



IMS Health & Quintiles are now



Konference Onkológia na Slovensku

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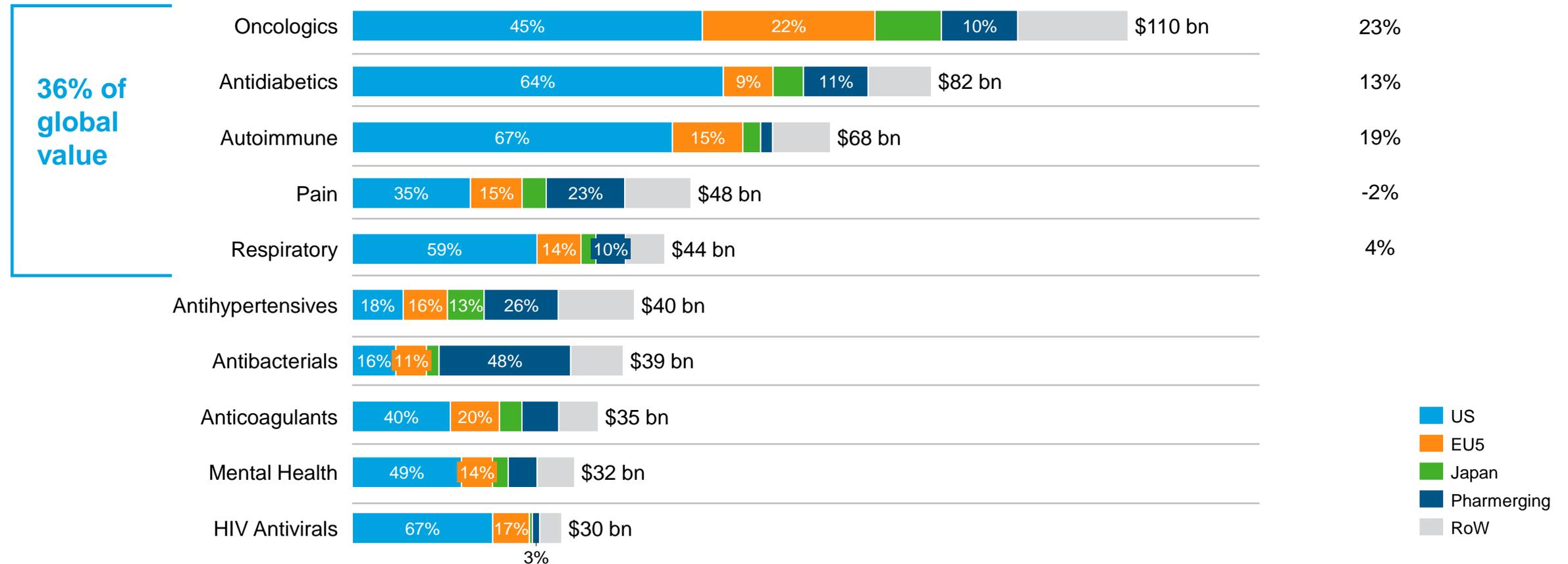
Bratislava, 30 May 2019

Selected global Oncology trends

A third of global value comes from five therapy areas and they contribute over 55% of global growth

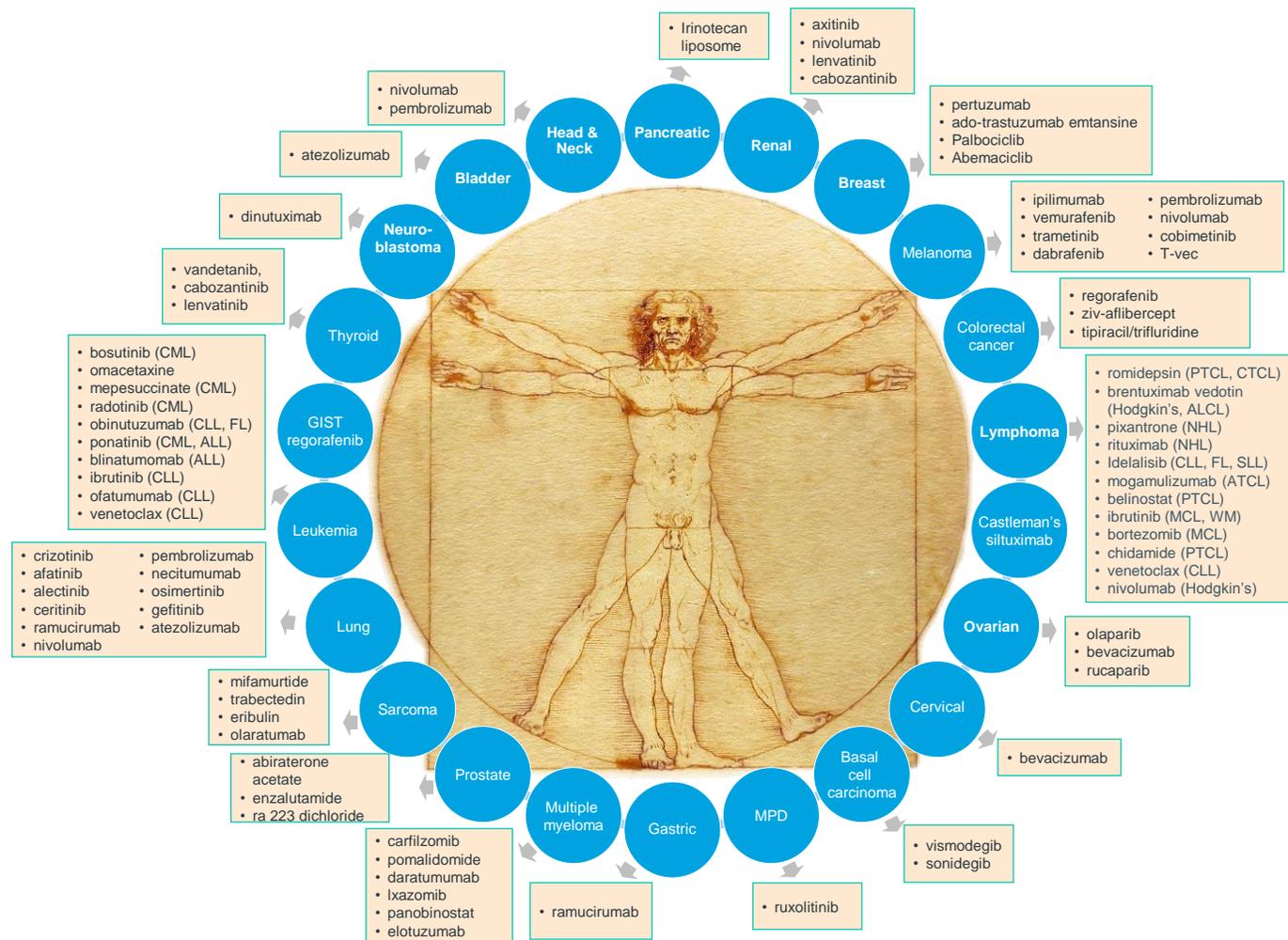
Therapy area sales (2017) bn USD

Share of global growth 2017

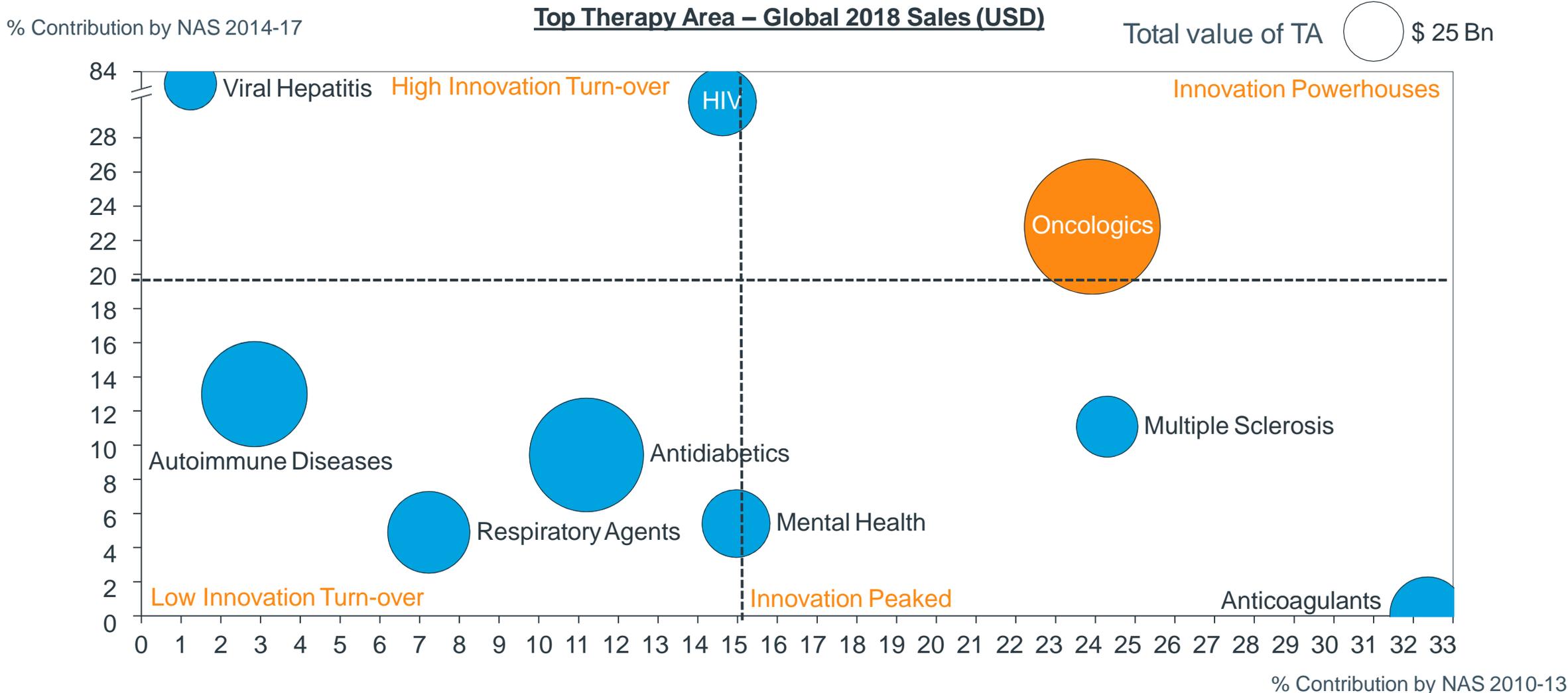


The cancer treatment landscape has been majorly transformed since 2011

New Active Substance Launches from 2011 by Indication



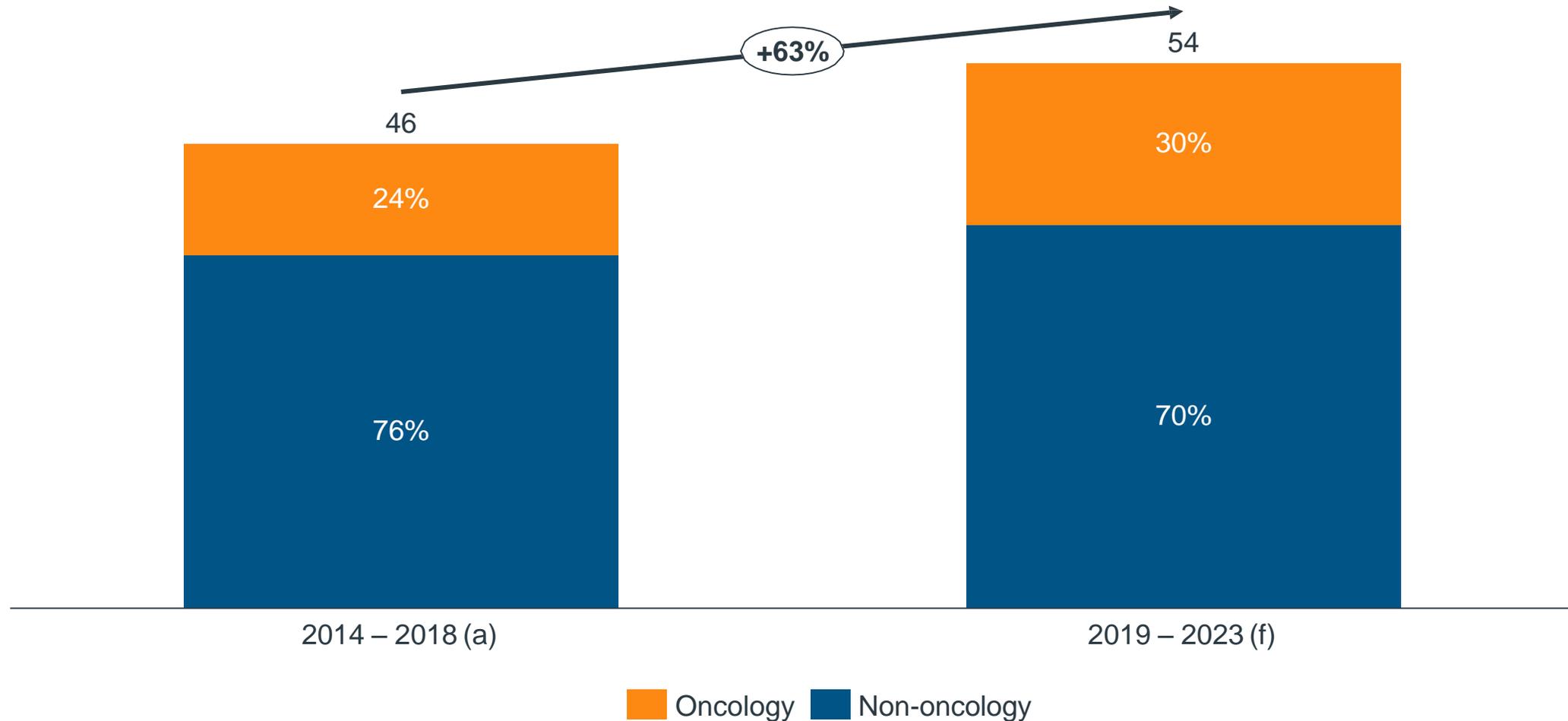
Oncology is the innovation powerhouse of the pharmaceutical industry



IQVIA forecasts an average of 17 new oncology products per annum



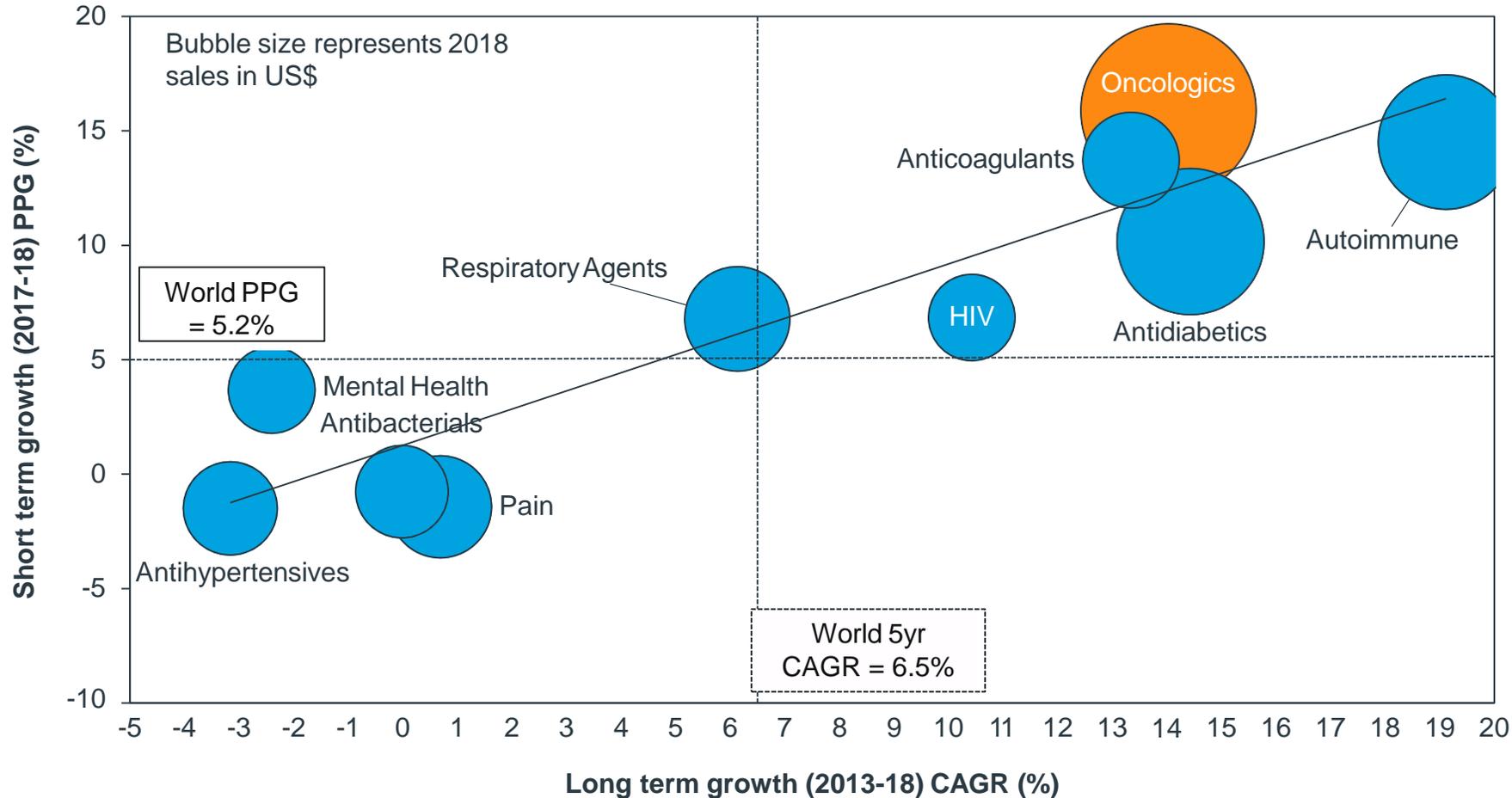
FDA NCE average approvals 2014-2023





Oncology is the #1 growth driver and the largest therapy area

Top-20 therapy area growth dynamics



Top-5 therapy area ranking

#	Therapy area	Growth (PPG)	
		2016 - 2017	2017 - 2018
1	Oncology	12%	16%
2	Autoimmune	17%	14.5%
3	Anticoagulant	13%	14%
4	Antidiabetics	9%	10%
5	HIV	9%	7%

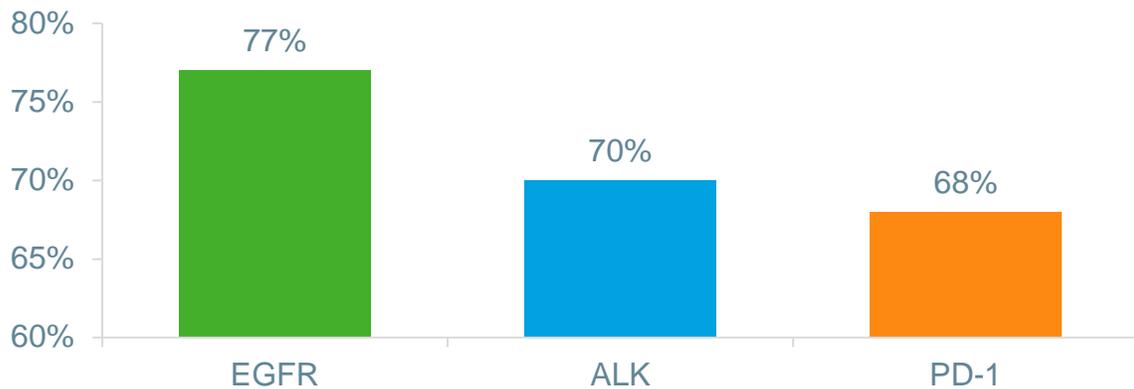
Note: Chinese Medicines have been excluded; growth in LCUS\$, Rx only Source: IQVIA MIDAS MAT Q4 2018



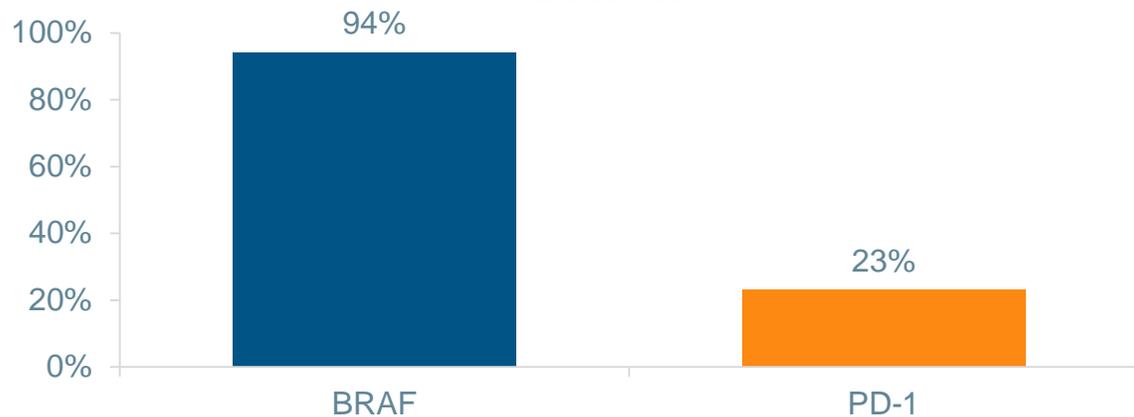
Many indications are becoming more and more complex and stratified through predictive biomarkers

% of Patients Tested by Biomarker and Cancer

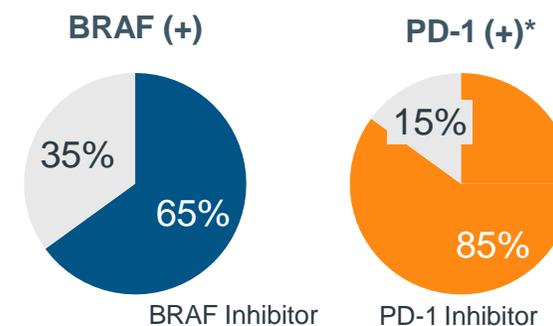
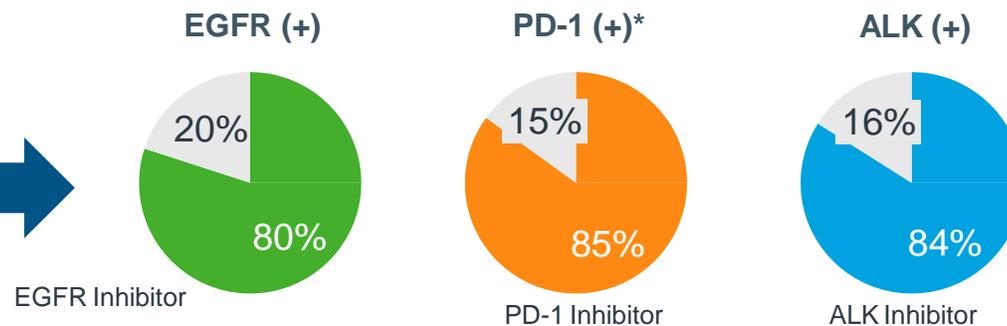
NSCLC



Melanoma



Once tested positive for that specific biomarker, the majority of the patients receive a drug targeting it



PD-1 inhibitors used in 31% of all NSCLC patients

PD-1 inhibitors are carving out their segment not necessarily driven by the biomarker

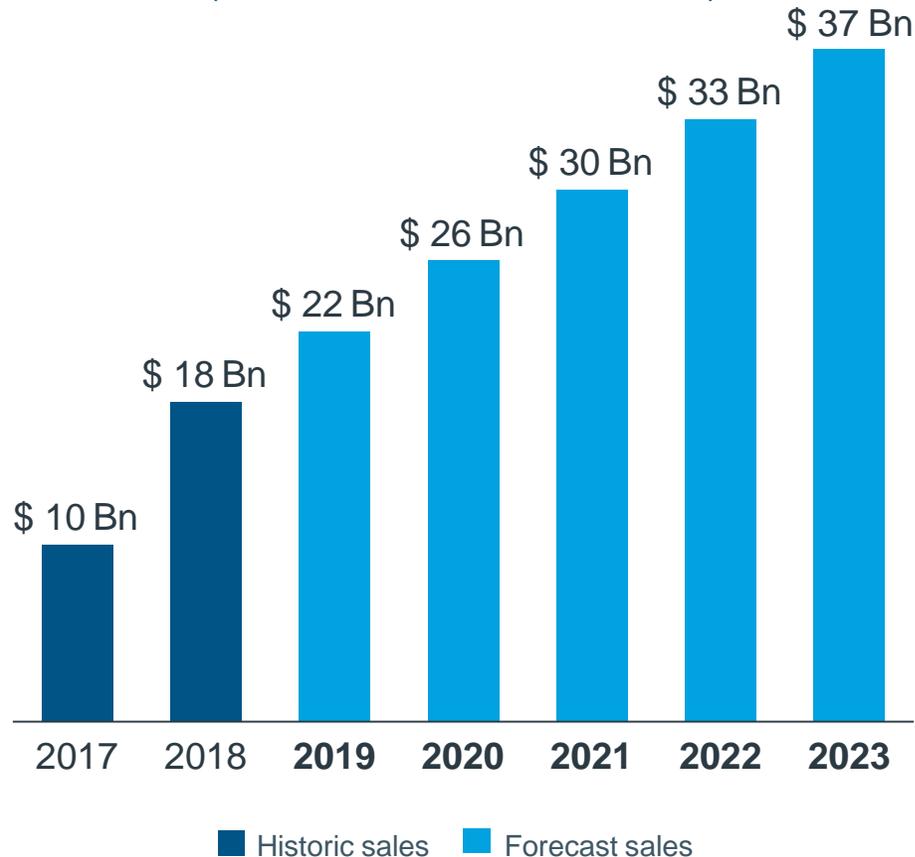
Note: PD-1 Positive defined as >50% expression



Immuno-oncology has become the major focus of growth

Checkpoint inhibitors expected to reach ~\$30 billion globally by 2022

Checkpoint inhibitor forecast
(Sales US\$ Bn, 2018-2022)



Immuno-oncology development highlights

>300 immuno-oncology therapies in development, phase 1 through pre-registration

60 immuno-oncology mechanisms investigated in early-stage pipeline vs. 4* in late-stage pipeline

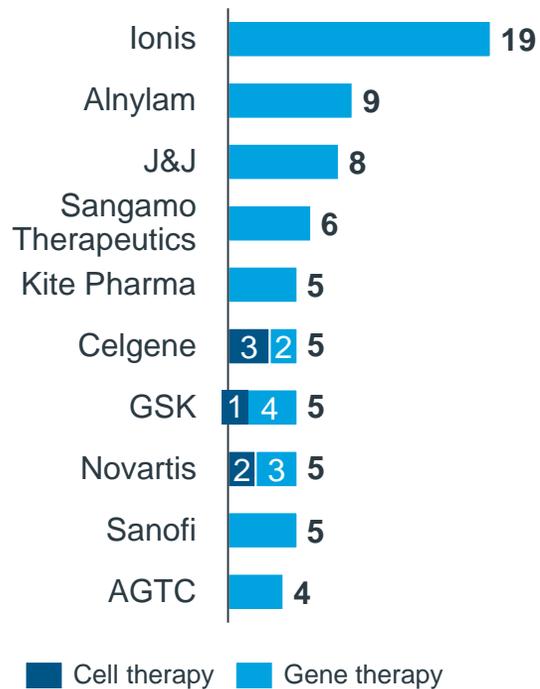
1/3 of IO phase 1 & 2 trials accounted for by anti-PD-1/-L1 and CD19 modulators

Immuno-oncology products have shown promise in a small number of haematological cancers

CAR T-cells, RNAi and CRISPR gene editing are the new therapy approaches – small companies dominate discovery

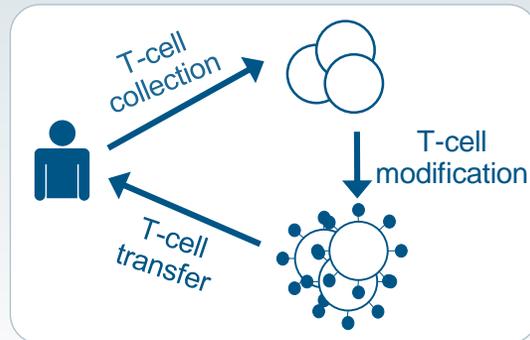
Number of pipeline in cell and gene therapy by Top 10 companies

Phase II to Reg



CAR T-cells

...are modified cells with engineered receptors, which **graft an arbitrary specificity onto an immune effector cell**

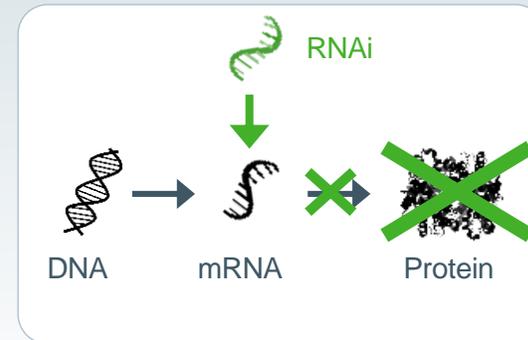


Key companies/partners
Novartis, Celgene, Merck, Amgen, Pfizer, Servier, GSK, Gilead/Kite Pharma, Juno, Cellectis, Celyad

Key therapy areas
Leukemia, cancer

RNAi (RNA interference/silencing)

...is an **efficient and stable** process in which RNA molecules **inhibit gene expression or translation**

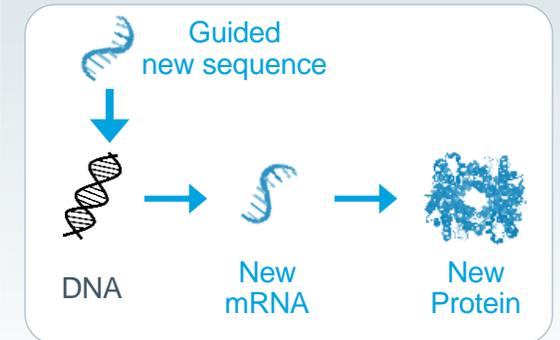


Key companies/partners
Ionis, Alnylam, Sanofi Genzyme, BMS, Quark Pharmaceuticals, Sylentis

Key therapy areas
Cancer, hepatitis, ophthalmological disorder

Gene editing technologies, including CRISPR

...are techniques which are **more powerful, rapid and less expensive** than any previously invented process



Key companies/partners
Caribou Biosciences, CRISPR Therap., Editas Medicine, Intelia Therap., Regeneron, Novartis, Vertex, Bayer, Juno

Key therapy areas
Rare genetic diseases, cancer, HIV, organ transplants

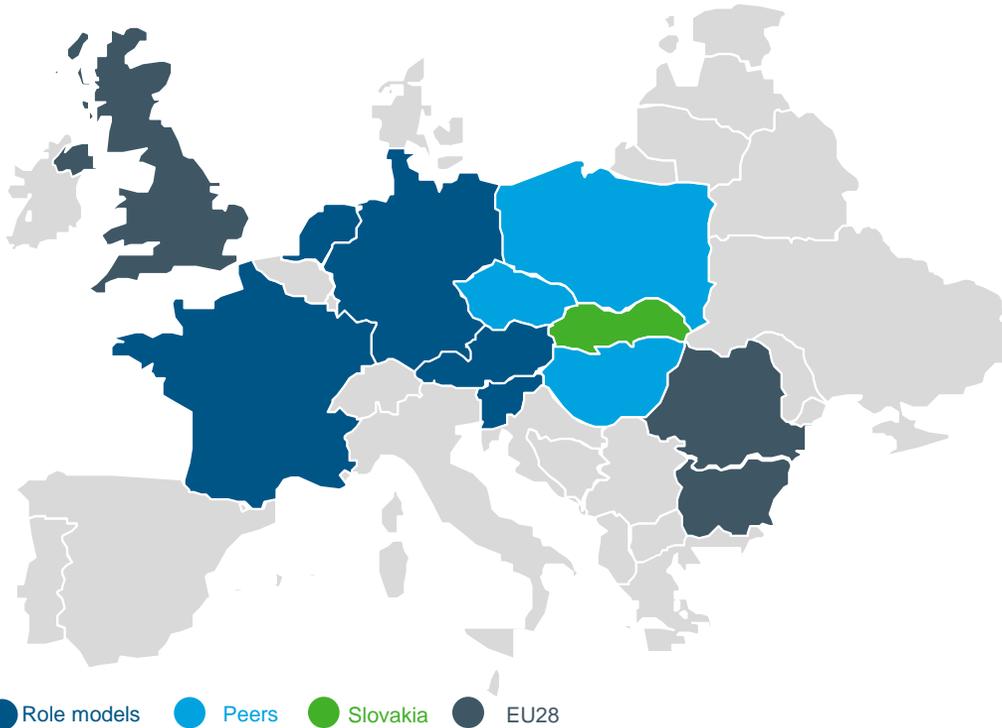
Look in recent past – Slovakia in 2018

Oncology landscape in Slovakia has been benchmarked with several EU countries to help with assessment of its development

Country benchmarking



Geographical coverage in the report¹⁾



Country	Market performance	Cancer burden	Economic assessment	Quantitative onco analysis	Qualitative onco analysis
● Austria	Role models	✓	✓	✓	✓
● France	Role models	✓	✓	✓	
● Germany	Role models	✓	✓	✓	✓
● Netherlands	Role models	✓	✓	✓	✓
● Slovenia	Role models	✓	✓	✓	✓
● Czechia	Peers	✓	✓	✓	✓
● Hungary	Peers	✓	✓	✓	✓
● Poland	Peers	✓	✓	✓	✓
● Bulgaria	EU28	✓		✓	✓
● Romania	EU28	✓		✓	
● UK	EU28	✓	✓		

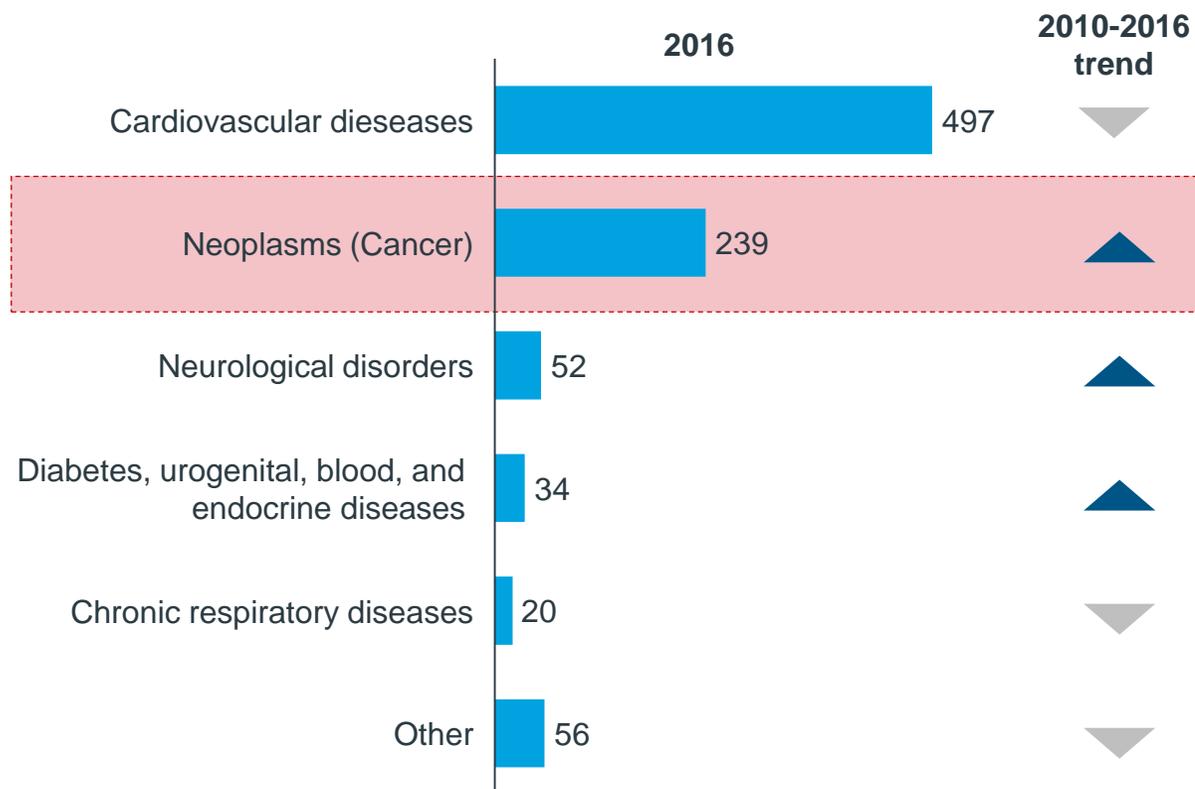
1) Selection of the scope countries has been defined by the Patient Association – Nie Rakovine Onkologia na Slovensku

Cancer to become the top killing disease in Slovakia

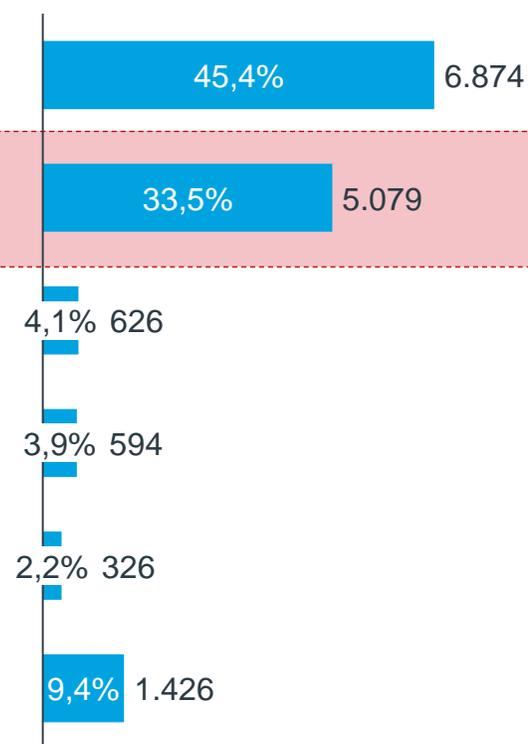
Causes of death – Slovakia



Rate of deaths by causes, 2016 [per 100k inhabitants]²⁾



Years of life lost, 2016 [per 100k inhabitants]²⁾



Commentary

- In Slovakia, and still globally, Cardiovascular diseases are top deadly diseases, causing the most deaths
- At the same time, the world is seeing fatality rates of CV fall, while Cancer rates grow, which will potentially bring Cancer related deaths in Slovakia to the top
- Cancer has already become top deadly disease in some of the EU countries – France (since 1998), UK, Italy, Spain and many more¹⁾
- **This report has been designed to assess, if Slovak healthcare system is ready for the challenge...**

Source: 1) European Heart Journal, Volume 37, Issue 42 - Cardiovascular disease in Europe: epidemiological update 2016 2) Global Health Burden - <http://ghdx.healthdata.org>

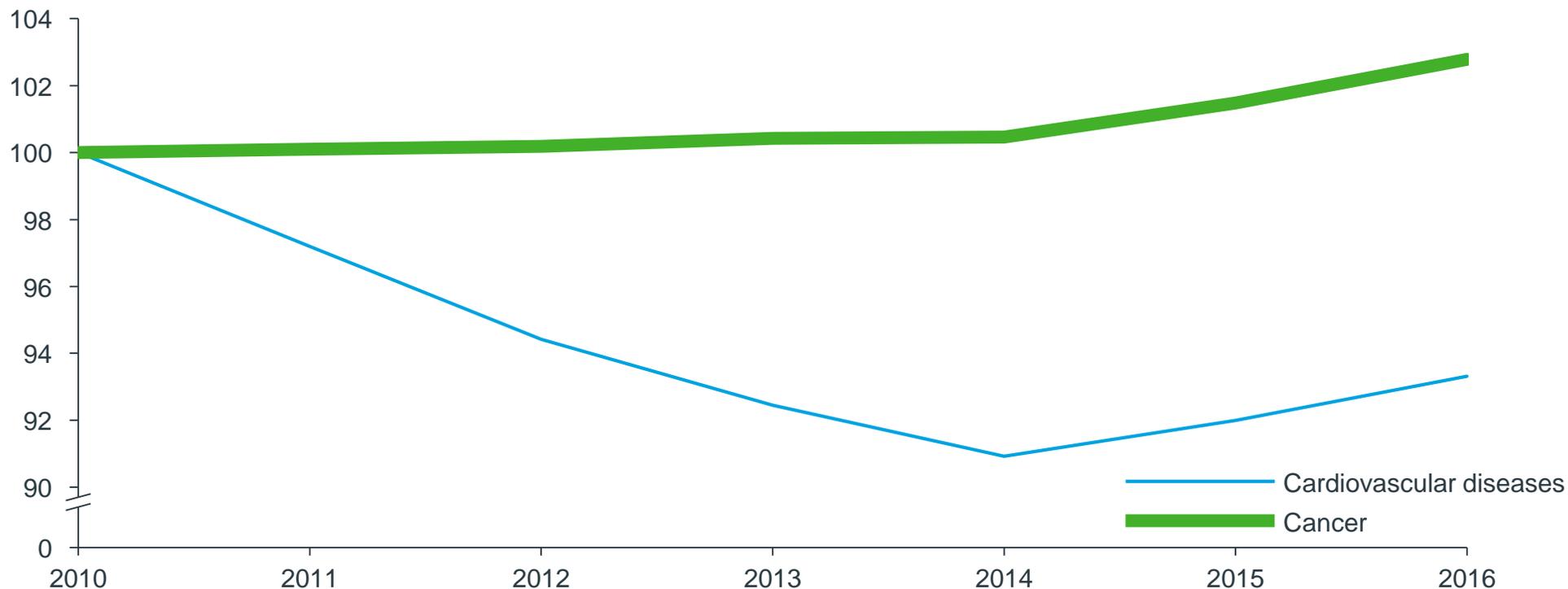
...and while cardio is going down thanks to better access to innovative drugs, oncology threat is growing

Cancer impact on society – Slovakia



Years of life lost (YLLs) index, 2010-2016

[2010 as a 100% index]



Commentary

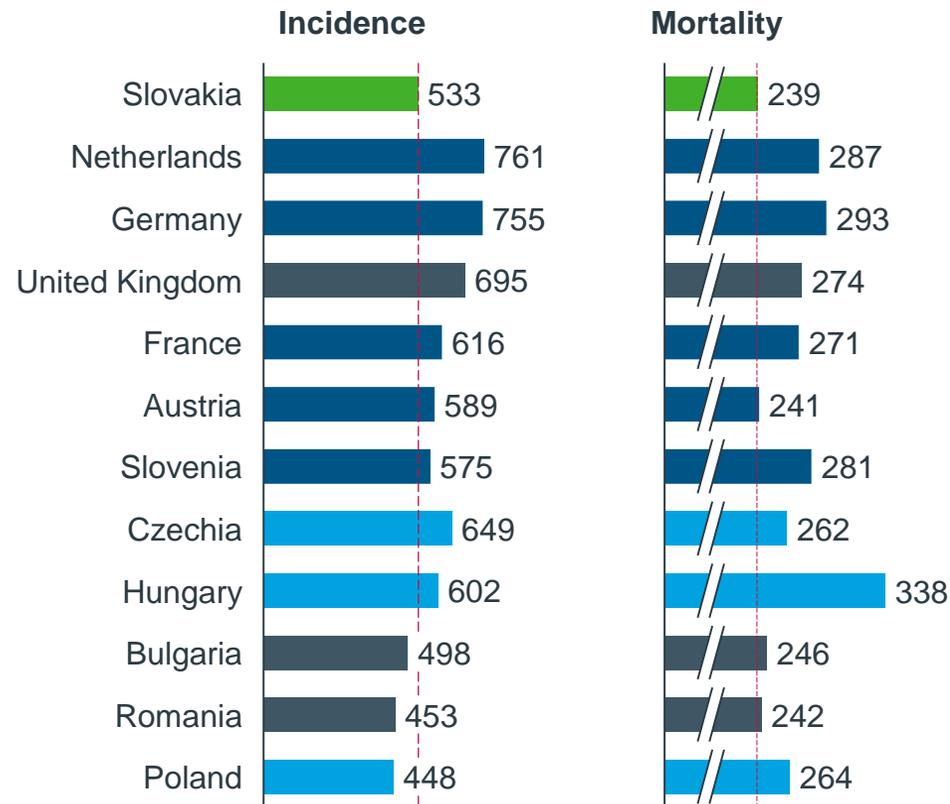
- In Slovakia, we already see the change in CV and Cancer Years of Life lost trend – clearly showing the growth in cancer burden
- Such development, shows that Slovakia should also be expected to join the Western Europe countries, that successfully dealt with CV risks, but will need to be increasingly focused on support and treatment of neoplasms affected patients
- **This report has been designed to assess, if Slovak healthcare system is ready for the challenge...**

Slovakia with one of the lowest cancer incidence and mortality – numbers are however mainly influenced by level of diagnostics

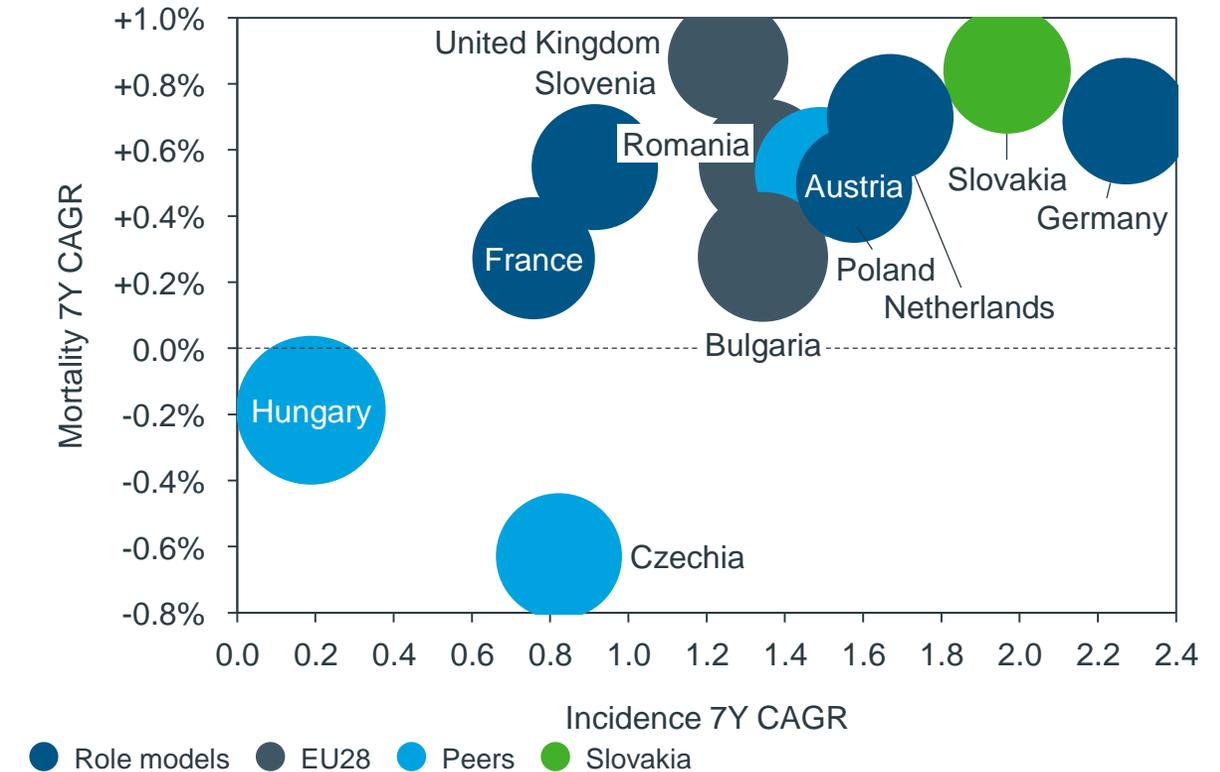
Cancer epidemiology – International



Cancer incidence and mortality per country, 2016 [per 100k inhabitants]



Cancer epidemiology dynamics, 2010-2016 [%]



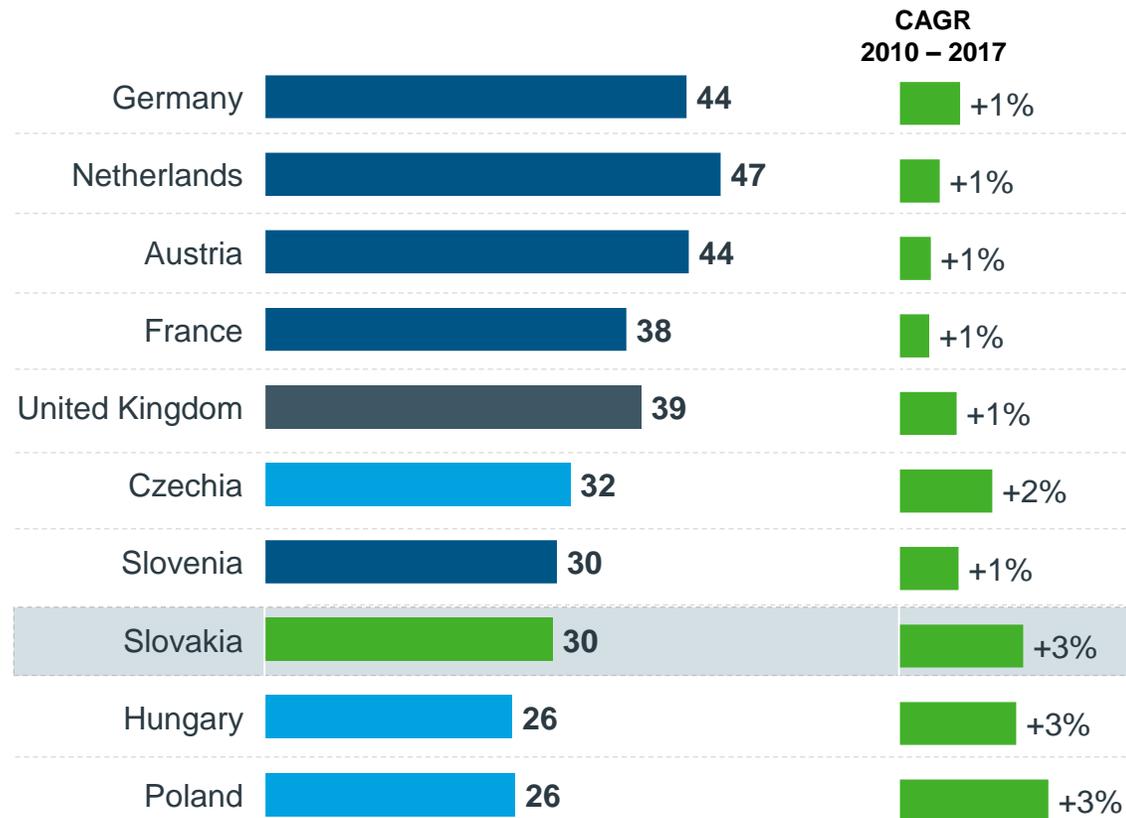
Source: Global Health Burden - <http://ghdx.healthdata.org>
Onkologia na Slovensku

Even though SK was catching up with role models in terms of GDP per capita, it did not follow with healthcare investments

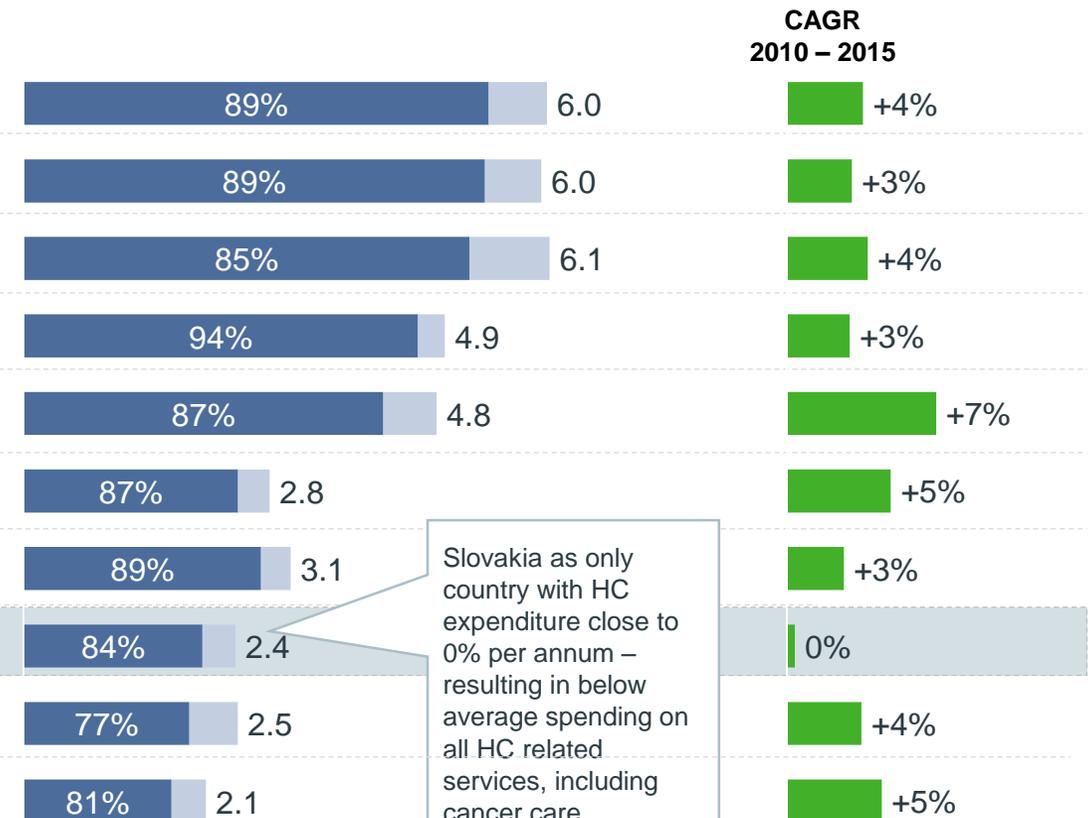
Healthcare financing



GDP per capita, 2017 [2010 PPP, USD ths, %]



Total healthcare cost per capita¹⁾, 2015 [USD ths, %]



Slovakia as only country with HC expenditure close to 0% per annum – resulting in below average spending on all HC related services, including cancer care

● Role models ● Peers ● Slovakia ● EU28

1) Includes public and private expenditure on services provided by healthcare system during the whole chain of care = total expenditure on health

Source: OECD (2018), Health spending (indicator). doi: 10.1787/8643de7e-en (Accessed on 11 June 2018), World Health Organization Global Health Expenditure and GDPA database (<http://apps.who.int/nha/database>)

At the same time, onco market in SK almost did not grow in value suggesting potential innovation problems

Onco market and growth; MAT 03/2018



	Value [EUR m]	Hospital share [%]	3y CAGR [%]	Volume [SU m]	Hospital share [%]	3y CAGR [%]
Germany	6,938	32.0%	+14.2%	416.3	4.4%	+2.0%
France	5,828	60.5%	+12.5%	379.7	5.9%	+2.9%
Austria	1,005	51.9%	+17.0%	46.0	4.64%	+3.1%
Poland	646	83.6%	+4.8%	152.4	10.3%	+3.8%
Hungary	390	58.8%	+12.8%	46.3	8.3%	+3.9%
Romania	313	37.8%	+2.6%	45.9	3.5%	+4.0%
Bulgaria	226	88.7%	+17.3%	19.9	21.7%	+6.7%
Czechia	378	91.0%	+8.8%	59.9	69.2%	+4.0%
Slovakia	216	53.8%	+1.4%	22.5	57.3%	+2.5%
Netherlands						
Slovenia	117	0.0%	+13.3%	11.9	0.0%	+3.3%

SK recorded lowest volumes out of V4 countries

Commentary

- Growth in value in Slovakia negligible compared with **other benchmark countries** – peers growing with **CAGR ~3-17%**
- Volume **increase in SK lays also in the lowest quartile – lowest among the peers (CZ, HU, PL)**
- Value dynamics in Slovakia, suggests **limited access to newer, more innovative treatments** that are usually priced higher than the market average

● Role models ● Peers ● Slovakia ● EU28

Trend also visible in the oncology drug consumption – SK the only one with decrease in value and zero growth of volumes

Consumption and growth per onco patient



	Value MAT 03/2018 [EUR ths/patient]	CAGR MAT 03/15 – 03/18 [%]	Volume MAT 03/2018 [SU/patient]	CAGR MAT 03/15 – 03/18 [%]
Germany	10.5	+10.8%	631.0	-1.1%
France	14.1	+10.9%	921.5	+1.4%
Austria	18.6	+14.0%	851.7	+0.4%
Poland	3.6	+2.9%	847.9	+2.0%
Hungary	6.5	+12.5%	773.7	+3.6%
Romania	3.5	+1.8%	516.2	+3.2%
Bulgaria	6.1	+16.0%	541.1	+5.5%
Czechia	5.4	+7.2%	849.2	+2.6%
Slovakia	7.3	-1.0%	752.0	+0.1%
Netherlands				
Slovenia	9.6	+12.0%	976.4	+2.1%

SK showed slowest growth of all short-listed countries

Commentary

- Overall, role model countries serve **higher volume per patient while also paying more money for more advanced therapies**
- Slovakia with no change in terms of oncology drugs consumption suggests **growing pressures on access to treatment for local patients – especially since, epidemiology trends suggest stable increase in incidence**

● Role models ● Peers ● Slovakia ● EU28

Source: SUKL, NCZI, MIDAS, IQVIA, values not discounted to real market prices
Onkologia na Slovensku

Innovative immunology molecules are being sold in SK and the country is on the peers average, lagging behind role models

Consumption and growth per onco patient – Immuno-oncology



	Value 2017 [EUR/patient]	CAGR 15-'17 [%]	Volume 2017 [SU/1000 patients]	CAGR 15-'17 [%]
Germany	571.7	99%	512.7	112%
France	1,099.7	94%	1,014.0	104%
Austria	1,732.3	169%	1,124.2	147%
Poland	145.0	725%	114.7	652%
Hungary *	305.1	440%	280.0	399%
Romania**	74.7	311%	78.8	361%
Bulgaria**	294.6	136%	176.7	158%
Czechia	201.4	479%	178.9	504%
Slovakia	98.6	181%	77.0	225%
Netherlands				
Slovenia	435.5	484%	352.1	442%

Commentary

- Evaluating the adoption of most innovative onco molecules, the **role models outperforms dominantly all peers countries**
- Looking on peers, Slovakia shows average numbers – PL, CZH and BG with higher adoption, while RO and HUN

SK is on par with RO, lags behind Peers

● Role models ● Peers ● Slovakia ● EU28 Note: Immunology market defined as Keytruda and Opdivo brands

* Keytruda and Opdivo in HUN are in itemized reimbursement. Drugs are procured centrally under the authority of MNHIF and all consumption data is classified. Stated values are estimated by IQVIA

** CAGR done only for last 2 years due to null values in first year

Market dynamics positions Slovakia as a country with limited innovation and decreasing access to oncology treatments

Onco market dynamics – MAT 03/2015-2018; [EUR m]



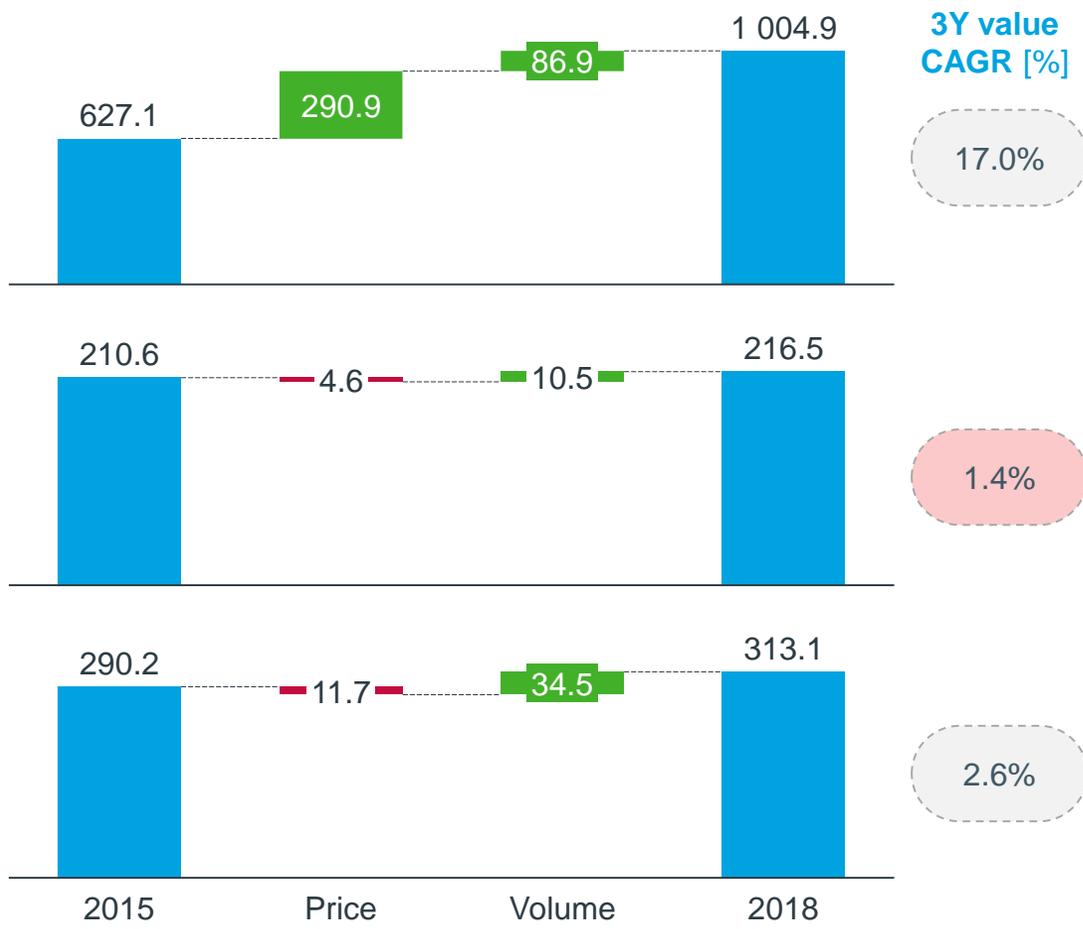
Price driven countries

- Austria
- Germany
- Slovenia
- France

Slovakia

Volume driven countries

- Romania
- Poland
- Czechia



Commentary

Markets with growing access to more advanced treatments

- Greatest **growth of average list price** (around 40%) in last 3y
- Level of **biosimilars rather low** (around 10%) and their growth is relatively stable

Limited innovation and almost no change in usage of oncology drugs – limiting the access for patients

- **List price decrease** over last 3 years
- Share of **biosimilars around 7%** with annual growth around 1 p.p,
- Negligible growth of the market, driven by slight **increase in volumes of low priced drugs**

Markets with lower innovativeness of oncology, but with increasing access to treatment

- **Stable average list price** or slight decrease (RO)
- **Price decrease** however **not driven by biosimilars** which share remains rather flat (around 15%)

Note: Slovakia for whole years 2015-2018, not MAT 03

In Slovakia, a number of SoC molecules is not categorized and thus much less likely to access

Standard of Care – overview per indication & SK reimbursement status

Lung		Breast		Melanoma		Prostate		Multiple Myeloma		CRC	
Alecensa	✗	Avastin	✓	Cotellic	✗	Jevtana	✗	Darzalex	✗	Avastin	✓
Avastin	✓	Halaven	✗	Keytruda	✗	Xtandi	✓	Farydak	✗	Cyramza	✗
Giotrif	✓	Herceptin	✓	Mekinist	✗	Zoladex	✓	Kyprolis	✗	Erbitux	✓
Iressa	✓	Ibrance	✗	Opdivo	✗	Zytiga	✓	Ninlaro	✗	Stivarga	✗
Keytruda	✗	Kadcyla	✗	Tafinlar	✗			Revlimid	✓	Vectibix	✓
Opdivo	✗	Kisqali	✗	Yervoy	✗			Velcade	✓	Zaltrap	✓
Tagrisso	✗	Perjeta	✗	Zelboraf	✗						
Tarceva	✓	Tyverb	✓								
Tecentriq	✗										
Xalkori	✗										
Zykadia	✗										

Note: Status as of June 2018, Bolded products are present in more than one indication within this analysis

✓ Reimbursed in SK

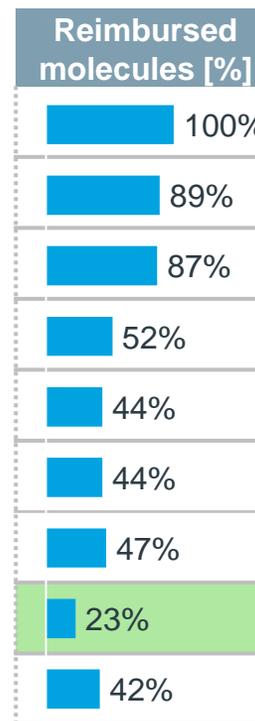
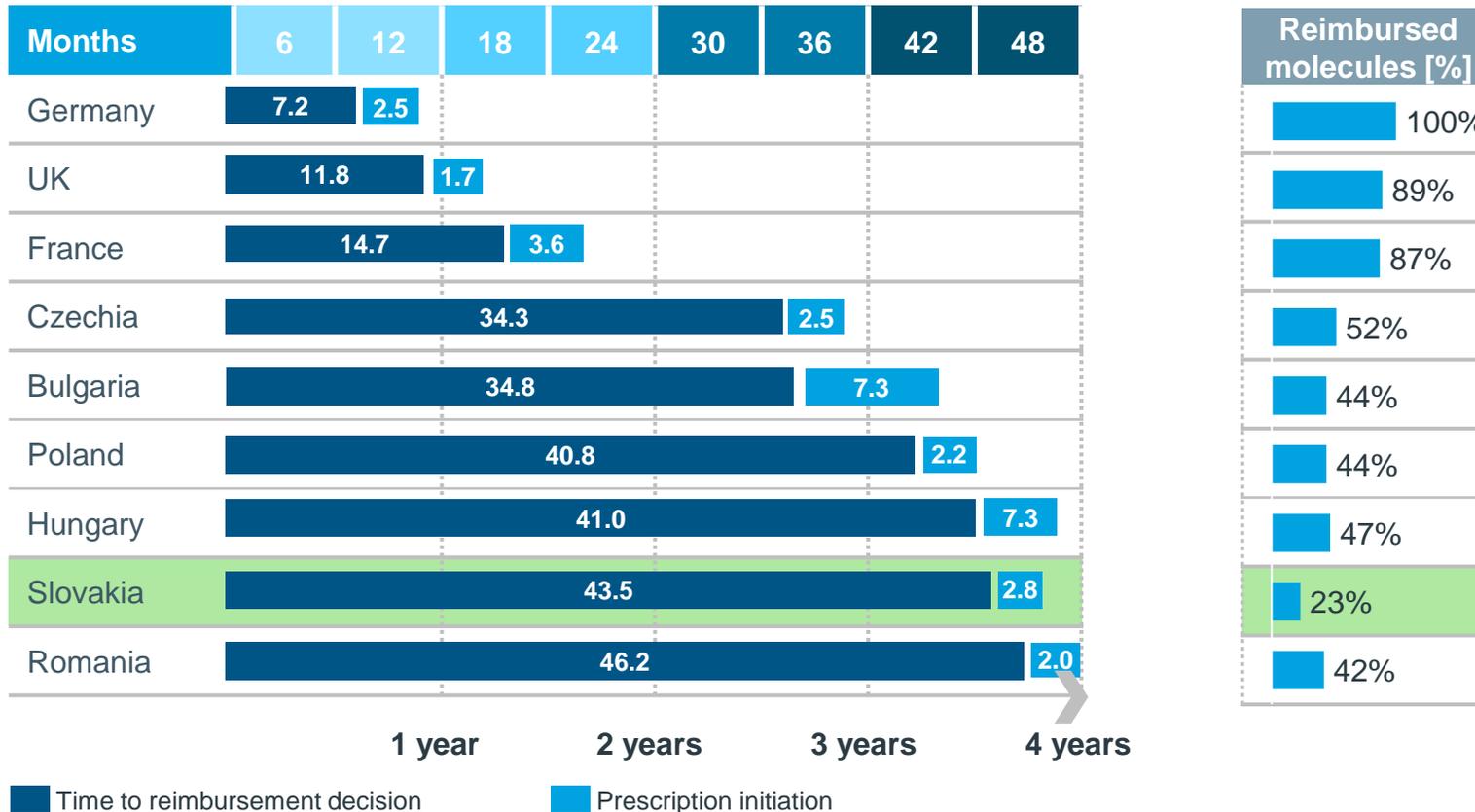
✗ Not reimbursed in SK

PLEASE NOTE THAT EVEN PARTIAL REIMBURSEMENT CONSIDERED AS "REIMBURSED" FOR THE ANALYSIS PURPOSES

Slovakia with lowest rate of reimbursed drugs and patients waiting 4 years to get the treatment that is already available elsewhere

Time to market for oncology drugs

Time to market – From EMA approval to 100% normalized sales



Comments

- Slovakia has the **lowest ratio of reimbursed onco molecules**
- Molecules reimbursed in **Slovakia** show the **one of the biggest delay among evaluated countries**
- When German patient gets the drug average Slovakian patients needs to wait additional average 3 years and in 4 out of 5 instances does not get it in the end
- **Role model countries** have **significantly shorter time to market** of innovative onco molecules while also substantially **greater number of molecules is given the reimbursement**

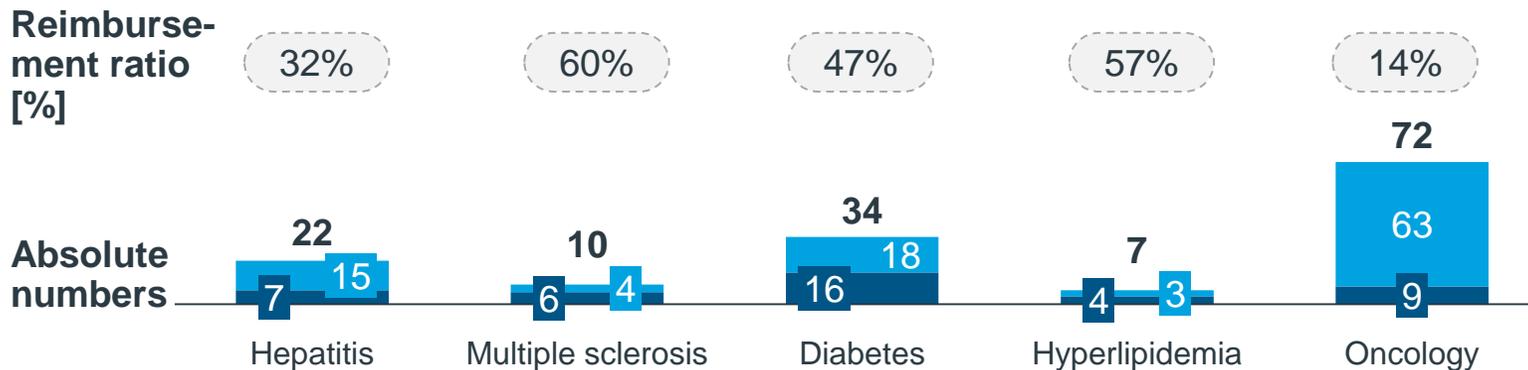
Note: Analysis based on 62 onco molecules approved by EMA from Jan 2009 to Jan 2017, status as of June 2018; Calculation based on the period between EMA approval and receipt of reimbursement status, if the molecule is still not reimbursed – the time as period between EMA approval and Jun 2018
PLEASE NOTE THAT EVEN PARTIAL REIMBURSEMENT CONSIDERED AS "REIMBURSED" FOR THE ANALISIS PURPOSES

At the same time, patients affected by other analyzed diseases received new treatments more often

Onco reimbursement vs other TAs



Approved and reimbursed molecules across TAs [MAT 03/2011-2018]



Commentary

- Reimbursement ratio shows that **oncology is the least prioritized therapeutic area** in terms of categorization
- **Only 14% of molecules approved by EMA from 2011 being categorized in SK** while this means also the highest number in absolute perspective since oncology is one of the most innovative treatment areas
- Number of **approved molecules by EMA is growing rapidly** – between years 2011 and 2017 the number more than doubled
- No innovative onco molecules approved by EMA since 2015 got the reimbursement

Year of EMA approval and reimbursement status as of June 2018 [# of molecules]



Note: Molecules analyzed are original meaning not generic molecules or biosimilars included in analysis, 2018 as of June 2018
PLEASE NOTE THAT EVEN PARTIAL REIMBURSEMENT CONSIDERED AS "REIMBURSED" FOR THE ANALYSIS PURPOSES

...moreover, when looking on QALY threshold the level is significantly lower compared to other countries

Oncology setting comparison – Selected peers



Country	Status	QALY	Funding and pricing	Onco accessibility		
Czechia	Peers	46,404 EUR	<ul style="list-style-type: none"> No specifically dedicated budget for onco mols Special temporary reimbursement status for highly innovative mols (VILP) Provision of best available treatment granted by law 		Screening system	✓
					Systematic treatment landscape	✓
					Outcomes data (registries)	✓
Hungary	Peers	71,644 EUR	<ul style="list-style-type: none"> Most of the onco mols in itemized list - medicines are procured under the payer authority (NEAK) Strict price control – blind bidding, preferred pricing Possibility of compassionate use of medicine 		Screening system	✓
					Systematic treatment landscape	✓
					Outcomes data (registries)	✓
Bulgaria	Peers	n/a	<ul style="list-style-type: none"> No specifically dedicated budget for onco mols Government initiatives to implement a centralized national tender procurement - maximum prices at which hospitals can finish their tenders 		Screening system	✓
					Systematic treatment landscape	✓
					Outcomes data (registries)	✓
Poland	Peers	73,186 EUR	<ul style="list-style-type: none"> Onco mols funded mainly via drug programs Price-volume agreements often used – outcomes-based schemes in discussion Reimbursement resubmission required every 2 years 		Screening system	✓
					Systematic treatment landscape	✓
					Outcomes data (registries)	✓

Slovakia		38,503 EUR	<ul style="list-style-type: none"> No special funding programs for onco mols Hospital tenders from 2013 and payers considering initiation of centralized procurement Compassionate use of medicine individually possible 		Screening system	✓
					Systematic treatment landscape	✓
					Outcomes data (registries)	✓

QALY threshold for reimbursement lowest in Slovakia and highly limiting access to new treatments for Slovak patients

Note: Oncology specifics not considered (○) / fully considered (●) in funding and pricing setting

Best (●) / Worst (○) oncology accessibility

✓ Element present and fully working

✓ Element present and not fully working or just planned

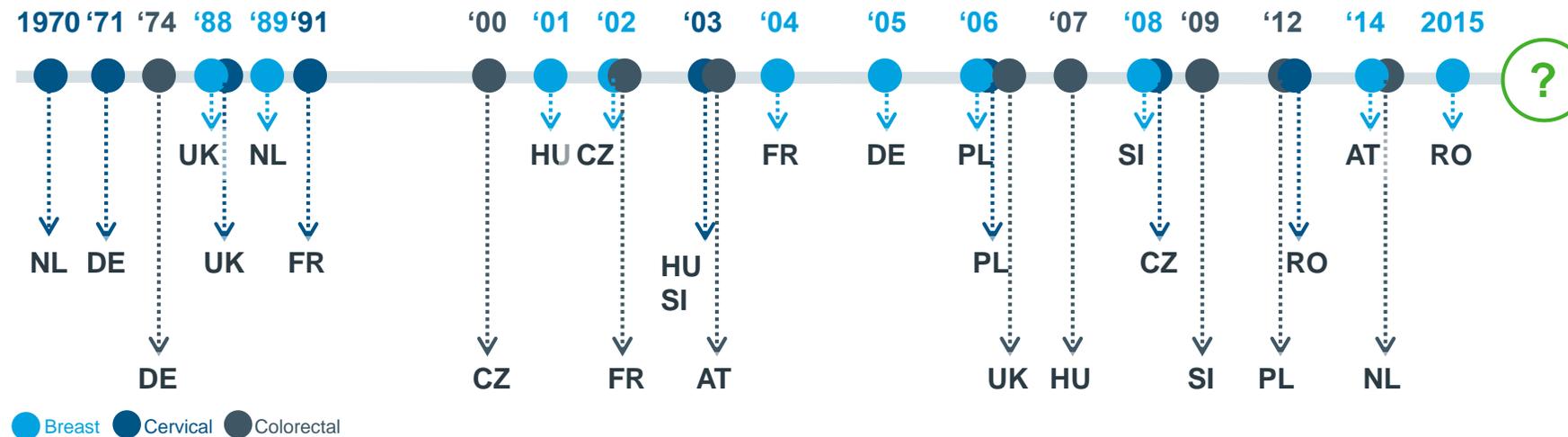
SK is almost the only country from the scope missing national screening for major cancer indications – roll out planned for 2019

Oncology accessibility – Screening



Nationwide screening programs – Timeline

Cancer	Pioneer	Last adopter	Usual screening age	No nationwide screening
● Breast	1988 – United Kingdom	2015 – Romania	45+	SK, BG
● Cervical	1970 – Netherlands	2012 – Romania	25+	SK, BG
● Colorectal	1974 – Germany	2014 – Netherlands	50+	SK, BG, RO



Slovakia



- MoH recently presented **National Oncology Program** including the schedule for national cancer screening
- Roll out is **planned from beginning of 2019**
- **Public communication** about the future national screening is planed from **September 2018**
- Screening program will cover all **3 major cancers** - Cervical and Colorectal in the first launching wave followed by Breast cancer screening
- **National Oncology Institute** will be responsible for **screening outcomes analysis**

Countries in scope: Peers, Role models, SK

Where should Slovakia go?

General so-what comments

- **Many more** oncology medicines will become available in the EU
- **Brand new** treatment & diagnostics schemes will **change the treatment landscape** prolonging patients' lives and their quality of life with the disease burden
- SK healthcare system should keep eye on these innovations and **reshape regulatory environment** to be ready for these challenges – mainly in via managed entry agreements financing and big data usage (e.g. Real world evidence)

Thank you for your attention!

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