExJ-ONC PM & Expert Board members

Early Launch of Oncology

ExJ-ONC @ NCC

- ExJ-Ped @ NCCHD
- ExJ-CCV @ NCVC
- ExJ-Neuro @ NCNP
- ExJ-Ger @ NCGG
- ExJ-Inf @ JIHS

ExJ-ONC Project Manager

(3) The 1st Consultation with non-confidential information

(4) Concluding the CDA (Signer: **EXJ Secretariat**)

(5) Receiving the Project Information Sheet

Project Info Sheet

- MoA
- Indication
- Target population
- Modality
- …

(6) Hearing the project details

(7) Creating the Hearing Report

Hearing Report

(8) Organizing the Expert Board

Expert Board Evaluation

- UMNs Matching Level
- Clinical Needs
- Clinical Dev Success
- Regulatory Success
- Trial Design
- Japan Market Situation
- Business Opportunity

Expert Report

(9) Go/No Go Decision

➡ **Go to Consulting Phase**

➡ No Go for Japan

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ENSEMBLExJ Operational Scheme: Stage 2 Consulting Phase

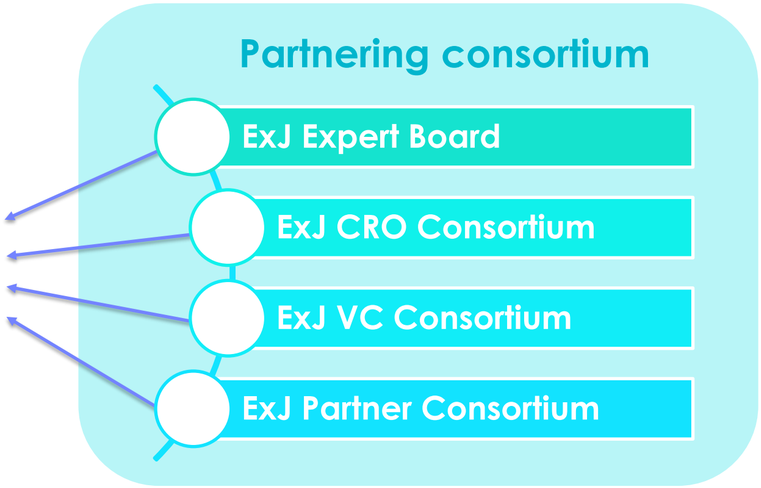
(10) Detailed discussion

Biotech

Expert Board

ExJ Secretariat @ NCC

CDA with ExJ



Joining the consortium is free of charge.

(11) The ExJ can identify partners to that fulfill the specified request

(12) The Global Biotech can pick up the companies and provides feedback to the ExJ

(13) The ExJ can make a match between Global Biotech and the Partners

Close the case and continue on-demand support

Why Developing in Japan Makes Strategic Sense?
- Market Share

Japan is Still Growing Market

Forecast of the Oncology Drug Market (B$)

	2023	2029	2034	CAGR
Japan	15-19	21-27	26-34	4-6%
US	80-90	120-140	160-190	6-7.5%
Germany	8-10	11-14	14-18	4.5-6%
UK	4-5	6-7	8-10	5-6.5%

CAGR: Compound Annual Growth Rate
Source: IQVIA, GlobalData, JPMA data

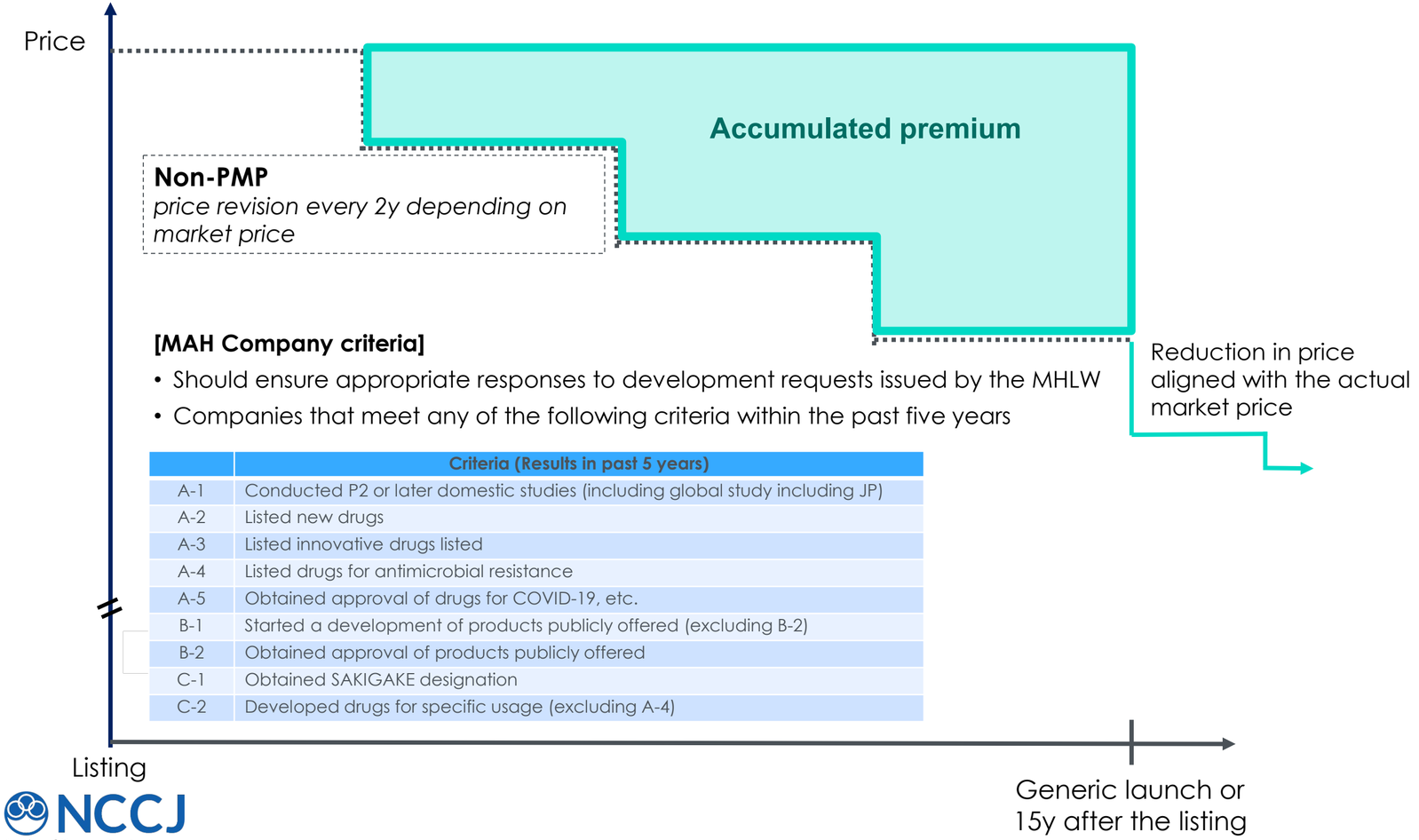
‘Earlier is Better’ Advantages to Involve Japan

Ten things you should know about entering Japanese Market

1. **Price Maintenance Premium (PMP)**
2. **Regulatory Excellence (Speed and Expand)**
3. Fast Track Regulatory Path
4. **Earlier is Better to involve Japan (1/4): ONC Clinical Strategy**
5. **Earlier is Better to involve Japan (2/4): Non-ONC Clinical Strategy**
6. Earlier is Better to involve Japan (3/4): Opt-Out Strategy
7. Earlier is Better to involve Japan (4/4): **Patent Term Extension Strategy**
8. **Real Data of Clinical Trial Capability**
9. CRO’s service as your clinical trial partner
10. Partnering opportunity in Japan

Ten things you should know:
1. Price Maintenance Premium (PMP)

A full understanding requires looking beyond drug price revisions to include Japan's incentive system for promoting new drug development



[MAH Company criteria]

- Should ensure appropriate responses to development requests issued by the MHLW
- Companies that meet any of the following criteria within the past five years

	Criteria (Results in past 5 years)
A-1	Conducted P2 or later domestic studies (including global study including JP)
A-2	Listed new drugs
A-3	Listed innovative drugs listed
A-4	Listed drugs for antimicrobial resistance
A-5	Obtained approval of drugs for COVID-19, etc.
B-1	Started a development of products publicly offered (excluding B-2)
B-2	Obtained approval of products publicly offered
C-1	Obtained SAKIGAKE designation
C-2	Developed drugs for specific usage (excluding A-4)

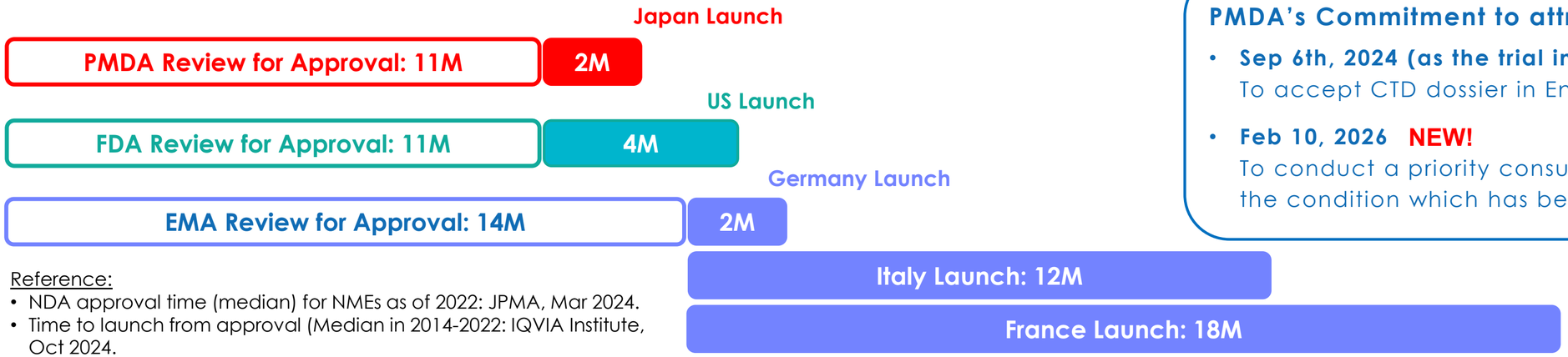
NME criteria

To be evaluated based on the innovativeness and usefulness, referring to the following.

1. Orphan drugs
2. Products publicly offered for development
3. Drugs granted premium pricing for innovativeness and usefulness, with adjustments based on operating profit margin (excluding drugs listed long after the first-in-market reference product was approved)
4. Drugs having a new MOA (meeting the innovativeness criteria)
5. Drugs approved within 3y of the first-in-class or reference product and ranked among the first three approval
6. Breakthrough drugs
7. Specific usage drugs
8. SAKIGAKE drugs
9. Drugs for pediatric indication
10. Drugs for antimicrobial resistance
11. Drugs listed promptly after the approval of the reference drug

Ten things you should know:
2. Regulatory Excellence

PMDA, Japan health authority, is one of the fastest countries from the review process to the actual launch.



Reference:
- NDA approval time (median) for NMEs as of 2022: JPMA, Mar 2024.
- Time to launch from approval (Median in 2014-2022: IQVIA Institute, Oct 2024.

NOTE

PMDA's Commitment to attract global Biotech

- **Sep 6th, 2024 (as the trial implementation)**
  To accept CTD dossier in English
- **Feb 10, 2026** **NEW!**
  To conduct a priority consultation for projects with fulfill the condition which has been consulted by ENSEMBLExJ

PMDA Approval encourages your access to Asian market with regulatory advantages

If JPMDA has approved a drug;

- **Philippine FDA:** Review time **[180d → 45d]**. If 2 or more referenced countries have approved, the time can be reduced to **[30d]**.
- **Indonesia NADFC:** Review time **[300d → 120d]** by providing PMDA review report.
- **Taiwan FDA:** Review time **[360d → 180]** if two out of ICH regions (US/EU/JPN) approvals or 120d with all approval.
- **Malasia, India, Australia and so on.**

Ten things you should know:
3. Fast Track Regulatory Path

SAKIGAKE Designation System

Promoting R&D in Japan aiming at early practical application for innovative pharmaceutical products, medical devices, and regenerative medicines.

[Criteria]

01 Innovative products

02 Life-threatening or no radical treatment

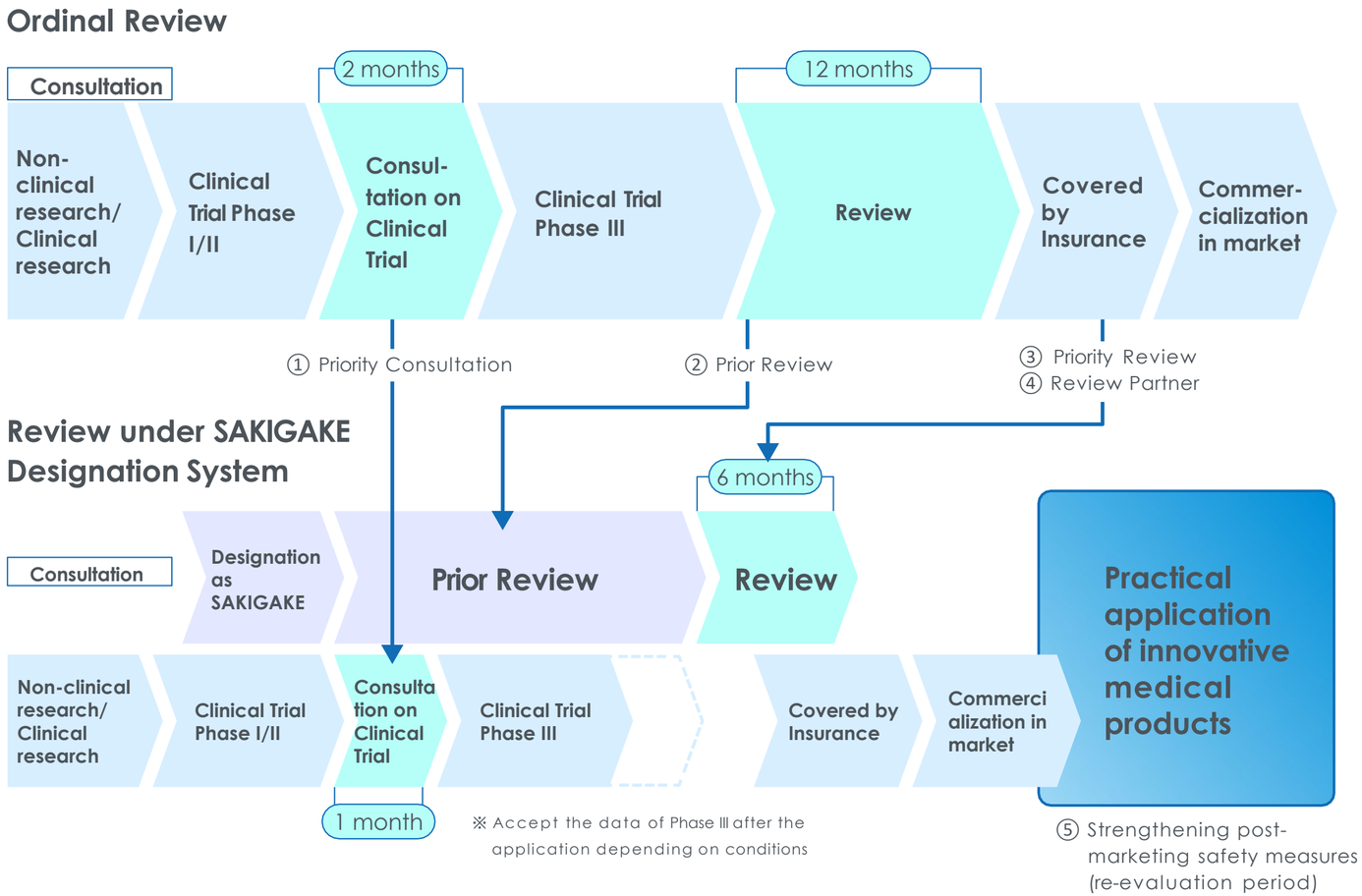
03 Prominent efficacy

04 First NDA in the world
(Global simultaneous NDA should be fine)

- Product for which FIH study was conducted in Japan

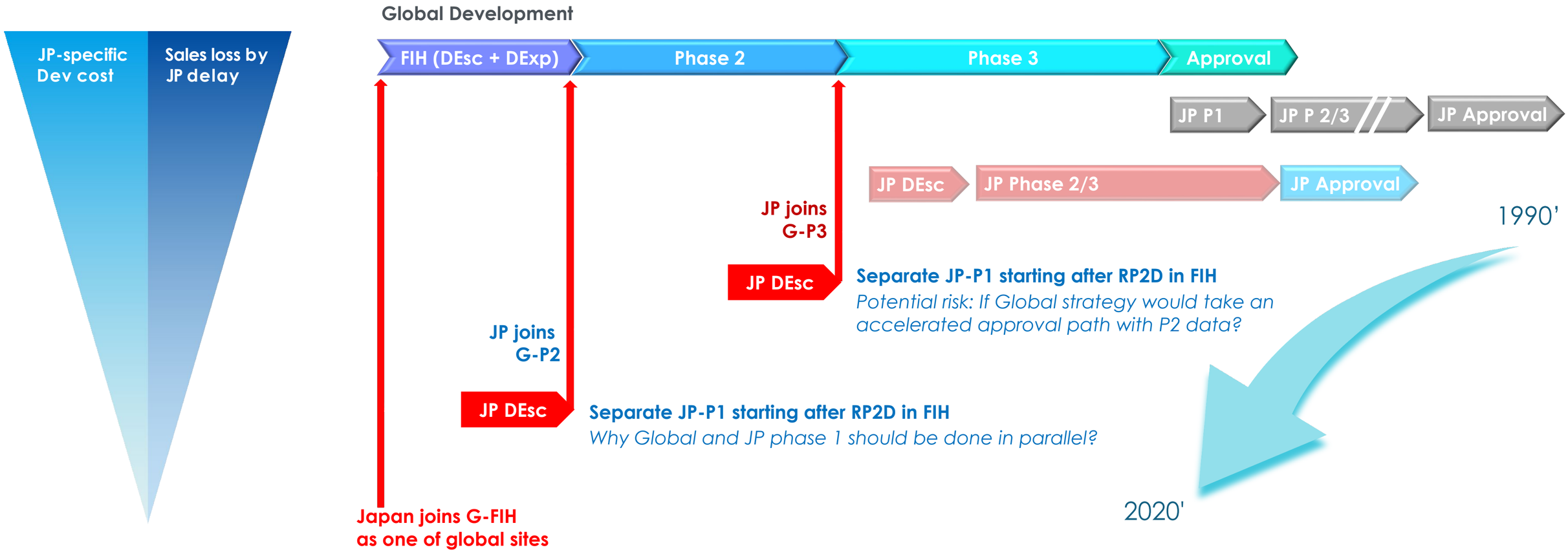
and/or

- Product for which POC study was conducted in Japan



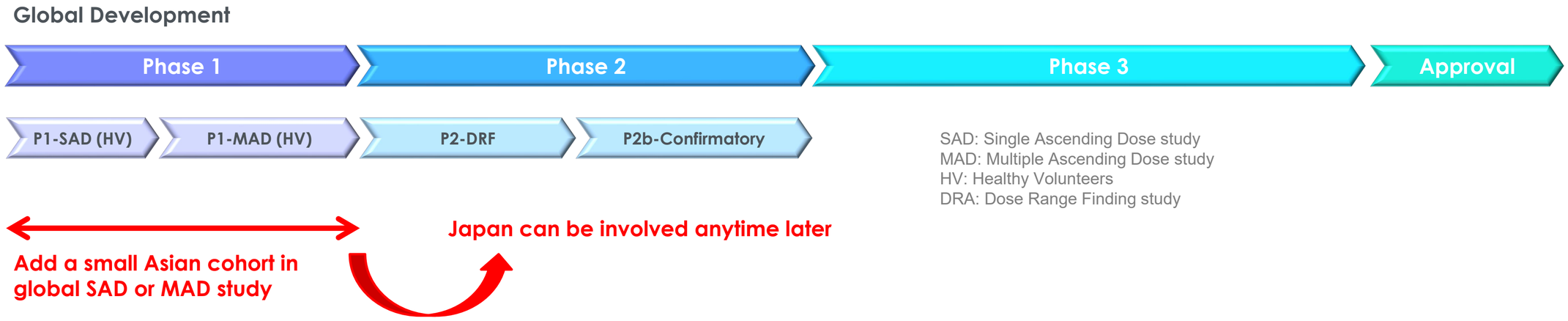
Ten things you should know:
4. Earlier is Better to involve Japan (1/4): ONC

Why have many Mega Pharma shifted the timing to involve Japan earlier (Oncology)



Ten things you should know:
5. Earlier is Better to involve Japan (2/4): Non-ONC

Why have many Mega Pharma shifted the timing to involve Japan earlier (Non-Oncology: e.g. the most cost/speed effective option)

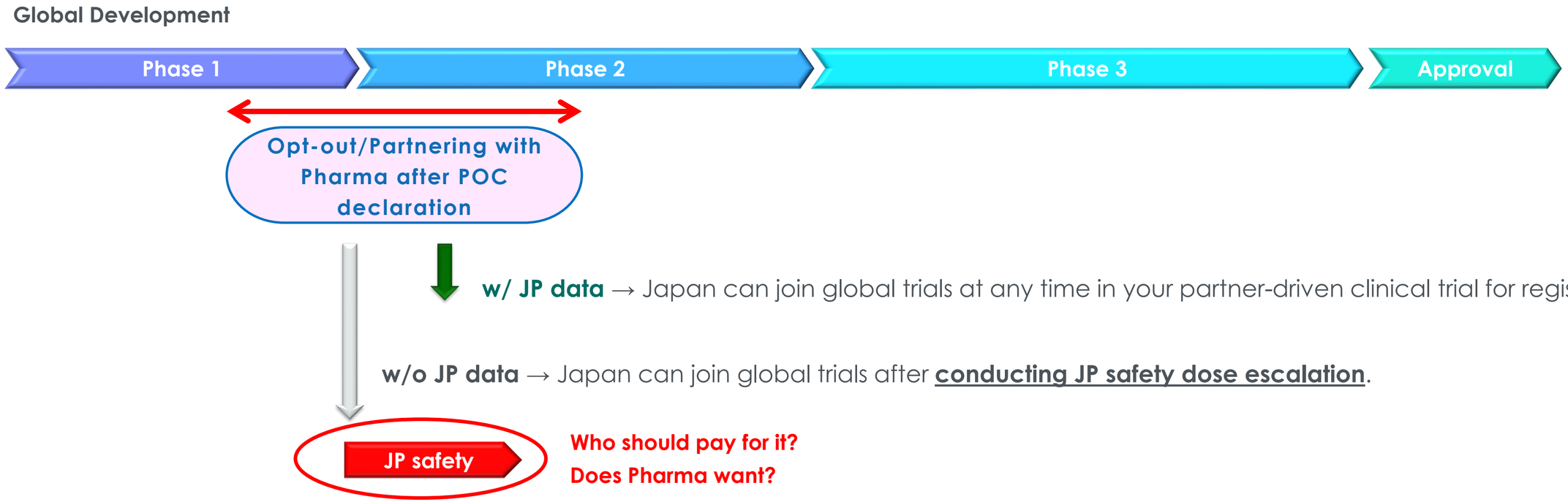


- Not mandatory to open the site in Japan/Asia, since Asian/Japanese population (Healthy Volunteers) can be enrolled at global Phase 1 sites, for example, Australia and the West Coast in US.
- Early confirmation whether ethnic differences are expected in safety and PK profiles and need to be taken into account in future development strategy

Ten things you should know:

6. Earlier is Better to involve Japan (3/4): Opt-Out

If your business model focuses the partnering/Opt-out after Clinical POC declaration

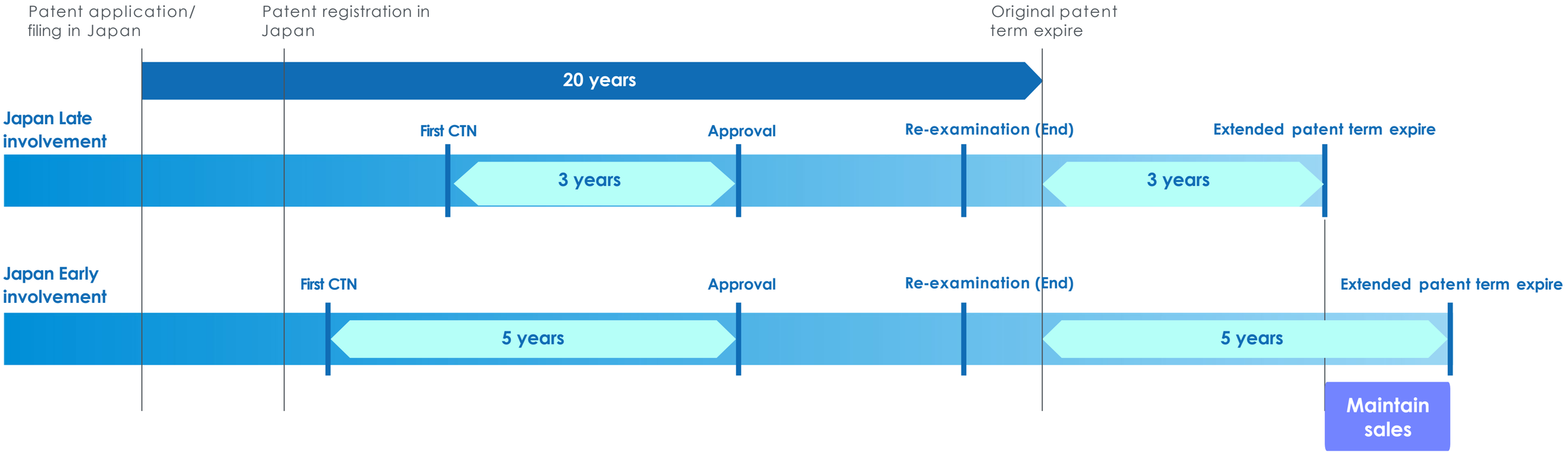


NOTE: Since 2023, PMDA has stated that JP P1 dose escalation study can be skipped, **if you can ensure Japanese safety** based on scientific rationale, considering ethnic differences in PK and MOA with available data.

Ten things you should know:
7. Earlier is Better to involve Japan (4/4): Patent

New Molecular Entity substance Patent Term Extension in Japan

- The period of a patent right is 20 years from the date of filing of the patent application.
- The period may be extended up to five years for pharmaceutical products and agricultural chemicals.
- The period from a patent registration **or first Clinical Trial Notification (CTN)**, whichever comes later, to approval should be determined as "the period during which the patented invention was unable to be worked". It would be added to the original patent duration.



Ten things you should know:
8. Real Data of Clinical Trial Capability

Speed & Cost in NCC Hospital's experience (NCC Japan's data for an example)

Clinical Development (FY2024)

Industry Sponsored Trials	982
Global Clinical Trials	821
First-in-Human Trials	227
Investigator Initiated Trials	103

Rapid preparation(site open)

- Ave. 30.7 days in FY2022
- From IRB submission (& review) to IRB: **25.8 days**
- From IRB to contract: **4.9 days**

Low price per case

- FIH, iv agent (ADC), q3wks, full-pk sampling, serial tumor biopsy, 4 cycles: **18,000 USD/case**
- FIH, oral agent, 3wks/cycle, full-pk sampling, serial tumor biopsy, 4 cycles: **21,500 USD/case**

You do not need to afford any hospitalization fee

- Hospitalization fee is paid by patient in Japan
- From 70 to 90% of hospitalization fee is covered by health insurance in Japan

Quality in NCC Hospital East's experience

- NCCHE has received FDA's on-site audit more than 10 times
- Then NCCHE received an endorsement from FDA to ensure their quality is likely to rank among **the top 5% globally!**
- The data will be generated under the global standard lab certification, e.g. **CAP and CLIA.**

NCCJ National Cancer Center Japan

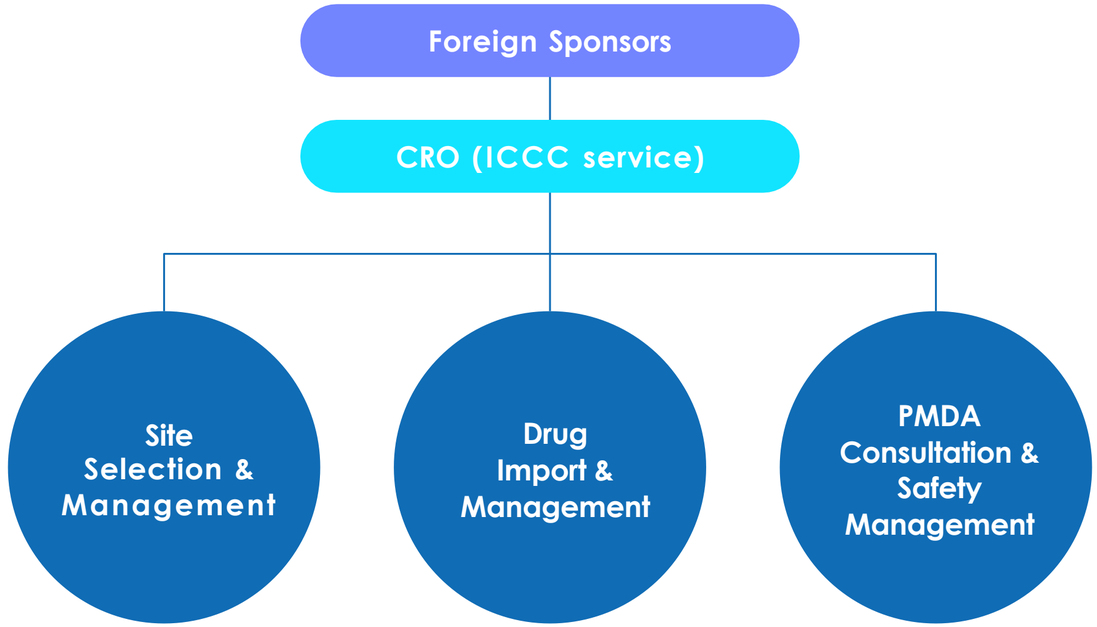
Ten things you should know:
9. CRO’s service as your clinical trial partner

In-Country Clinical Caretaker (ICCC)

- There is a regulatory system for companies outside Japan (foreign sponsors) to promote drug development in Japan through outsourcing the operations of clinical trials to Contract Research Organizations (CROs).
- The following is described in the Ministerial Ordinance on Good Clinical Practice for Drugs (J-GCP: Attachment 1-1).

Clinical Trial In-Country Representative

In order to take the necessary measures to prevent the occurrence or spread of health hazards due to drugs used in the clinical trial, a person who intends to sponsor a clinical trial and resides outside Japan shall appoint a person eligible for sponsoring the clinical trial on behalf of the person who intends to sponsor a clinical trial from among persons residing in Japan (including the head of a Japanese business office of a foreign company) to have him or her (hereinafter referred to as “Clinical Trial In-Country Representative*”) conduct the procedures for sponsoring the clinical trial (J-GCP Article 15).

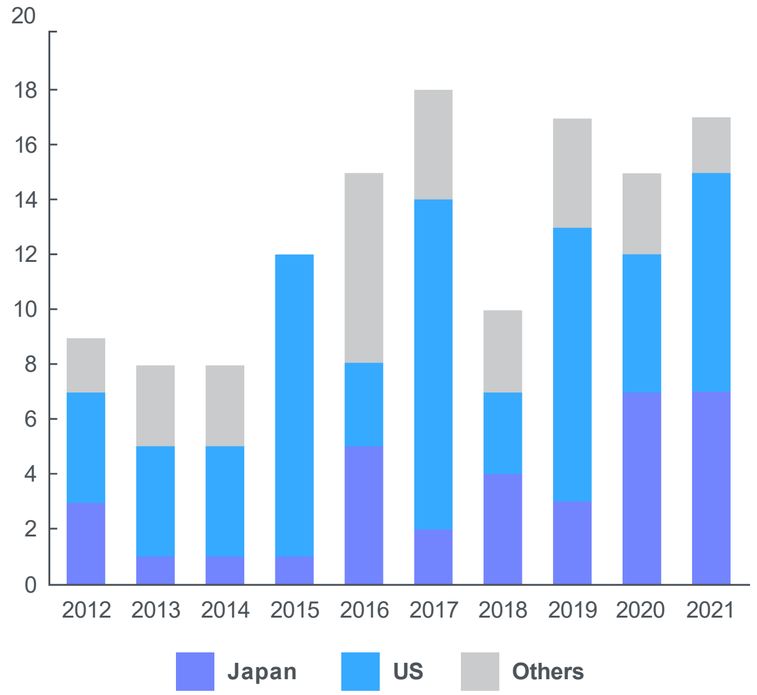


Ref: Japan CRO Association website

Ten things you should know:
10. Partnering opportunity in Japan

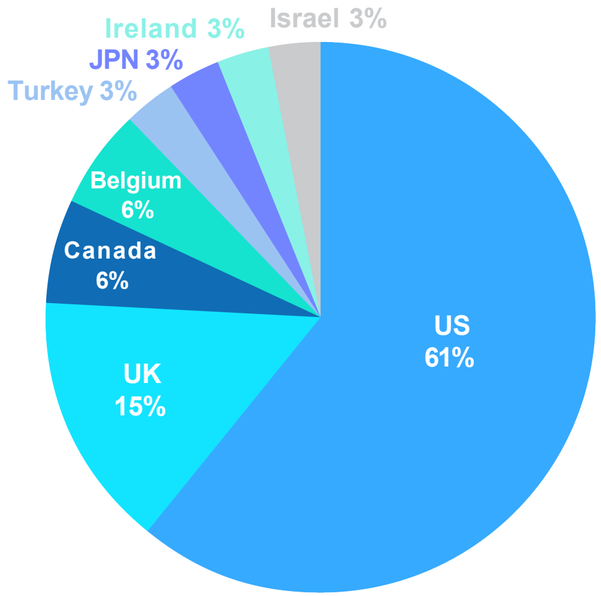
- The data indicated Japan domestic companies have maximize their business in partnership with Bio Tech companies
- Challenge is how effectively matching opportunity is identified!

#of Licensing contract by Japanese Pharma

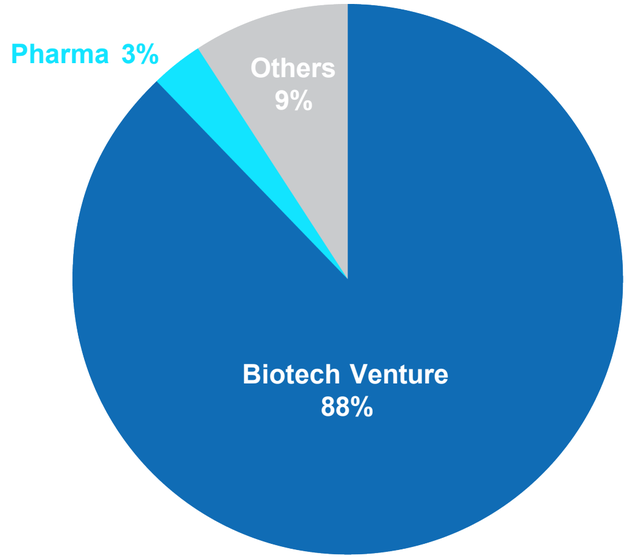


Profile of acquired company by Japanese Pharma

Country of acquired company
(N=33)

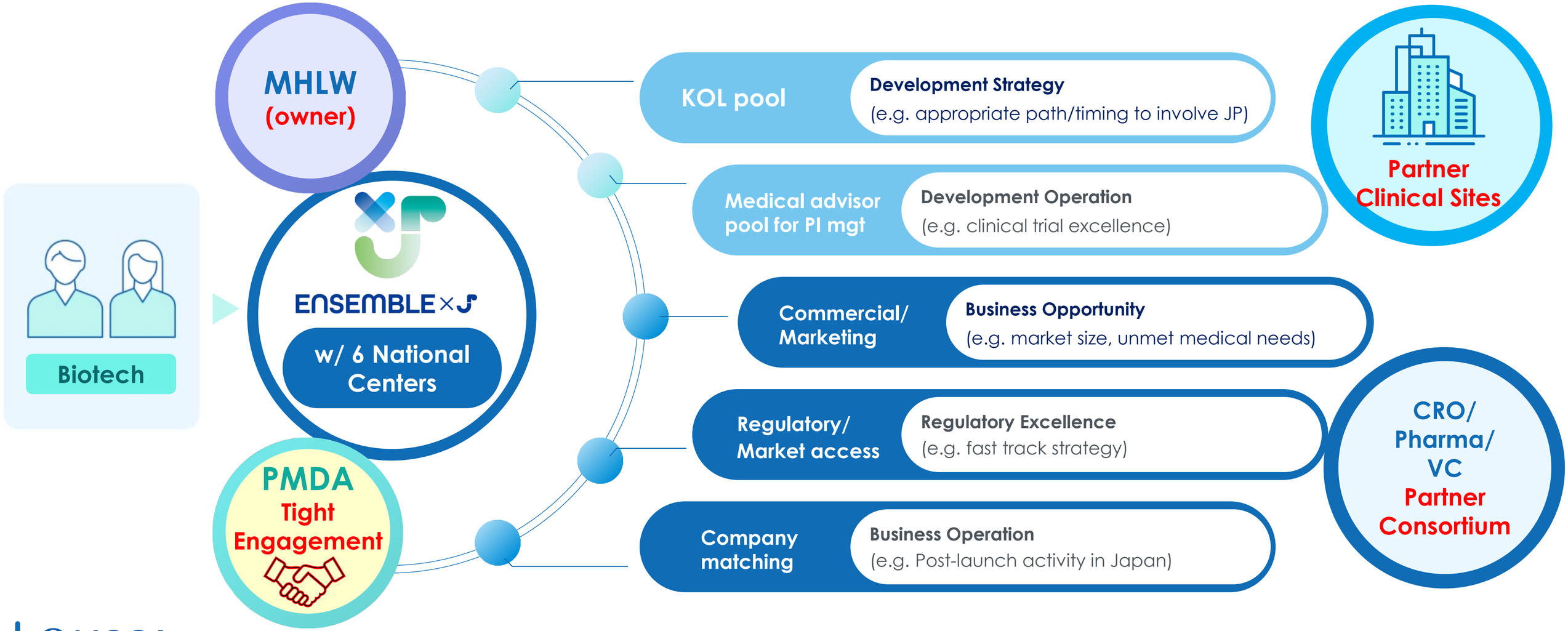


Business type of acquired company
(N=33)



Ref: OPIR News Views and Action by Office of Pharmaceutical Industry Research, No.68, Mar 2023

ENSEMBLExJ Supports You like Your Own Japan Team



What is “Win” for Japan?

Status of Drug Lag/Loss in Japan

- New Molecular Entities (NMEs) approved in US/EU in 2016-2020 are **436** products.
- **143**[*1]/436 products are not yet approved in Japan.

	Approved	Not approved yet	In development	Not yet in development[*2]
US	136	7	3	4
EU	86	57	26	31
Japan	0	143	57	86

NMEs by Biotech[*3]	56 %
NMEs as orphan drugs[*4]	47 %
NMEs for pediatric use[*5]	37 %
Others	16 %

Resource: Counted by MHLW and Office of Pharmaceutical Industry Research based on official info from PMDA, FDA, EMA, Asu-no-Shinyaku (Technomics, Inc)
※1 : # of NMEs approved in US and/or EU in 2016-2020 but not yet in Japan as of the end of 2022
※2 : As of March 2023
※3 : Companies defined as developers that obtained US and/or EU approval within 30 years of founding and reported revenues of less than USD 500 million in the year prior to approval
※4 : Products that received orphan drug designation in the US and/or EU prior to approval
※5 : Products that had obtained pediatric indications in the US and/or EU as of the end of 2022

Your “Win” to Maximize a Business Opportunity is Our “Win” to Resolve Drug Lag/Loss in Japan

MHLW’s initiatives to resolve Drug Lag/Loss in Japan

Unapproved Drugs and Off-Label Use Rapid Resolution Promotion Program

Pediatric Drug Development Network Support Program

First in Human Infrastructure Program for Novel Modalities

ENSEMBLExJ International Join Clinical Trial One-Stop Consultation Window Program

Feel Free to Contact Us Anytime!

Contact & Information

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[ENSEMBLExJ Movie (1min)]

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