# FY2022 1st Half Business Results
# November 15, 2022

**Perseus Proteomics Inc.**

**(Securities code: 4882)**

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# 01 About Perseus Proteomics

# Company outline

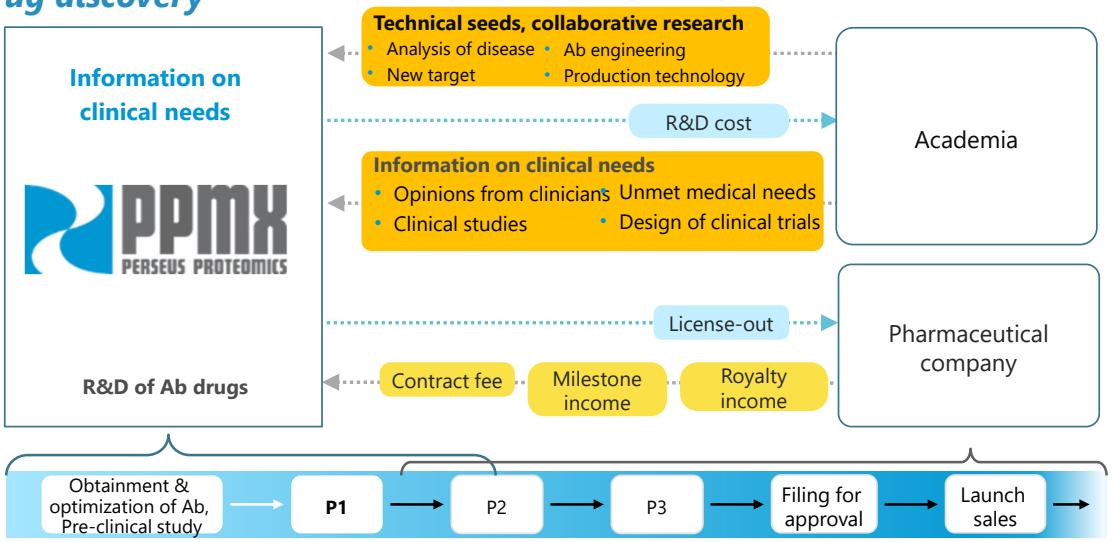
| | |
|---|---|
| Business | ● Develop Ab drugs<br>● Support research on Ab<br>● Sales of Abs/reagents |
| Company name | Perseus Proteomics Inc. |
| Established | February 2001 |
| Office | HQ/Laboratory: 4-7-6 Komaba, Meguro-ku, Tokyo, Japan<br>Nagoya Laboratory: 2-22-8 Chikusa-ku, Nagoya-shi, Aichi, Japan |
| Capital | 1,939 million yen* |
| Employee | 24<br>(R&D, Business Development: 19, Administration: 5) * |

*as of Sep.30, 2022

- 2001.2 **Established**
- 2005.9 Sales of Ab against 48 nuclear receptors starts
- 2006.9 **PPMX-T001 licensed out to Chugai Pharmaceuticals**
- 2011.1 **PPMX-T002 licensed out to FUJIFILM** (2022.3 returned)
- 2014.12 **PPMX-T003** selected as JST drug discovery project (940 M yen)
- 2015.9 **PPMX-T004 licensed out to FUJIFILM** (2022.3 returned)
- 2019.1 Nagoya Laboratory opens
- 2019.11 **PPMX-T003 in-house** P1 starts
- 2021.6 **Listed on Mothers (Growth) TSE**
- 2022.3 **PPMX-T003** adopted as AMED project on ANKL (250 M yen)
- 2022.9 **FUJIFILM** no longer “other associated company”

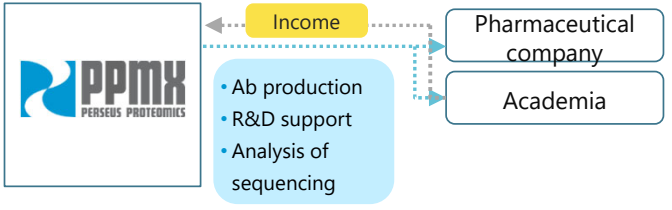
# Business model

## 1. Drug discovery

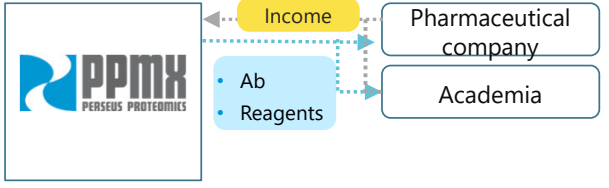



Flexibly decides license- out timing depending on situation

## 2. Support of Ab research

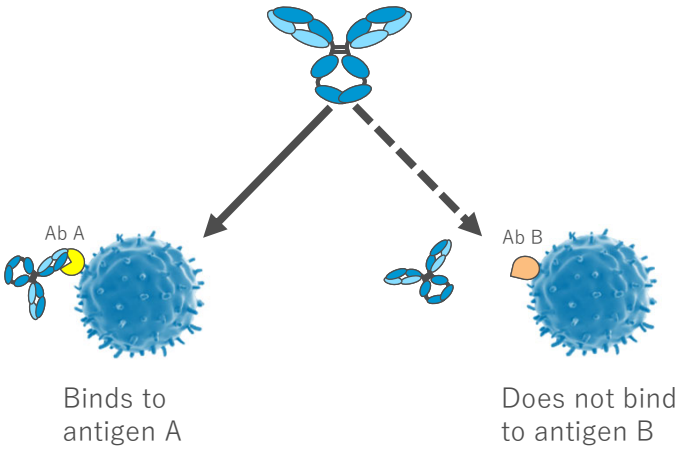



## 3. Sales of Abs/reagents



# What are Ab drugs?

- **Abs: substances that remove foreign objects in human body**




**Binds to specific antigens only**

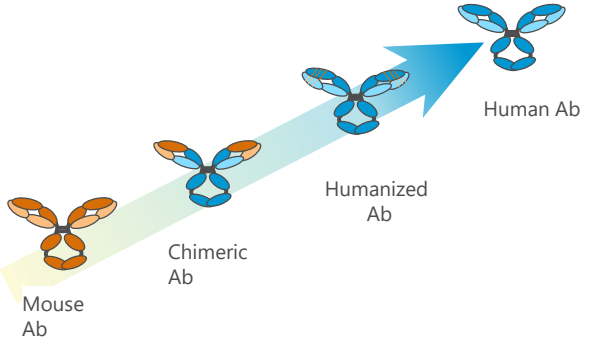
## Ab drugs:

**Abs designed to bind to targets expressed on cancers or pathogens**

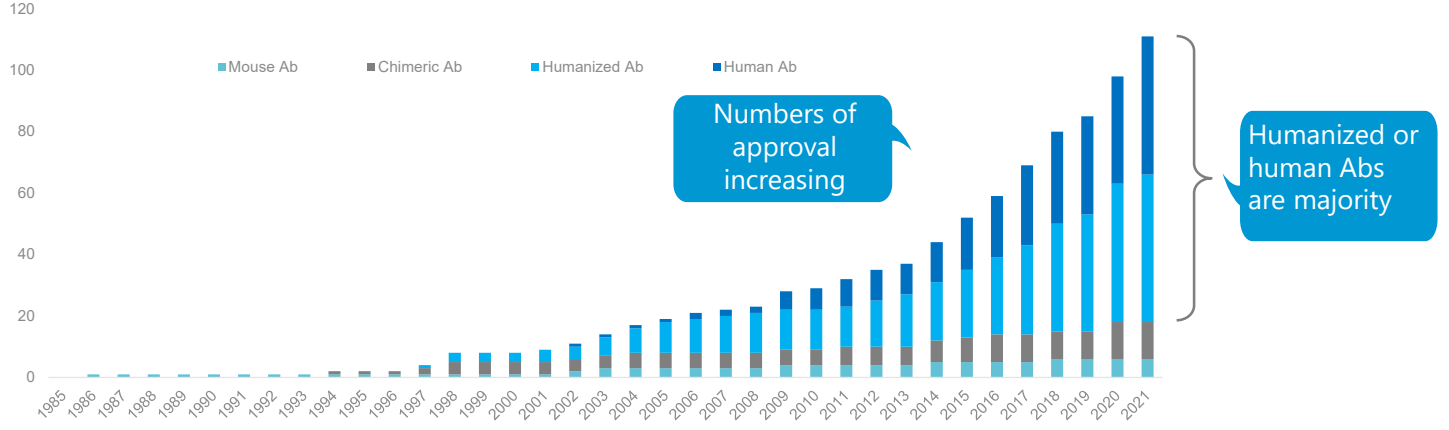
- Blocks signal transmission and inhibits multiplication functions, etc.
- Activates immune cells including T cells to induce cytotoxicity
- Activates physiological functions
- Transmits drugs to cells where targets are expressed

# What are Ab drugs?

## Evolution of Ab

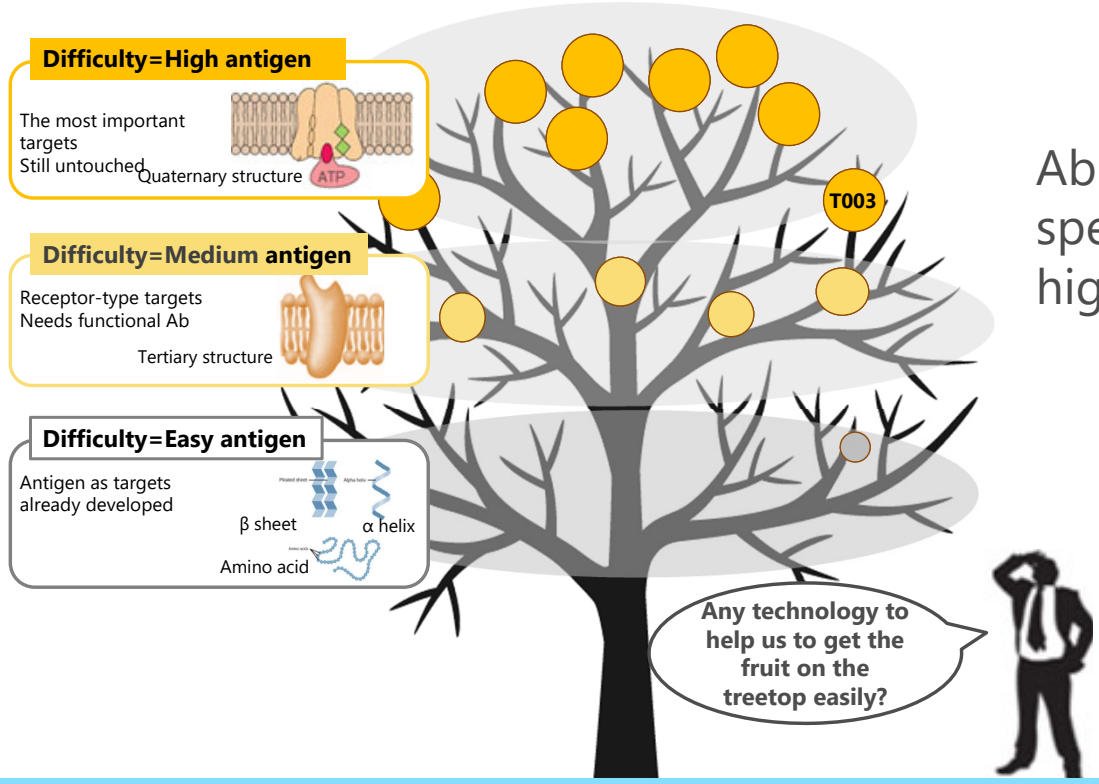



## Number of Ab drugs approval in JP/US/EU




Source: data from National Institute of Health Sciences
Calculated based on Approval date in Japan, USA and Europe

# Ab creation technology now required

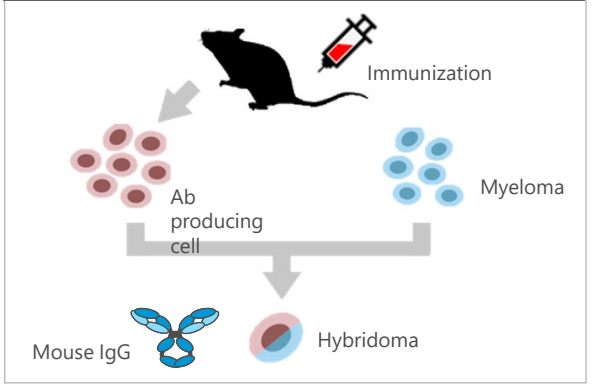



Ab that binds to specific part with high affinity

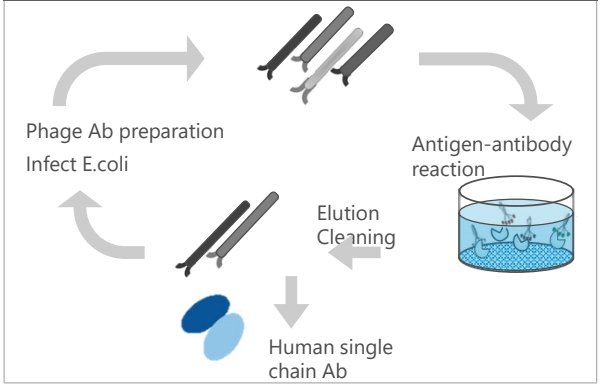
**Technology required for obtaining Abs efficiently against medium to high level antigens**

# Our technology to obtain Abs

## Hybridoma method




## Phage display method




**Merit**

- Easy method, established technique
- Increased biological affinity
- Low cost

- Possible to obtain human Ab
- No animals used
- No need to consider biological toxicity
- Rich in screening conditions

**Problem**

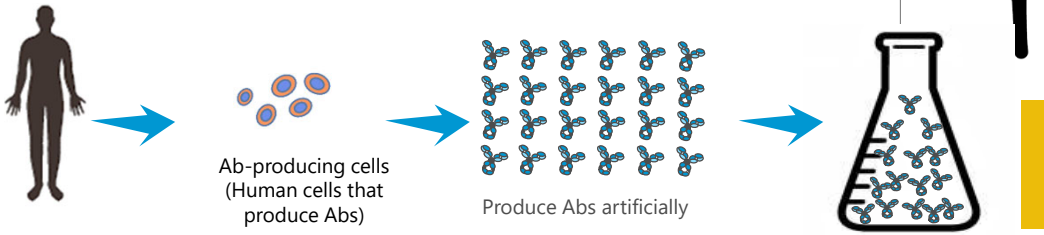
- Abs with species crossing are hard to obtain
- Needs humanization due to immunogenicity
- Abs against complex antigens are hard to obtain
- Easy-to-obtain Abs already developed
  ⇒ Focusing on new targets and modified Abs including ADC*1 and RIT*2

- Skills in creation of libraries required
- More expensive than animal immunization
- Low affinity of antigen-antibody
  ⇒ PPMX conquered this problem by maximizing library diversity

*1 ADC: Antibody drug conjugate. It delivers drug combined with Ab by utilizing Ab function.
*2 RIT: Radioimmunotherapy. Radioisotope combined with Ab irradiates cancer cells by utilizing Ab function.

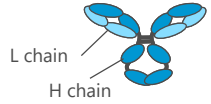
# Our strength: Phage Ab library

## 1 What is phage Ab library?

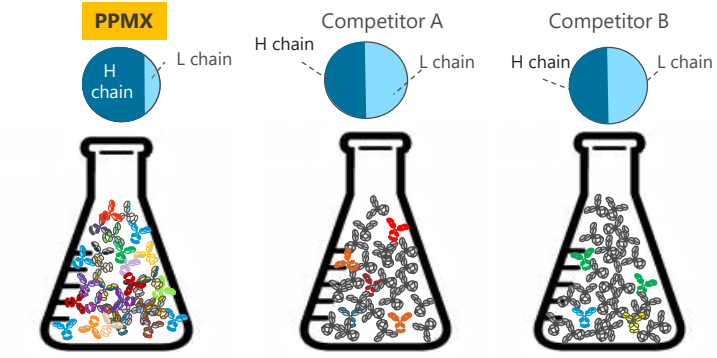



A mass of approx. 100 billion ($10^{11}$) different Abs to obtain Ab that binds to specific antigen

## 2 Our design of phage Ab library




**We maximize diversity of H chain by focusing on H chain (our unique library)**




While numbers of Abs are the same 10 billion, diversities are different

**Phage display method utilizing maximized diversity of Ab library**

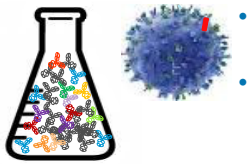
# Our strength: Ab screening using cell (PPMX exclusive method)

**Problem 1**

During preparation of antigen, steric structure is lost.

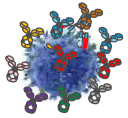
**Solution**

**Ab screening using living cells**



- Reflects complex steric structure through using living cells
- Directly obtains Abs against antigens on cell membrane

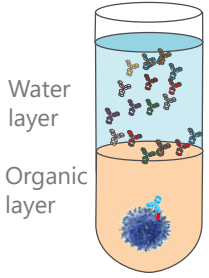
**Problem 2**



Numerous unrelated Abs also bind to cells.

**Solution**

**ICOS* method: Ab screening utilizing organic solvent**




- Obtains Abs that bind to antigen only
- Patent registered

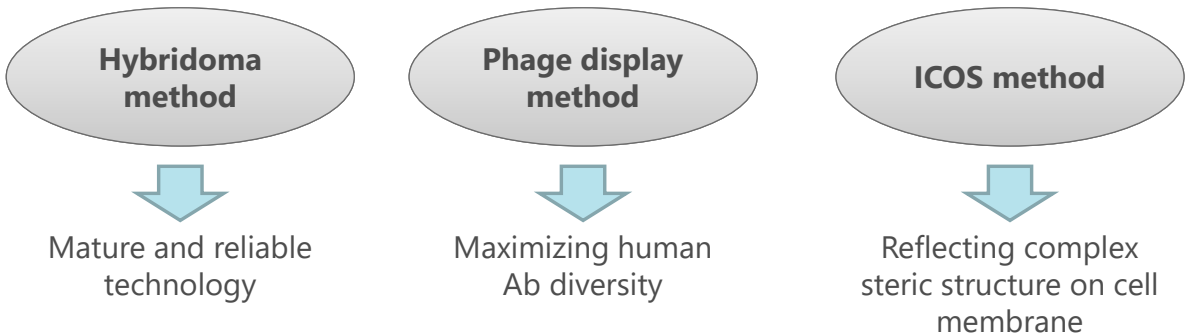
**Efficiently separates Abs difficult to obtain by targeting cells**

*Isolation of antigen/antibody Complexes through Organic Solvent

# Summary of technology to obtain Abs

## Our technology on Ab drug development

Our unique technology platform sophisticated
to aim at drug discovery for highly difficult targets




Showing our maximum value
in developing anti-cancer drugs

**PPMX's sophisticated Ab obtaining platform**

# 02 Topics

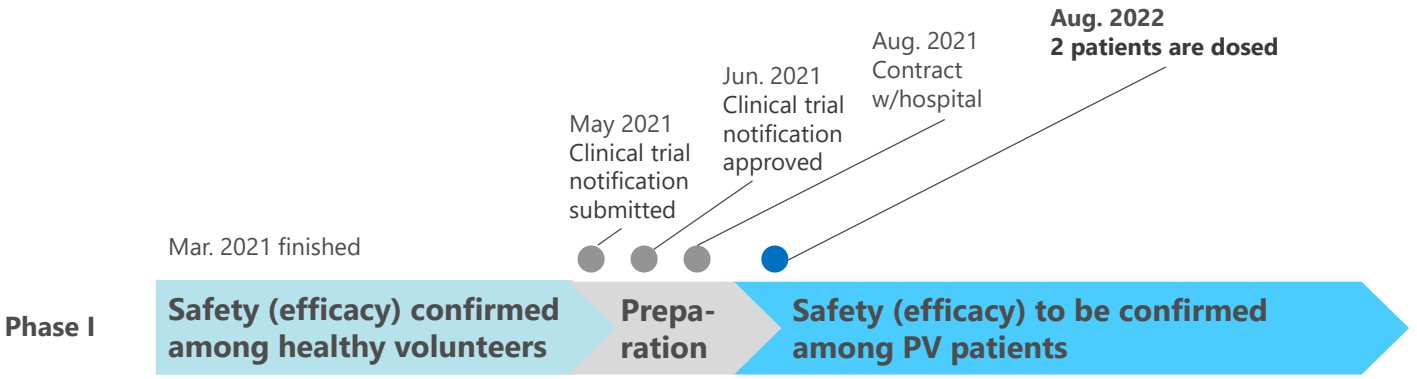
# Topics

1. **PPMX-T003:**
   **FPI in phase I clinical trial among polycythemia vera patients**

2. **FUJIFILM is no longer “other associated company”:**
   **Aims at out-licensing of PPMX-T002/T004 to global pharmaceutical companies**

3. **Drug discovery support:**
   **Started collaboration with Axcelead DDP**

# 1 PPMX-T003: FPI in phase I clinical trial among polycythemia vera patients




- Kansai Medical University Hospital
- Osaka Metropolitan University Hospital

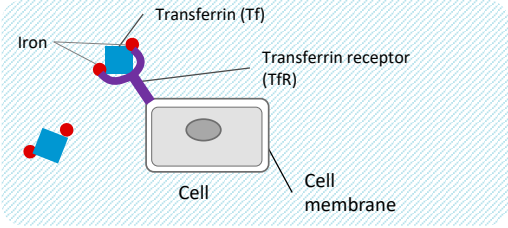
**Clinical trial information**

jRCT
jRCT2051210083: https://jrct.niph.go.jp/en-latest-detail/jRCT2051210083
clinicaltrials.gov
NCT05074550: https://clinicaltrials.gov/ct2/show/NCT05074550

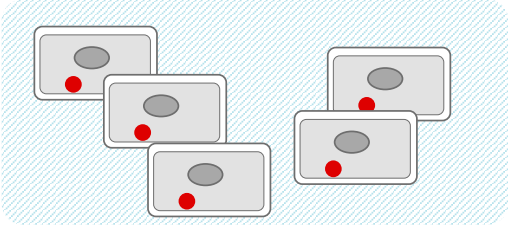
# PPMX-T003:
# First-in-class anti-cancer drug candidate targeting transferrin receptor

**Transferrin receptor (TfR):**
- Strong target molecule for anti-cancer drug
- Expressed on cell membrane.  Binds to transferrin (Tf) carrying iron for cellular iron uptake

1 TfR binds to Tf




2 Cell proliferation



**[ Cells where TfR is highly expressed ]**

- Erythroblast (normal cell, RBC producing cell)
- Cancer cell (especially acute cancer which is actively proliferating)

**Well-known concept**

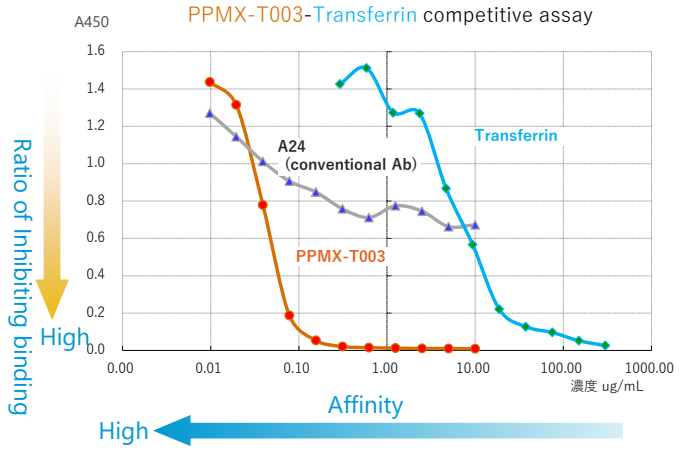
**Blocking iron**
**⇒ Death or inhibition of cell proliferation**

**Inhibiting cellular iron uptake leads to death/proliferation inhibition of cancer cells**

* Erythroblast: primitive red blood cell (RBC)

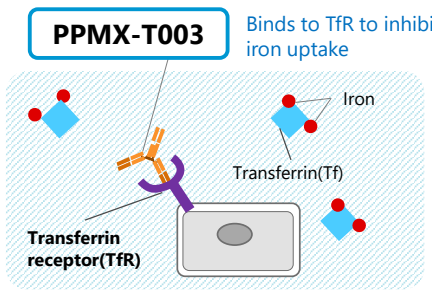
# PPMX-T003:
# Highly functional Ab obtained by our phage display technology

**Shows unprecedented result in inhibiting ratio of binding Tf to TfR**
**Inhibits iron uptake into erythroblast and cancer cells and leads to cell death/proliferation inhibition**

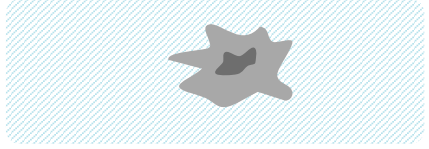



Inhibition of iron uptake has been difficult, however, PPMX-T003 is expected to bring it to reality as the first therapeutic drug for cancer and PV.

1 PPMX-T003 **binds to TfR more tightly than Tf**




2 Iron uptake inhibited. Cell death or proliferation inhibition of cells



**Anti-Transferrin receptor Ab with incomparable function of inhibiting binding**

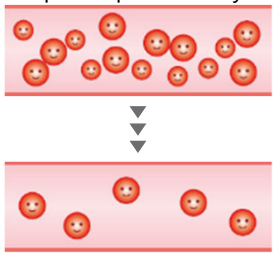
# PPMX-T003:
# Indication: Polycythemia vera (PV)

- RBC increases to an abnormal level.
- Thrombosis is easily formed due to thick and slow blood flow.  Various organs are affected by thrombosis.
- 2 out of 100,000 people develop this disease.  Number of patients in Japan: 30,000 (estimated by PPMX.  Average life expectancy: 16 yrs)

## Current therapeutics

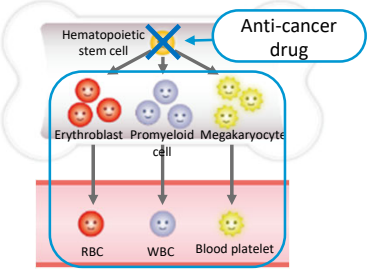
### Therapeutic phlebotomy

Half of patients are treated by therapeutic phlebotomy only.



- Anemia
- Lassitude
- Depression
- Restless hands and legs
- Other diseases by iron deficiency

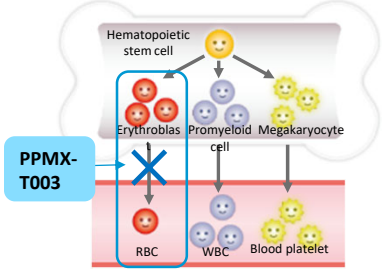
### Anti-cancer drug, etc.




- Entire hematopoietic stem cell affected
- Secondary cancer risk
- Many side effects

## New candidate

### PPMX – T003

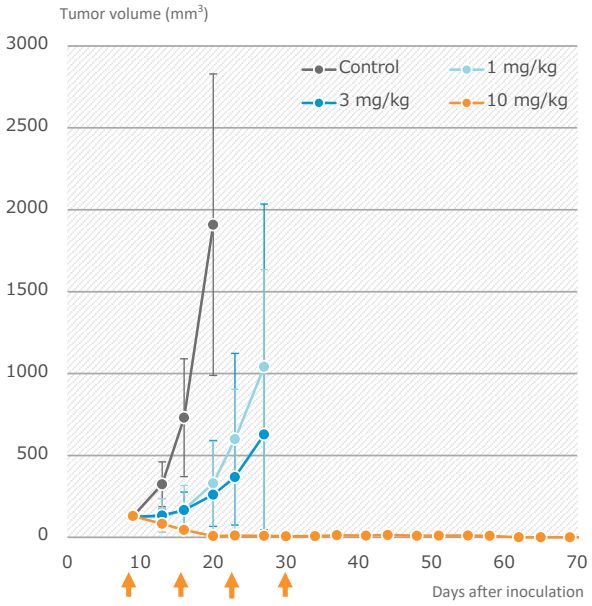



- **Acts only on erythroblast**
- **Few side effects**
- **Safe to use**

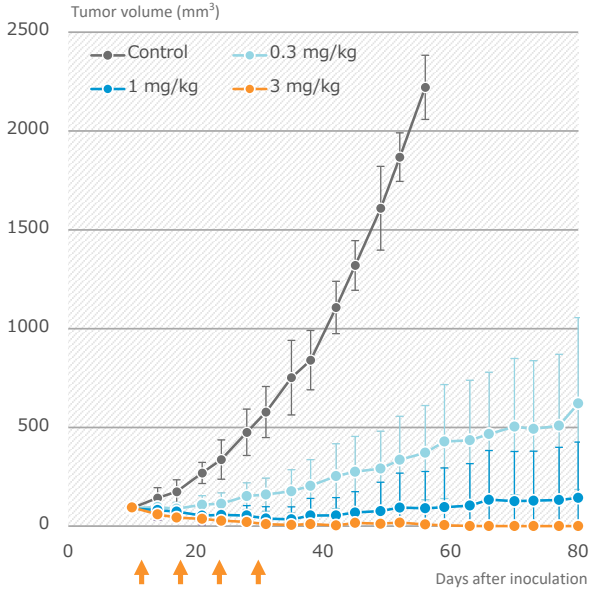
**PPMX-T003: effects on inhibiting abnormal proliferation of RBC expected**

# PPMX-T003:
# Confirmed efficacy against blood cancers in mice

● AML



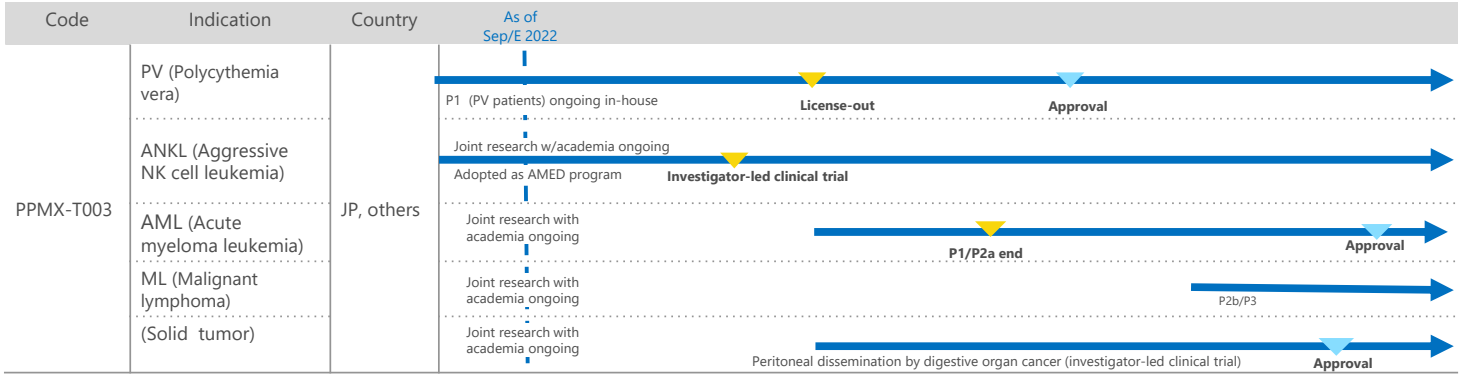

● Malignant Lymphoma




**Excellent efficacy against AML and various blood cancers is confirmed**

Source: Zhang et al.(2017) AACR Annual Meeting, Chicago, USA DOI: 10.1158/1538-7445.AM2017-5586

# PPMX-T003: Development plan

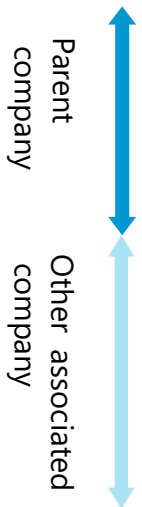



Number of patients

| Indication | | No. of patients ww (rounded) | Note |
|---|---|---|---|
| PV (Polycythemia vera) | Chronic blood disease | 280,000 | Calculated with onset risk rate at 2 in 100,000*, life expectancy at 14 years*, population at 1 billion (developed countries) |
| AML (Acute myeloma leukemia) | Blood cancer | 200,000 | WHO data (assumes 40% of leukemia) |
| Malignant lymphoma | Blood cancer | 590,000 | WHO data (number of non-Hodgkin lymphoma patients) |
| Multiple myeloma | Blood cancer | 190,000 | WHO data |
| Peritoneal dissemination of cancer | Solid tumor | N/A | Over 10,000 and several thousand new patients annually in Japan |

* This chart is based on our assumption and does not guarantee the progress as shown here.
* All the development after out-licensing is determined by the development strategies of licensing partners.

# 2 FUJIFILM is no longer “other associated company”:




| | |
|---|---|
| 2009.1 | FUJIFILM becomes parent company of PPMX |
| 2011.1 | PPMX out-licenses PPMX-T002 |
| 2015.9 | PPMX out-licenses PPMX-T004 |
| 2018.3 | FUJIFILM becomes other associated company of PPMX |
| 2021.6 | Stocks of PPMX are listed on Mothers (currently Growth) market |
| 2021.9 | FUJIFILM announces transfer of radiopharmaceutical business |
| 2022.3 | Licensing agreements of PPMX-T002/T004 are terminated |
| 2022.9 | FUJIFILM is no longer other associated company of PPMX |

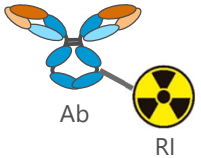
# 2 Aims at out-licensing of PPMX-T002/T004 to global pharmaceutical companies

**Target＝Cadherin 3 (CDH3)**

Highly expressed on various solid tumors

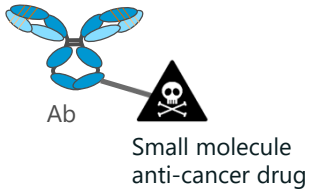
Head & neck cancer | Ovarium cancer | Biliary tract cancer | Pulmonary adenocarcinoma | Large bowel cancer

## PPMX-T002 RI-labelled Ab




- Change to new code
- Co-development w/PeptiDream group under study
- Enhance efficacy through finding a global out-licensing partner

## PPMX-T004 ADC



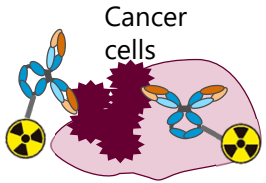

- Change to new code
- Develop as a new ADC
- Find a global out-licensing partner

# PPMX-T002:
# Co-development with PeptiDream Group under study
## ---Develop as a new RI labelled Ab

**1 Function of RI labelled Ab**



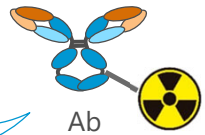
Dose PPMX-T002
to a patient




PPMX-T002 Ab accumulates on CDH3 on cancer cells
and RI kills cancer cells

**2 Structure of new PPMX-T002**

Confirmed accumulation on cancer cells
Use it as is

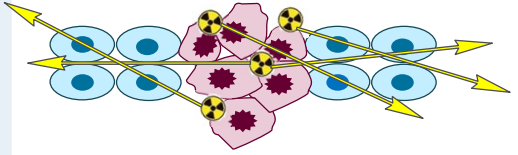
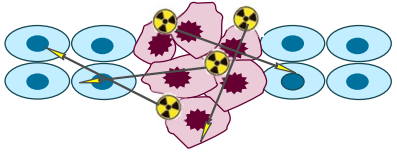
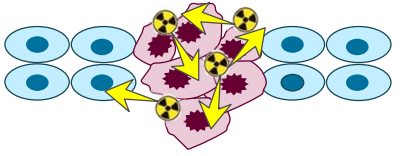



$^{90}$Y(β emitter)

**$^{177}$Lu (β emitter)**
or
**$^{225}$Ac (α emitter)**

**Utilize Ab as is and change RI from $^{90}$Y to that w/higher effectiveness**

# PPMX-T002:
# Promote development through increasing efficacy by RI change

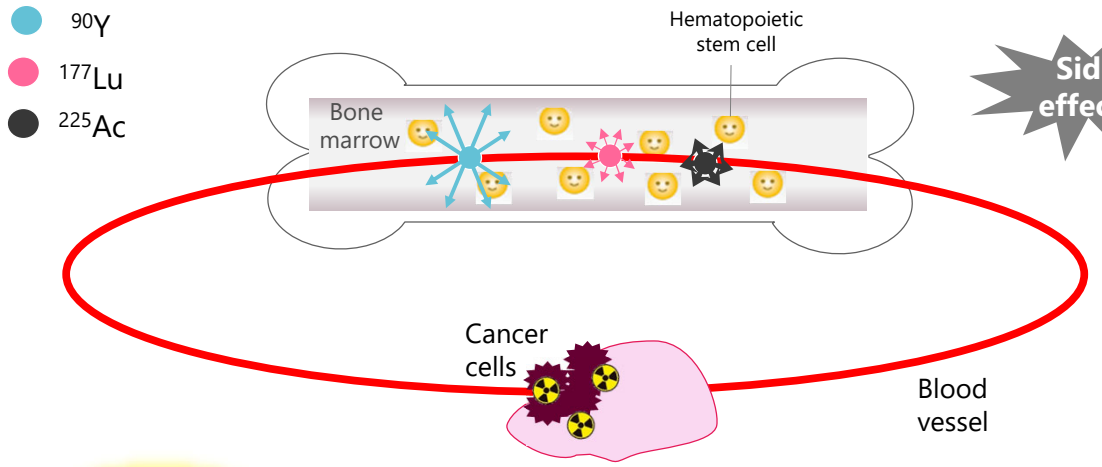
| | $^{90}$Y | $^{177}$Lu | $^{225}$Ac |
|---|---|---|---|
| Radiation | β emitter | β emitter | α emitter |
| Energy(MeV) | 2.3 | 0.5 | 5,830 |
| Max range (No of cells) | 11.0 mm (～a few hundreds) | 2.2 mm (～100) | 0.090 mm (a few) |
| Half-life | 2.7 days | 6.7 days | 10 days |
| Approved RI drug targeting molecules | Zevalin (2002/US, 2008/JP) | Lutathera (2018/US, 2020/JP)<br>Pluvicto (2022/US) | - * |
| Feature |  Normal cells can be damaged as this β emitter has a long range. |  Side effects are fewer as this β emitter has a shorter range than $^{90}$Y. More dose can be possible. |  This α emitter has a range of only a few cells. Attacks cancer cells effectively with high energy. Next generation RIT. |




*The world-first α emitter drug, Xofigo($^{223}$Ra), was approved in 2013 in US.

# PPMX-T002:
# Points to consider in selecting RI

## Impacts on hematopoietic stem cells are the key to determining RI and dosage




**Side effects**

Damages/Kills hematopoietic stem cells when passing through bone marrow

**Efficacy**

Ab accumulates on cancer cells, radiation from RI damages/kills cancer cells

**Select the best RI after study of side effects and efficacy**

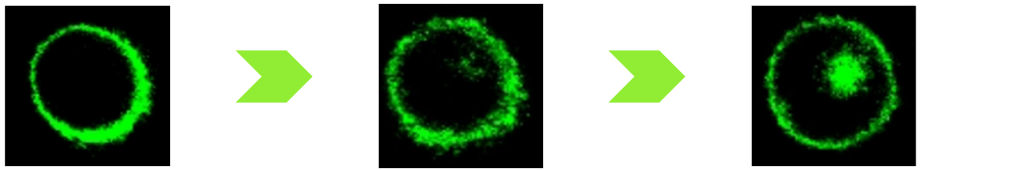
# PPMX-T004:
# Leading development as new ADC

## 1 Function of ADC

Let ADC in cancer cells to kill them by releasing anti-cancer drug inside

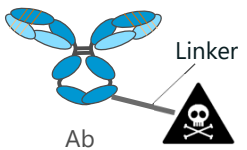


Dose PPMX-T004
to a patient



PPMX-T004 Ab and drug taken into a human cancer cell. Already confirmed functionality of Ab

## 2 Study of new PPMX-T004




Controls release of small molecule anti-cancer drug

Induces cell death

**Studying to decide the best combination of the latest drug and linker**

# 3 Drug discovery support: Started collaboration with Axcelead DDP (Takeda spin-off)

## Started collaboration in Aug. 2022

Wide platform function for drug discovery

AXCELEAD Drug Discovery Partners

- Non-clinical tests (including in vitro/in vivo efficacy evaluation)

×

Cutting-edge Ab generating technology accumulated in drug discovery

PPMX PERSEUS PROTEOMICS

- Ab generation
- Screening
- Humanization
- Improvement of physical properties

**One-stop**

High quality Ab drug discovery support service



# Pipeline progress

| Code | Indication | Region | Drug discovery/ Research | Preclinical | P1 | P2 | P3 | Notes |
|---|---|---|---|---|---|---|---|---|
| **PPMX-T002 ➔ New code** | Solid tumor | USA Japan | RI labelled Ab | | | | | • Co-development w/PeptiDream group under study<br>• Change of RI under study<br>• To be developed under new code |
| **PPMX-T004 ➔ New code** | Solid tumor | | ADC | | | | | • Study of optimization of therapeutic drugs and linkers<br>• To be developed under new code |
| **PPMX-T003** | PV*1 | Japan | | | | | | FPI in Aug, 2022 |
| | ANKL*2 | Japan | | | | | | • Adopted as AMED program<br>• Investigator-led clinical trial under preparation |

*1 PV: polycythemia vera *2 ANKL: aggressive NK-cell leukemia

# 03 FY2022 1st Half Business Results

# FY2022 1st half business results
# Profit & Loss highlights

(million yen)

| | FY2021 1st half | FY2022 1st half | FY2022 forecast |
|---|---|---|---|
| **Sales** | **29** | **47** | **77** |
| **Gross profit** | 29 | 44 | 72 |
| **SG & A** | **275** | **351** | **776** |
| R&D cost | 154 | 214 | 522 |
| Other | 120 | 137 | 253 |
| **Operating income** | **(245)** | **(306)** | **(703)** |
| **Ordinary income** | **(263)** | **(288)** | **(736)** |
| Extraordinary loss | 9 | 73 | 116 |
| **Net income** | **(274)** | **(363)** | **(854)** |

**Ab/reagent sales**
**Ab research support**

**PPMX-T003 P1 cost**

**Impairment loss due to capex increase**

- Sales/Profit: favorable progress
- SG&A: P1 among PV patients of PPMX-T003

# FY2022 1st half business results
# Balance Sheet highlights

(million yen)

| Assets | 2022/3/31 | 2022/9/30 |
|---|---|---|
| Cash & deposits | 3,214 | 2,820 |
| **Total current assets** | **3,290** | **2,879** |
| **Non-current assets** | **9** | **9** |
| **Total assets** | **3,300** | **2,889** |

| Liabilities | 2022/3/31 | 2022/9/30 |
|---|---|---|
| Current liabilities | 148 | 64 |
| Non-current liabilities | - | 25 |
| **Total liabilities** | **148** | **89** |
| **Total net assets** | **3,152** | **2,799** |
| **Total liabilities and net assets** | **3,300** | **2,889** |

- Non-current liabilities: long-term deposits due to adoption of PPMX-T003 (ANKL therapeutic drug development) as AMED program
- Capital ratio: 96.5％

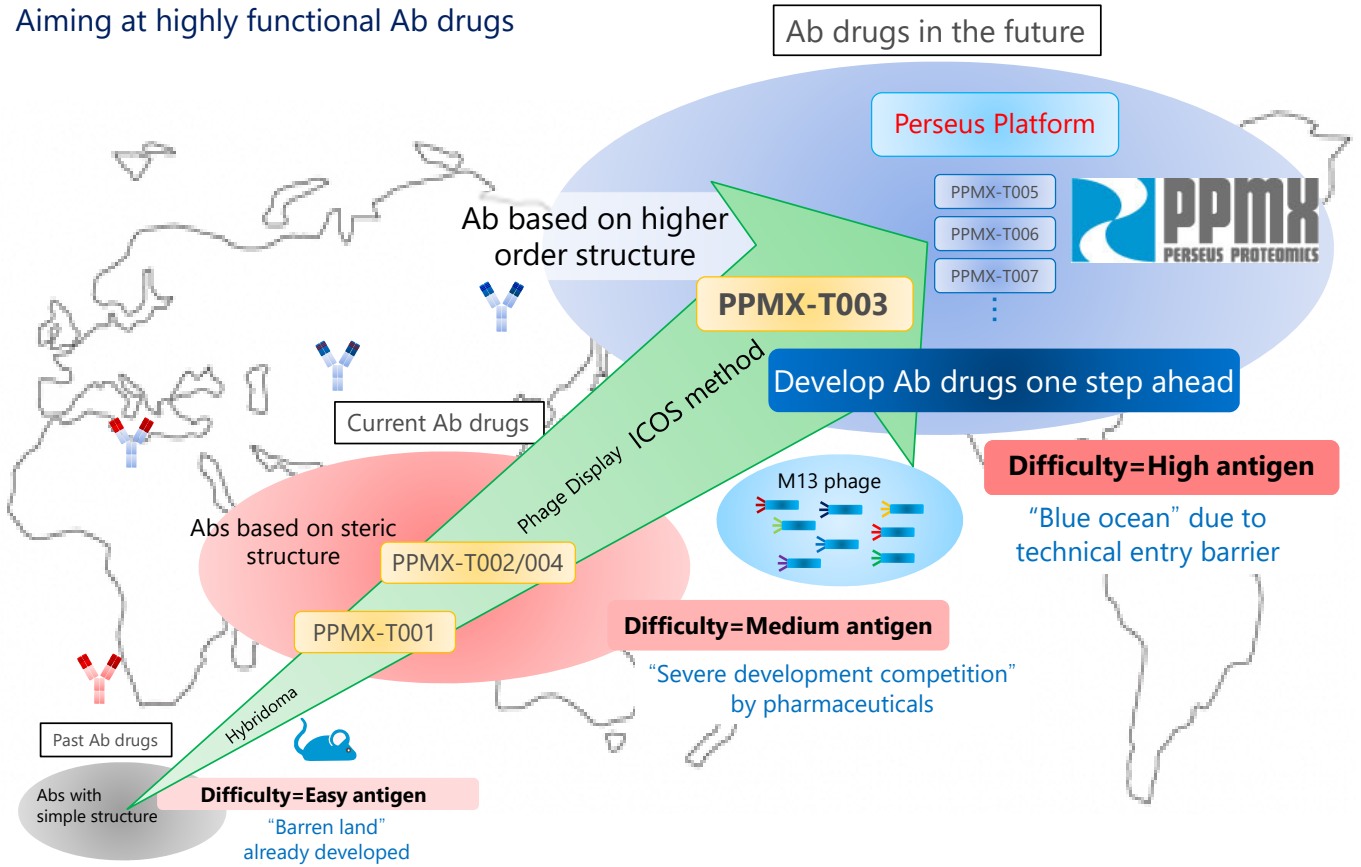
# 04 Progress of FY2022 Business Plans

# Progress of FY2022 Plans

| | | |
|---|---|---|
| 1 | PPMX-T003:<br>Start and finish administration in P1 among PV patients | **First/Second patients in** |
| 2 | PPMX-T003:<br>Develop medical drug for ANKL – finish preparation for investigator-led clinical trial | **Preparing for submission of protocol of investigator-led clinical trial** |
| 3 | PPMX-T002:<br>Determine new partner | **Determination process of RI development company as a partner** |
| 4 | PPMX-T004:<br>Plan re-development | **Optimization of drug and linker ongoing for re-development plan** |

# Bring more Ab drugs to patients

Aiming at highly functional Ab drugs



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