How to build a sustainable biotech hub in an emerging economy

Poland as the new source of biomedical innovation

Pawel Przewiezlikowski

Krakow, 15 April 2024

RYVU THERAPEUTICS | Developing therapeutics at the forefront of oncology

CDDF Cancer Drug Development Forum
FACILITATE. DEBATE. ACTIVATE. INNOVATE.

Agenda

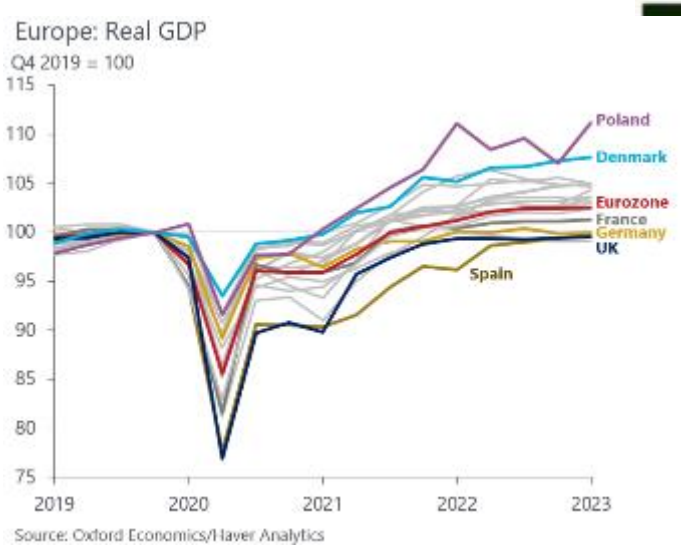
- **Poland:**
  Economic demographic foundations
  Capital markets
- **Scientific potential and track record**
- **Polish biotech companies**
- **Clinical trials in Poland**
- **Secret Polish recipe for biomedical success**

Poland – growing economy forms a strong foundation for biomedical research
Among major economies Poland has trailed only China in growth in the last 30 years

Key facts

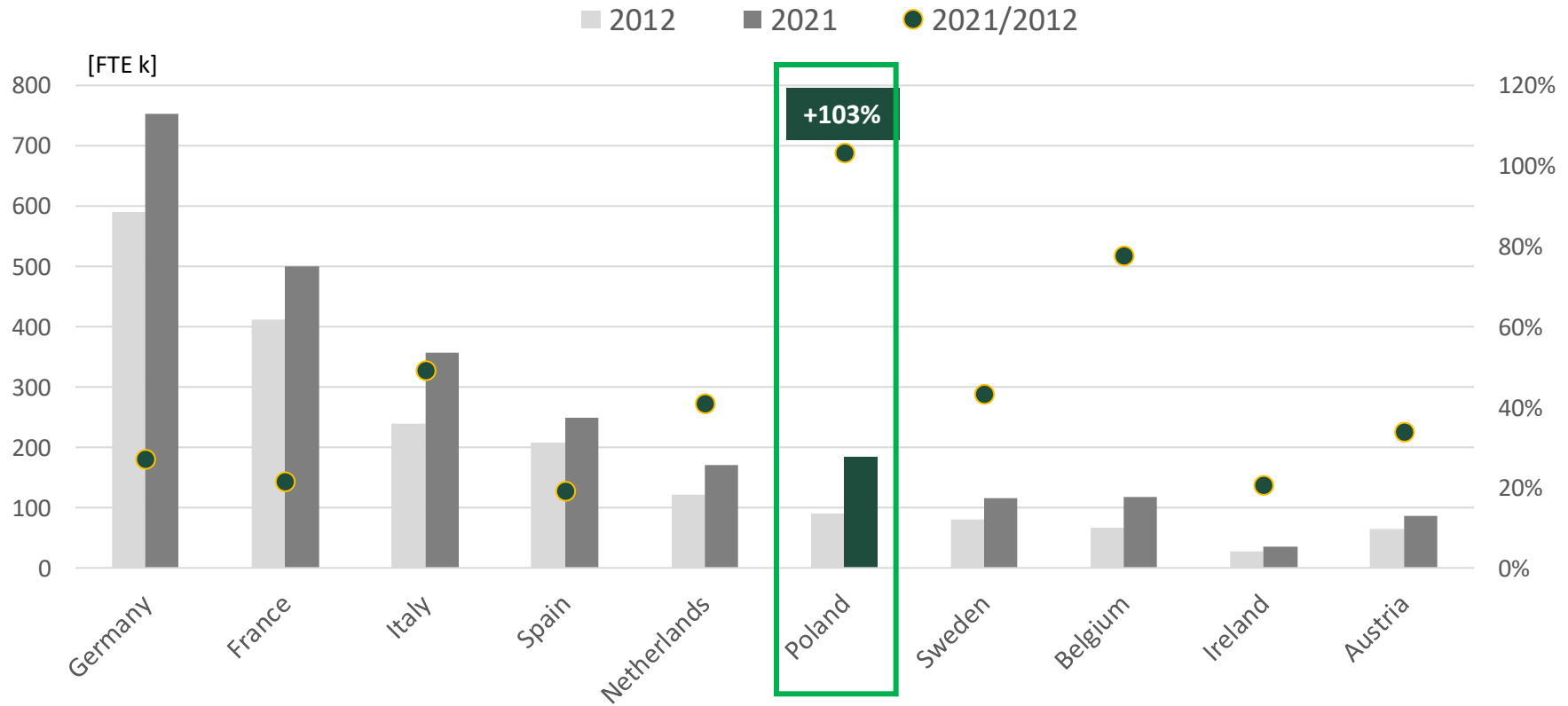
- Poland is the **largest economy in Central and Eastern Europe** as well as the **fifth biggest economy (PPP*) in the European Union** (behind Germany, France, Italy and Spain).
- In 2024, Poland will record **the largest GDP growth** among Europe's big economies (2.7 %)
- Characterized by the **strong domestic market, low private debt, low unemployment rate** and **flexible currency**, Poland is a regional economic leader with a high potential for dynamic future growth.

Population	**38M (+2M UA refugees)**
GDP (Nominal)[1]	**US$ 880B**
GDP Per Capita (Nominal)[1]	**US$ 23.4 K**
GDP (PPP*)[1]	**US$ 1.4T**
GDP Per Capita (PPP*)[1]	**US$ 47.7K**
Unemployment Rate (IMF)	**2.9%**
Inflation (consumer prices)	**2.8%**
Public Debt (As % of GDP)	**52%**



Poland is ranked 5th in the EU by the number of scientists and enjoyed the strongest growth in the last decade

R&D personnel in TOP10 EU economies[1]



Qualified R&D labour force and thousands of well-educated graduates every year

38 of ~400 European Universities with biotechnology studies are located in Poland[2]

BLUME GROWTH ADVISORY

Sources: (1) Eurostat, OECD; (2) Polish Federation of Biotechnology

Two engines of Central and Eastern European biotechnology and pharmaceutical sectors

Short-term: competition on the cost of labor

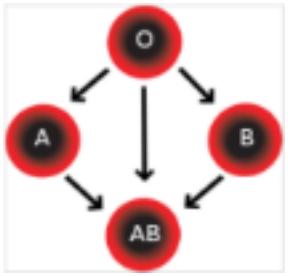
- Production of high-value-added drugs (difficult-to-synthesize generics, biosimilars)
- Contract research on drugs
- Clinical trials
- Outsourcing centers (BPO)
- Bioinformatics services

Long-term: Innovation

- Innovative drugs should be developed based on our know-how used for internal use and export
- Artificial intelligence-based precision medicine products

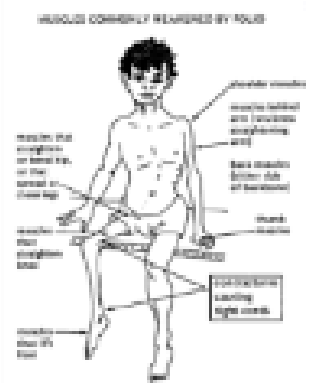
Famous Polish biomedical scientists and their discoveries/projects

Cybulski
1899



Hirszfeld
1912

Funk
1910



Koprowski
1950

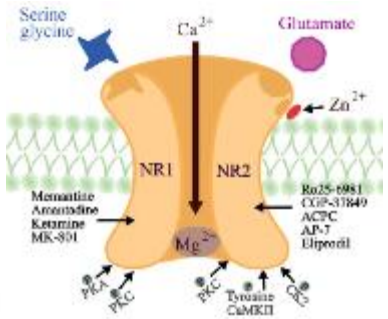
Chomczyński
1987

Machoń
1970

Reichstein
1950

Andruszkiewicz
1988

Mroczkowski
2007

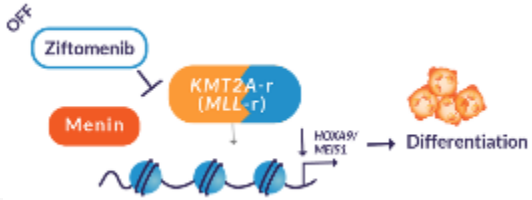


Maj, Vetulani,
Nowak, Popik
1980-1995

Jemielity
2007

Sternbach
1959

Fotin-Mleczek
2013

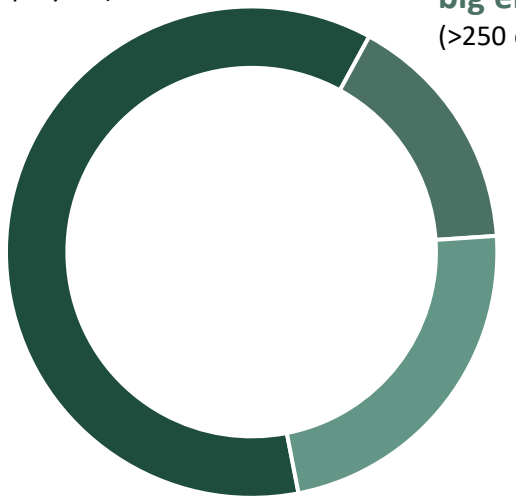


Grembecka,
Cierpicki, Klossowski
2017

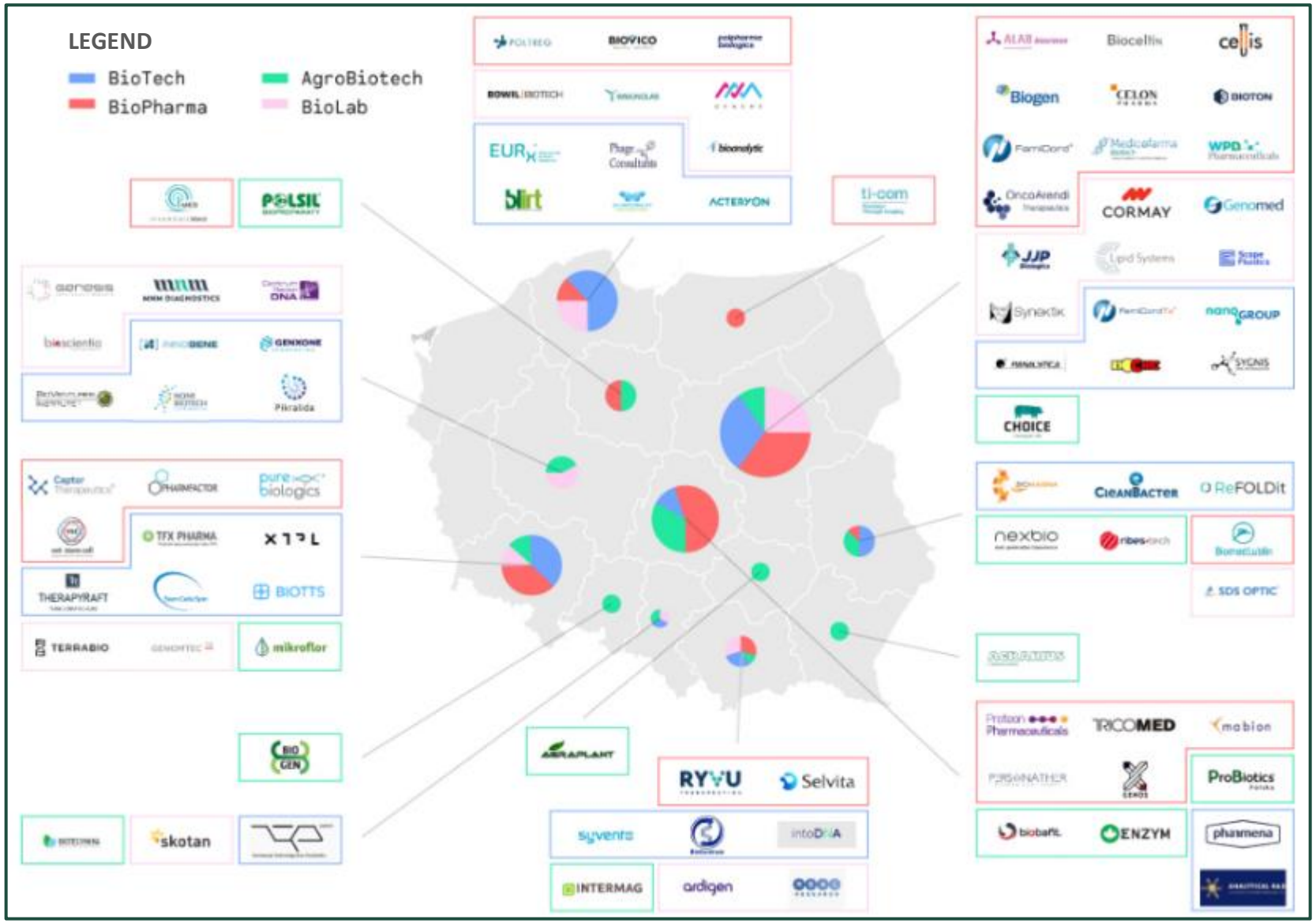
Poland has 217 registered biotech entities……

61%
small enterprises
(<50 employees)

16%
big enterprises
(>250 employees)



23%
medium enterprises
(50-249 employees)



BLUME GROWTH ADVISORY

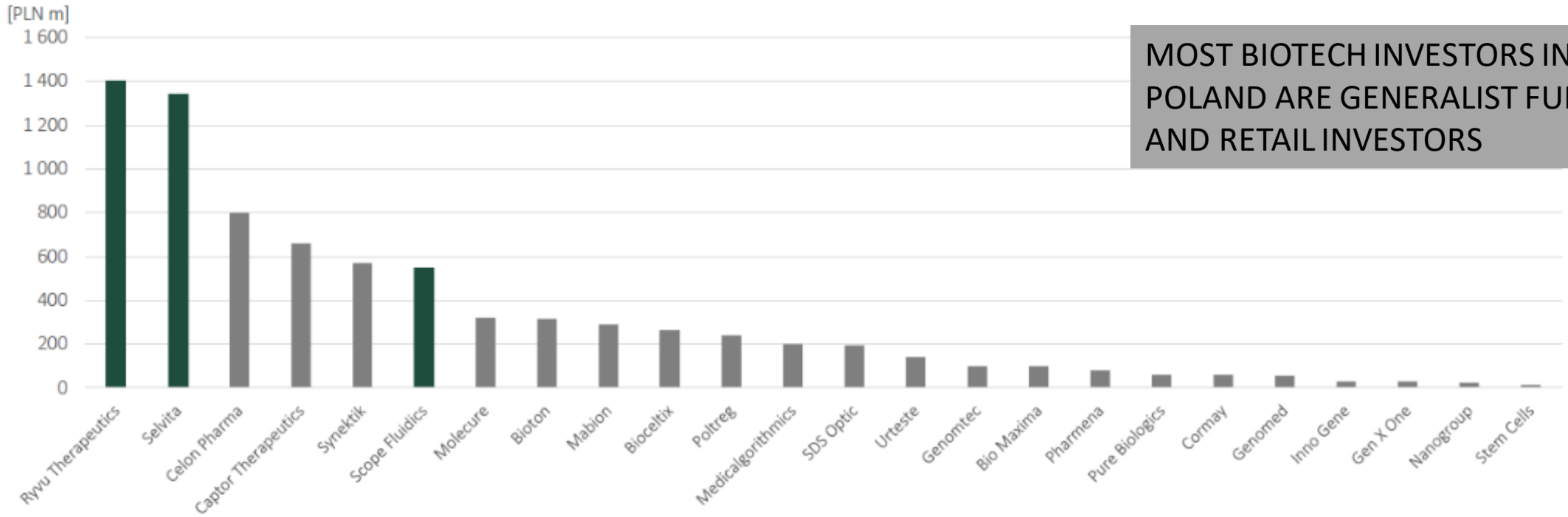
Sources: (1) Stat.gov.pl (2021); (map) BioForum

20 years of innovative biomedical sector in Poland - Milestones

2002	**Celon Pharma** is established - the first Polish pharmaceutical company whose main value is innovative projects
2007	**National Center for Research and Development** is established - the first funding agency for commercial biomedical R&D
2009	**ReadGene** company debuts on the NewConnect market
	Adamed launches diabetes drug into clinical trials - Poland's first commercial innovation drug
	Medicalgorithmics - first Polish AI-driven medical device approved by the US. FDA (mobile Holter – cardiac telemetry)
2010	Collaboration **Selvita (Ryvu)** / Orion on the basis of technology from IF-PAN - first international commercialization in Polish biotechnology
2011	**University of Warsaw** BioNTech contract for RNA stabilization technology
2013	**Mabion** debuts on WSE's main market
2014	Ryvu - Merck collaboration - first big Pharma appreciates Polish innovators
2016	**Braster** Breast Cancer Tester on the Polish Medical Device Market
2017	SEL24 Ryvu in Phase I clinical trial - Poland's first innovative oncology drug in the clinic
2019	**Medical Research Agency** is established
	Celon Pharma's esketamine for drug-resistant depression - Poland's first innovative drug in phase II clinical trials
2020	Galapagos - **Molecure** (Oncoarendi) collaboration - first partnership contract with initial payment > 100 MPLN
	Selvita acquires Croatian Fidelta - first foreign acquisition of Polish biotech company
2021	Adamed - Acadia collaboration in CNS
2022	Two M&As over $100 M: Acquisition of **Blirt** by Qiagen and **Curiosity Diagnostics** by Biorad
	Polpharma's biosimilar drug approved by FDA - Poland enters the medium level of bio innovation
	Captor - Ono collaboration on protein degraders in CNS and Ryvu with BioNTech in oncology
2023	First GMP-compliant Treg cell drug produced at **Poltreg** plant

Poland developed the only public capital market in CEE capable of financing the biotech/medtech sector

Market capitalization of Polish biotech/medtech companies listed on the Warsaw Stock Exchange and NewConnect(1)



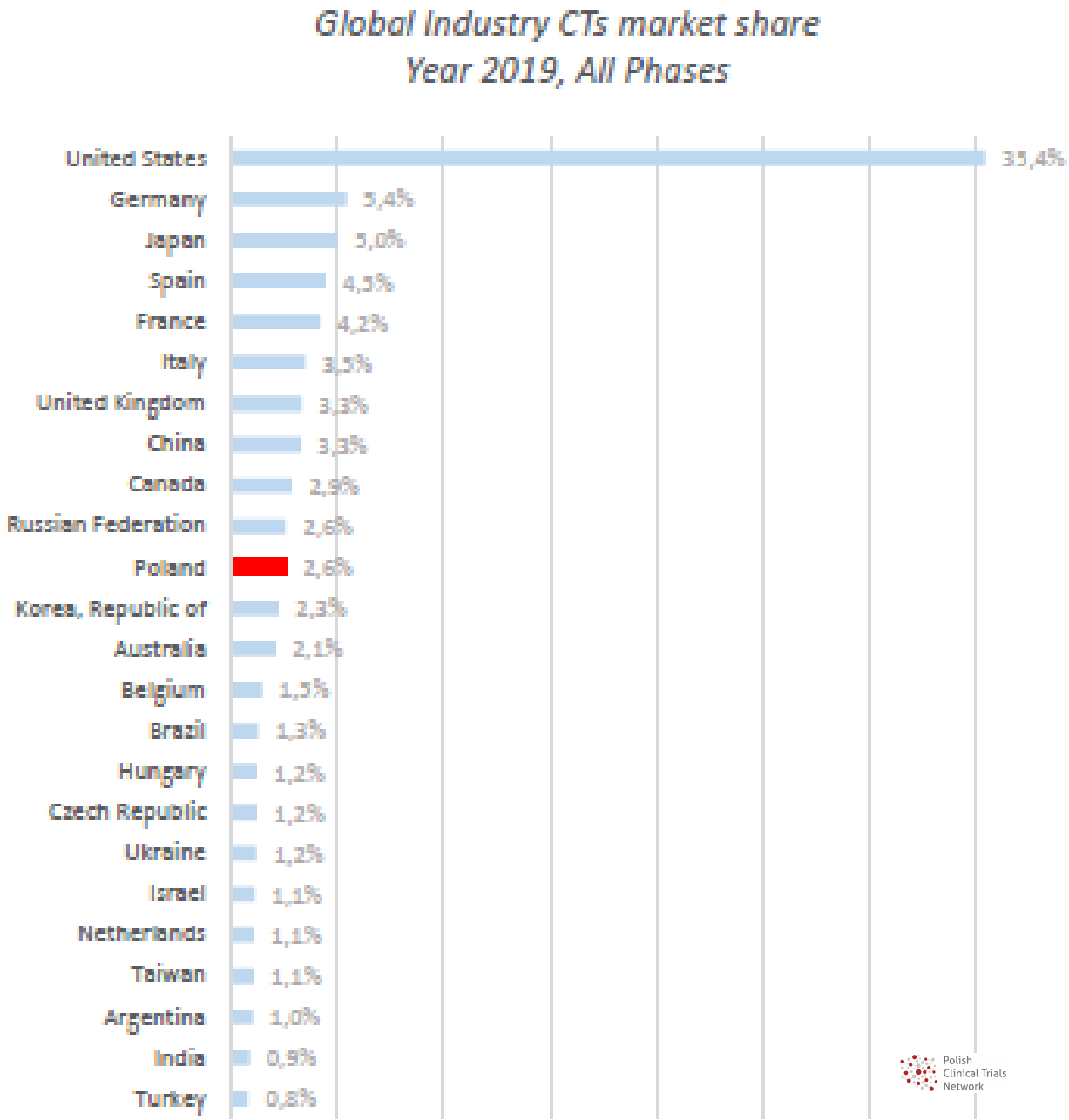
MOST BIOTECH INVESTORS IN POLAND ARE GENERALIST FUNDS AND RETAIL INVESTORS

>PLN 8 bn (>EUR 1.7 bn) sector value on the Polish public market

BLUME GROWTH ADVISORY Source: (1) Stooq.pl (as of 9.06.2023)

Poland is a major global clinical research hub

- 559 clinical trials initiated in 2021
- The majority are Phase 3 (203) and Phase 2 (144) trials
- 25% oncology, 15% neurology, 10% cardiology, 10% infectious disorders
- 25 000 patients
- Several dedicated oncology Phase I units established in recent years (eg. Gdansk, Warsaw)
- 645 clinical trials initiated in 2022



Polish Clinical Trials Network

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Poland’s strong position in clinical research

- Higher productivity of clinical trial sites in relation to other markets.
- Centralized healthcare system with competent researchers attracting and retaining large numbers of patients for clinical trials.
- Lower costs of conducting clinical trials compared to other markets, including lower start-up costs.
- Comparing to other CEE countries still relatively small saturation of clinical trials to country population
- Polish Clinical Trials Network (PCTN)

MEDICAL RESEARCH AGENCY

Polish Clinical Trials Network

Global Clinical Operations hubs in Poland (incl. headcount)

Regional Clinical Operations HQ:

- AbbVie
- AZ
- BMS
- Roche
- GSK

Ways to overcome barriers to the development of the CEE biotechnology industry

International clients and development partners

International managerial practices

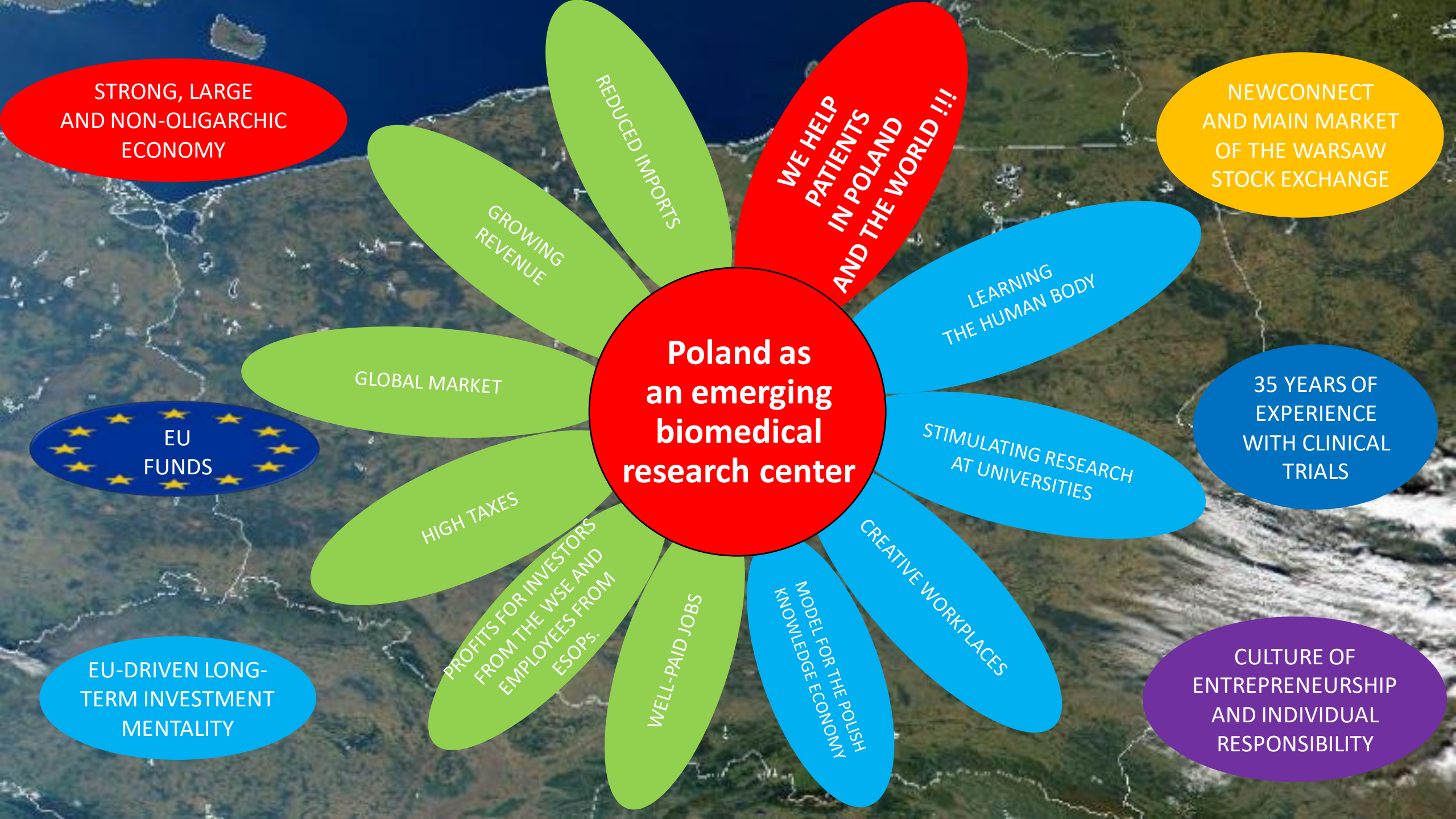
Regulatory knowledge

Specialized investors

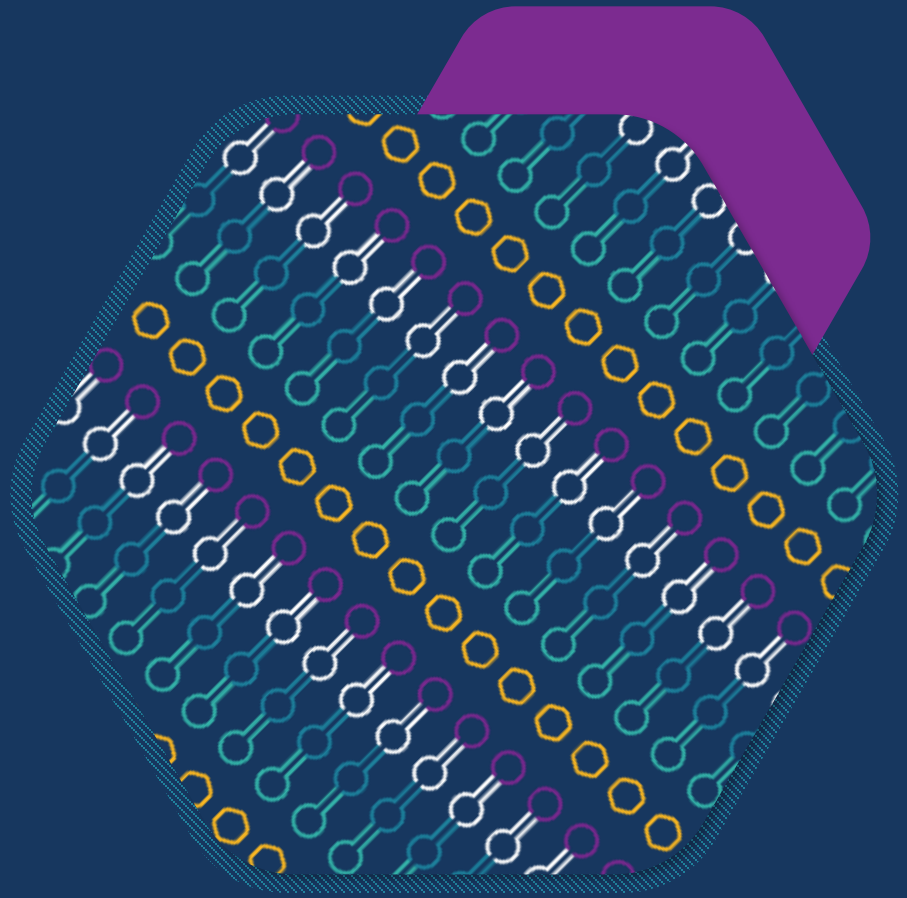
Global distribution network

Government support for R&D in biotechnology

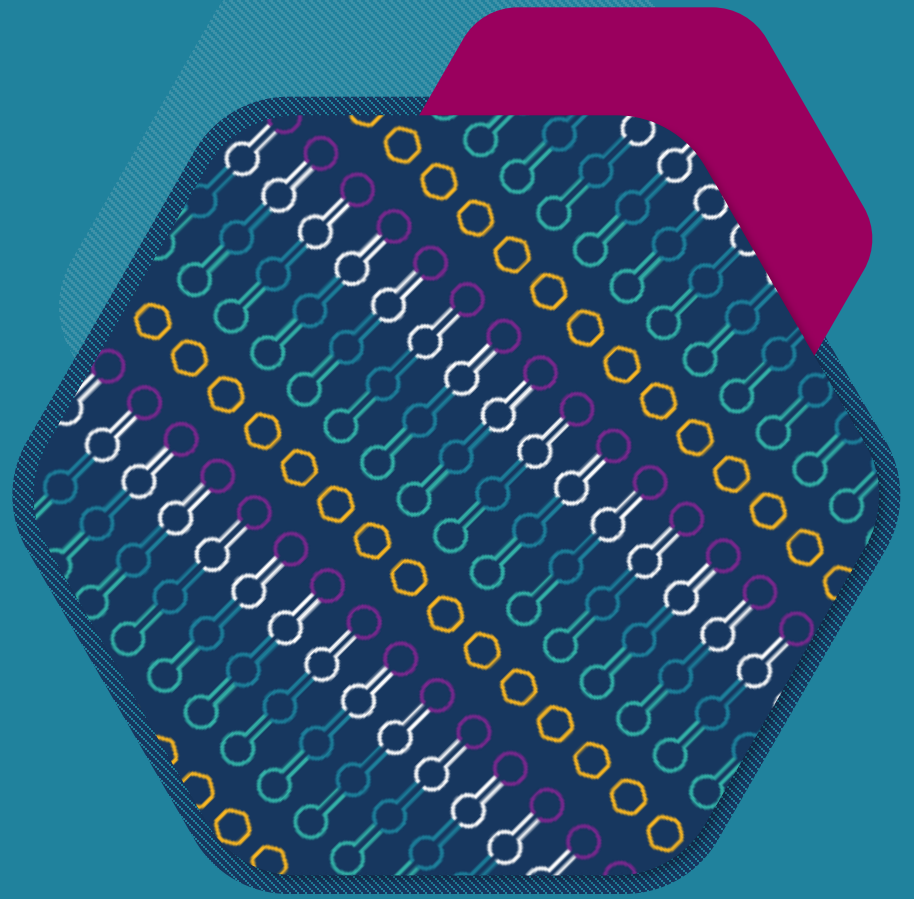
Reverse brain drain


STRONG, LARGE AND NON-OLIGARCHIC ECONOMY
REDUCED IMPORTS
GROWING REVENUE
WE HELP PATIENTS IN POLAND AND THE WORLD !!!
NEWCONNECT AND MAIN MARKET OF THE WARSAW STOCK EXCHANGE
LEARNING THE HUMAN BODY
GLOBAL MARKET
Poland as an emerging biomedical research center
35 YEARS OF EXPERIENCE WITH CLINICAL TRIALS
EU FUNDS
STIMULATING RESEARCH AT UNIVERSITIES
HIGH TAXES
CREATIVE WORKPLACES
PROFITS FOR INVESTORS FROM THE WSE AND EMPLOYEES FROM ESOPs.
WELL-PAID JOBS
MODEL FOR THE POLISH KNOWLEDGE ECONOMY
EU-DRIVEN LONG-TERM INVESTMENT MENTALITY
CULTURE OF ENTREPRENEURSHIP AND INDIVIDUAL RESPONSIBILITY

Thank you



APPENDIX



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Developing therapeutics
at the forefront of oncology

Discovered in CEE - available in CEE?

- No CEE biotech or pharmaceutical company will fund a full drug development cycle alone
- Partnerships with multinationals are needed
- Corporations need to have a consistent pricing policy in developed markets
- Reimbursement level in CEE is insufficient to cover prices of many breakthrough drugs
- For partnering agreements for drugs discovered in CEE, creative schemes are needed to ensure future access to drugs for CEE patients at a price level acceptable to the CEE payers
  - Example method - increased royalties to the licensor in CEE and use of the surplus to subsidize accessibility
  - Condition of the R&D grant for the project

Poland - a strong partner for the international biomedical industry

Large potential

- 20 largest economy in the world by PPP
- 40 million people (including 2 milion Ukrainian refugees)
- The fastest growing developed economy in the world since 1989

Low risk and long-term stability

- Debt/GDP <55%
- EU and NATO member (quality, security, environment)
- Member of the European Patent Organization
- Transparent legal system

Dynamic scientific developments including biotech

- 40 000 scientists in biomedial research
- Fast-growing R&D thanks to GDP growth and EU funding
- Experienced scientific returnees and international specialists
- Fast growing biotech sector

Affordable costs

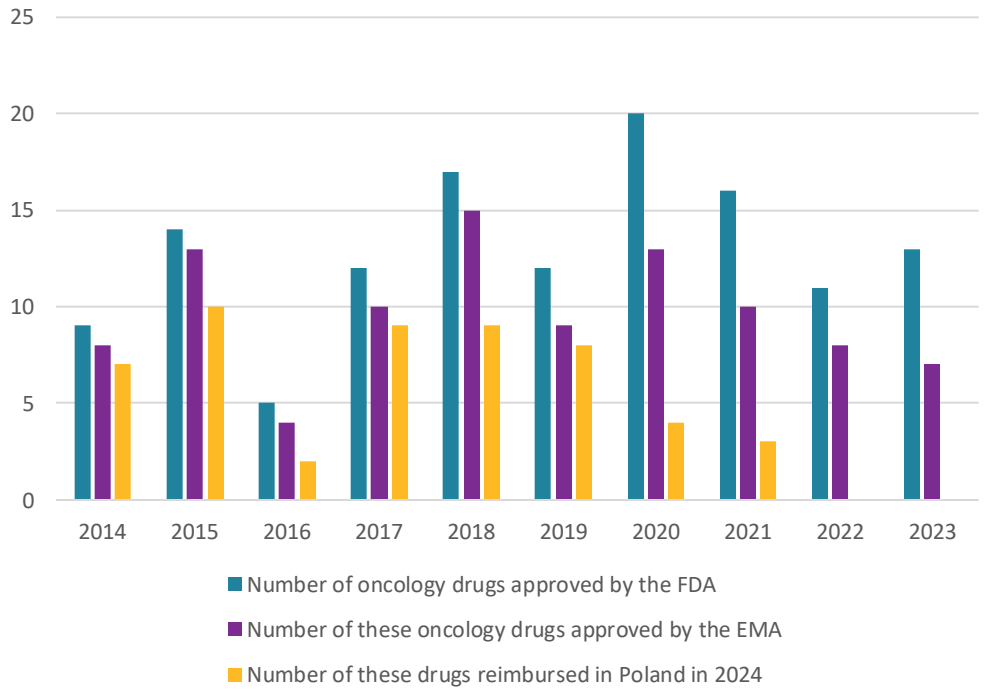
- Cost of living 50-60% lower than in major biotech hubs
- Low income taxes

Good project management and communications

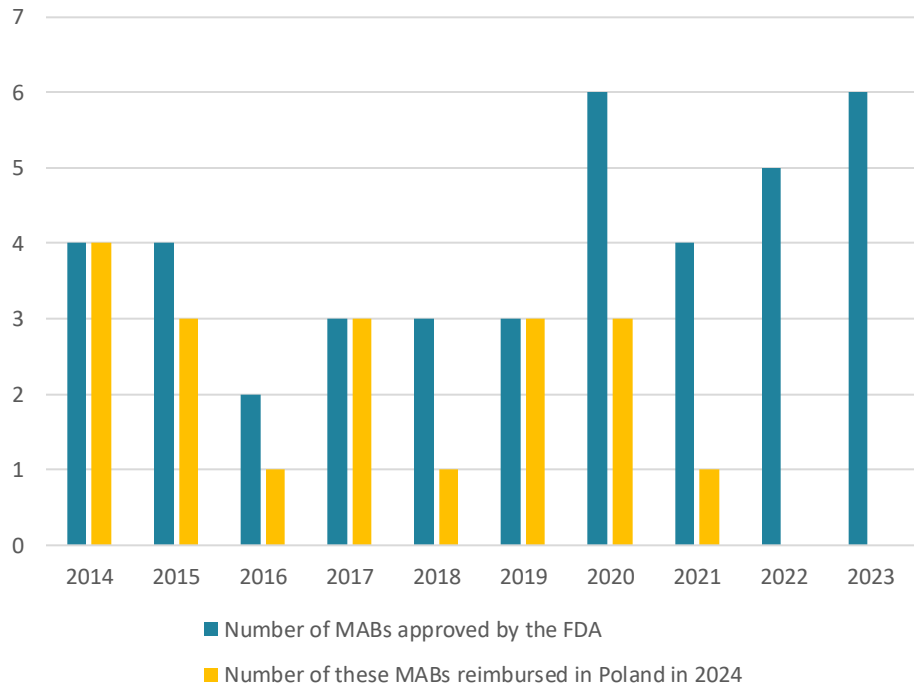
- Good logistics (flights, highways)
- Geographical proximity
- English is the standard internal language at biotech companies
- Well-established collaboration practices
- Low corruption index

Poland is not the optimum territory for efficient enrollment of immunotherapy-naïve patients – usually a three-year gap in full reimbursement vs. the USA

Availability and reimbursement of FDA-approved oncology drugs in PL



Availability and reimbursement of FDA-approved monoclonal antibodies in Poland



Availability of modern oncology drugs in Poland

Oncology drugs approved by FDA in years 2014-2024

DRUGS AVAILABLE (REIMBURSED) IN POLAND

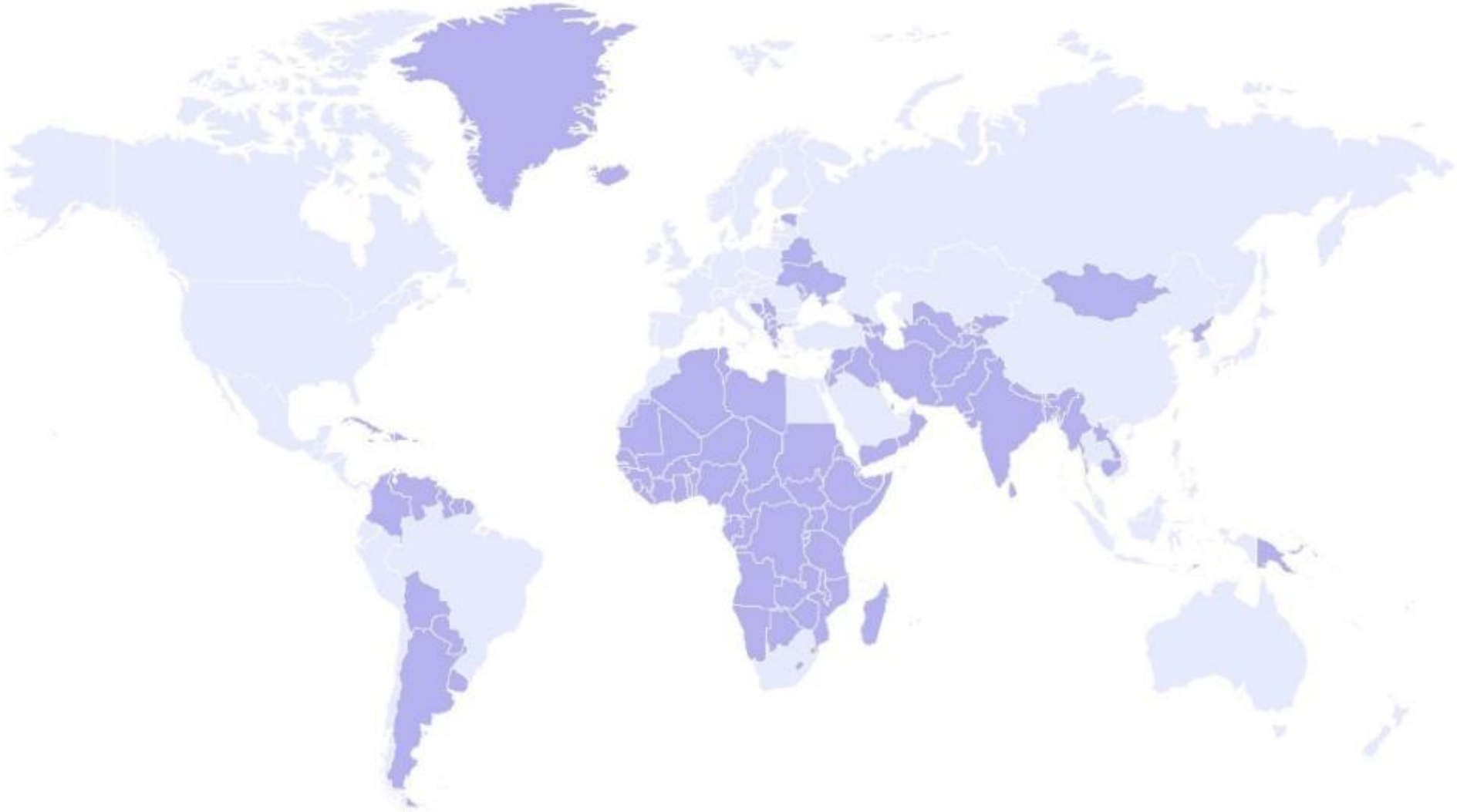
	Drug Name	Active Ingredient	FDA Approval
1.	Scemblix	asciminib	2021
2.	Lumakras	sotorasib	2021
3.	Jemperli	dostarlimab-gxly	2021
4.	Monjuvi	tafasitamab-cxix	2020
5.	Trodelvy	sacituzumab govitecan-hziy	2020
6.	Tukysa	tucatinib	2020
7.	Sarclisa	isatuximab	2020
8.	Enhertu	fam-trastuzumab deruxtecan-nxki	2019
9.	Padcev	enfortumab vedotin-ejfv	2019
10.	Brukinsa	zanubrutinib	2019
11.	Inrebic	fedratinib	2019
12.	Rozlytrek	entrectinib	2019
13.	Nubeqa	darolutamide	2019
14.	Polivy	polatuzumab vedotin-piiq	2019
15.	Piqray	alpelisib	2019
16.	Xospata	gilteritinib	2018
17.	Vitrakvi	larotrectinib	2018
18.	Lorbrena	lorlatinib	2018
19.	Talzenna	talazoparib	2018
20.	Libtayo	cemiplimab-rwlc	2018
21.	Braftovi	encorafenib	2018
22.	Mektovi	binimetinib	2018
23.	Erleada	apalutamide	2018
24.	Lutathera	lutetium Lu 177 dotatate	2018
25.	Calquence	acalabrutinib	2017
26.	Verzenio	abemaciclib	2017
27.	Besponsa	inotuzumab ozogamicin	2017
28.	Imfinzi	durvalumab	2017
29.	Rydapt	midostaurin	2017
30.	Alunbrig	brigatinib	2017
31.	Zejula	niraparib	2017
32.	Bavencio	avelumab	2017
33.	Kisqali	ribociclib	2017
34.	Tecentriq	atezolizumab	2016
35.	Venclexta	venetoclax	2016
36.	Alecensa	alectinib	2015
37.	Empliciti	elotuzumab	2015
38.	Ninlaro	ixazomib	2015
39.	Darzalex	daratumumab	2015
40.	Tagrisso	osimertinib	2015
41.	Cotellic	cobimetinib	2015
42.	Yondelis	trabectedin	2015
43.	Lonsurf	trifluridine and tipiracil	2015
44.	Qarziba / Unituxin	dinutuximab	2015
45.	Ibrance	palbociclib	2015
46.	Cyramza	Ramucirumab	2014
47.	Blincyto	Blinatumomab	2014
48.	Zykadia	Ceritinib	2014
49.	Akynzeo	Netupitant and palonosetron	2014
50.	Opdivo	Nivolumab	2014
51.	Olaparib	Lynparza	2014
52.	Keytruda	Pembrolizumab	2014

DRUGS UNAVAILABLE NOT (REIMBURSED) IN POLAND

	Drug Name	Active Ingredient	FDA Approval
1.	Ogsiveo	nirogacestat	2023
2.	Truqap	capivasertib	2023
3.	Augtyro	repotrectinib	2023
4.	Fruzaqla	fruquintinib	2023
5.	Loqtorzi	toripalimab-tpzi	2023
6.	Ojjaara	momelotinib	2023
7.	Elrexfio	elranatamab-bcmm	2023
8.	Talvey	talquetamab-tgvs	2023
9.	Vanflyta	quizartinib	2023
10.	Columvi	glofitamab-gxbm	2023
11.	Epkinly	epcoritamab-bysp	2023
12.	Zynyz	retifanlimab-dlwr	2023
13.	Jaypirca	pirtobrutinib	2023
14.	Lunsumio	mosunetuzumab-axgb	2022
15.	Krazati	adagrasib	2022
16.	Rezlidhia	olutasidenib	2022
17.	Elahere	mirvetuximab soravtansine-gynx	2022
18.	Tecvayli	teclistamab-cqyv	2022
19.	Imjudo	tremelimumab	2022
20.	Lytgobi	futibatinib	2022
21.	Pluvicto	lutetium (177Lu) vipivotide tetraxetan	2022
22.	Opdualag	nivolumab and relatlimab-rmbw	2022
23.	Vonjo	pacritinib	2022
24.	Kimmtrak	tebentafusp-tebn	2022
25.	Pylarify	piflufolastat F 18	2021
26.	Cytalux	pafolacianine	2021
27.	Tivdak	tisotumab vedotin-tftv	2021
28.	Exkivity	mobocertinib	2021
29.	Rylaze	asparaginase erwinia chrysanthemi (recombinant)-rywn	2021
30.	Truseltiq	infigratinib	2021
31.	Rybrevant	amivantamab-vmjw	2021
32.	Zynlonta	loncastuximab tesirine-lpyl	2021
33.	Fotivda	tivozanib	2021
34.	Pepaxto	melphalan flufenamide	2021
35.	Cosela	trilaciclib	2021
36.	Ukoniq	umbralisib	2021
37.	Tepmetko	tepotinib	2021
38.	Orgovyx	relugolix	2020
39.	Margenza	margetuximab (anti-HER2 mAb	2020
40.	Danyelza	naxitamab-gqgk	2020
41.	Gavreto	pralsetinib	2020
42.	Detectnet	copper Cu 64 dotatate	2020
43.	Blenrep	belantamab mafodotin-blmf	2020
44.	Zepzelca	lurbinectedin	2020
45.	Cerianna	fluoroestradiol F18	2020
46.	Qinlock	ripretinib	2020
47.	Retevmo	selpercatinib	2020
48.	Tabrecta	capmatinib	2020
49.	Pemazyre	pemigatinib	2020
50.	Koselugo	selumetinib	2020
51.	Tazverik	tazemetostat	2020
52.	Ayvakit	avapritinib	2020
53.	Gallium 68 PSMA-11	Gallium 68 PSMA-11	2020
54.	Ga-68-DOTATOC	Ga-68-DOTATOC	2019
55.	Turalio	pexidartinib	2019
56.	Xpovio	selinexor	2019
57.	Balversa	erdafitinib	2019
58.	Elzonris	tagraxofusp-erzs	2018
59.	Asparlas	calaspargase pegol-mknl	2018
60.	Daurismo	glasdegib	2018
61.	Vizimpro	dacomitinib	2018
62.	Copiktra	duvelisib	2018
63.	Lumoxiti	moxetumomab pasudotox-tdfk	2018
64.	Poteligeo	mogamulizumab-kpkc	2018
65.	Tibsovo	ivosidenib	2018
66.	Aliqopa	copanlisib	2017
67.	Idhifa	enasidenib	2017
68.	Nerlynx	neratinib maleate	2017
69.	Rubraca	rucaparib	2016
70.	Lartruvo	olaratumab	2016
71.	Axumin	flucidovine F 18	2016
72.	Portrazza	necitumumab	2015
73.	Odomzo	sonidegib	2015
74.	Farydak	panobinostat	2015
75.	Lenvima	lenvatinib	2015
76.	Beleodaq	Belinostat	2014
77.	Zydelig	Idelalisib	2014

The majority of the most frequently prescribed modern drugs (including IO therapies) are available for patients in Poland and reimbursed by the healthcare system

Countries where key PD-1 Abs are currently unavailable: Potential recruitment of immunotherapy-naïve patients



Source: Evotec

Ryvu's history of corporate development

2007-2014

2007: Selvita, a hybrid biotechnology company, a combination of service segment (CRO) and innovative drug discovery

2014: IPO on the WSE

2019

Corporate division, spin-off of Selvita (services segment) from Ryvu Therapeutics

>250 mUSD increase in value for Ryvu shareholders

2019-2022

SEL24
- Successfully completed phase I clinical trial in AML
- Positive Phase II clinical data
- Cohort expansion among AML patients with IDH mutations

RVU120
- Preliminary positive clinical and preclinical phase I
- Administration of drug to first patient in phase I/II trial in solid tumors

CORPORATE DEVELOPMENT PLAN:

RVU120
- Phase II clinical trial of RVU120, as monotherapy, in AML/HR-MDS, with a potential strategy for rapid market introduction
- Initiation of Phase I/II clinical development of RVU 120 in combination regimens and monotherapy in other indications

2022-2024

SEL24 (MEN1703)
- Support for further clinical development conducted by the Menarini Group

EARLY PHASE PROJECTS
- Complete preclinical development and enter Phase I clinical trials of one
- Strengthening the development of the Synthetic Lethality Platform