medicines patent pool

PRIORITISATION OF MEDICINES FOR IN-LICENSING

ANNUAL REPORT 2025

Medicines Patent Pool
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Index

Introduction

The mission of the Medicines Patent Pool (MPP) is to facilitate the development of- and increase access to, life-saving medicines and health technologies for low- and middle-income countries (LMICs) through public-health oriented voluntary licensing and technology transfer.

To do so, the first step for MPP is to identify suitable candidates for access-enabling licensing using a prioritisation framework that is applied to assess products of potential interest in all health areas. In line with MPP's current mandate[1], products assessed include biotherapeutics and novel medical technologies.
This prioritisation process contributes to ensuring MPP focuses its efforts on medicines for which licensing could have the greatest public health impact. By using a robust framework, MPP evaluates product candidates and publishes a list of prioritised and watchlist medicines and health innovations in a range of health areas, for which a potential MPP intervention may support increased access.

Scope

Following its foundation in 2010, MPP initially focused on medicines for human immunodeficiency virus (HIV), with subsequent expansion to other infectious diseases, namely viral hepatitis and tuberculosis (TB) in 2015[2]. This work led to licences that resulted in high public health impact, as outlined in a MPP impact assessment modeling study published in 2022[3].

In 2018, MPP's mandate expanded to target patented medicines included in the World Health Organisation (WHO) Model List of Essential Medicines (EML) or with potential for future inclusion, which encompass a whole range of disease areas, including cancers, diabetes and cardiovascular diseases, and is exploring other areas of intervention, as relevant. Additionally, MPP contributed to the COVID-19 response and its current mandate includes pandemic preparedness and response.
MPP's strategy for the 2023-2025 period embraces a disease agnostic approach, by which patented medicines for which an MPP intervention would potentially make a difference in public health, might be considered for public-health oriented agreements with innovators, regardless of the health area.

MPP's work started with small molecules, and after conducting a feasibility study[4] on expanding access to biotherapeutics in 2022, expanded its mandate to biologics. Moreover, given their ground-breaking potential impact, long-acting technologies and formulations designed to achieve longer exposure to medicines are considered for prioritisation since 2021, together with any relevant medical technologies for which an MPP intervention might generate positive impact for public health.

1 MPP Focus areas

2 Annual MPP prioritisation reports archives

3 The economic and public health impact of intellectual property licensing of medicines for low-income and middle-income countries: a modelling study. w, Sébastien et al. The Lancet Public Health, Volume 7, Issue 2, e169 - e176

4 Exploring the Expansion of the Medicines Patent Pool's Mandate to Patented Essential Medicines: A Feasibility Study of the Public Health Needs and Potential Impact, The Medicines Patent Pool, 24 March 2018

MPP prioritisation

MPP's prioritisation process generates two lists - a priority list and a watchlist - of medicines and health technologies for which expanded access in LMICs could provide significant health benefits over standards of care, and where a voluntary agreement, including licensing and/or technology transfer, through MPP could lead to substantial public health impact. These lists guide MPP in-licensing efforts. Figure 2 represents the priority and watchlist products for 2025.

PRIORITY LIST

MPP's priority list of medicines includes medicines and health innovations for which voluntary licensing and/or technology transfer through MPP would lead to expanded access, significant health benefits, and substantial public health impact compared to standards of care.

WATCHLIST

Products in MPP's watchlist are medicines and health innovations for which expanded access could provide significant health benefits but for which supporting data are lacking and/or key challenges need to be addressed for expanded access through MPP licensing to lead to public health impact.

Additionally, medicines are sometimes provisionally added to the watchlist when a potential added benefit might be obtained through an MPP licence, but where a full assessment is still ongoing.

It should be noted that MPP does not include in its prioritisation list, the medicines and health innovations for which it has already signed agreements. The list of MPP previously signed agreements to enable access are available on MPP's website[5].

In the next sections of the report, priority and watchlist products are listed, and graphical summaries compiling assessed featured are presented for the prioritised products.

5 MPP licences and sub-licenses

Prioritisation framework

The products classification into priority and watchlist medicines is guided by MPP's prioritisation framework[6] and based on available evidence. The framework was developed through several iterations by MPP experts and with the support of MPP's Scientific[7] and Community[8] Advisory Panels members. Both lists are reassessed periodically based on new clinical evidence, changes to WHO recommendations and other recognised public health guidelines, changes in intellectual property landscape, evolution in access programmes, changes in prices or market forecasts, or any other relevant event.

MPP's prioritisation list based on this framework was recognised in the 2024 Access to Medicines Index[9]. The authors of the report invited pharmaceutical companies to *"use MPP's priority list as a guide for identifying products for which licensing would have the biggest public health impact"*.

Another testimony of the MPP prioritisation framework robustness as a public-health oriented rationalisation for impact in LMICs, several global health organisations and initiatives have engaged with MPP to discuss the framework, and tailor some elements of it to their needs, expertise and capacity.

In order to guide products' assessments, the framework addresses the following considerations, as guiding principles:

Does the product address a public health need?

This question is assessed through the public health pillar of the framework, where the burden of the health condition is assessed, as well as the advantages of the candidate product over existing alternatives of care for this condition.

Are there any access hurdles (anticipated or existing) for the product in low-and-middle-income countries?

This question is assessed through the access pillar. It includes access considerations on which MPP directly intervenes through licensing and technology transfer (e.g., intellectual property, including patents and know how), as well as additional access considerations which may be important in the treatment cascade (e.g. access to diagnostics, access companion treatments or availability of health system enablers).

What would be the effect of an MPP intervention on access?

This question elaborates on both public health and access pillars, and ensures that medicines are prioritised where an MPP intervention could yield substantial health (and sometimes economic) impact.

6 MPP prioritisation framework – 2024 version

7 MPP's Scientific Advisory Panel

8 MPP's Community Advisory Panel

9 2024 access to medicines index – insight related to MPP's scope

By addressing these questions, MPP collects insights about public health and access dimensions of the products assessed, as well as insights to assess the potential impact of an MPP intervention.

The framework is structured into seven pillars as shown on the next page.
These are:

1. the clinical relevance of the candidate,
2. the burden of disease that is targeted,
3. the product's intellectual property landscape,
4. the service delivery enablers to be considered fo the product implementation,
5. regulatory approval and quality-assurance aspects,
6. development and manufacturing requirements,
7. market prospects.

Within each pillar, several criteria are considered. These are further broken down into subcriteria. Figure 1: MPP prioritisation framework shows MPP's prioritisation pillars and criteria, while the annex details sub-criteria.

Figure 1: MPP prioritisation framework (see annex for full framework)

MPP prioritised and watchlist products 2025

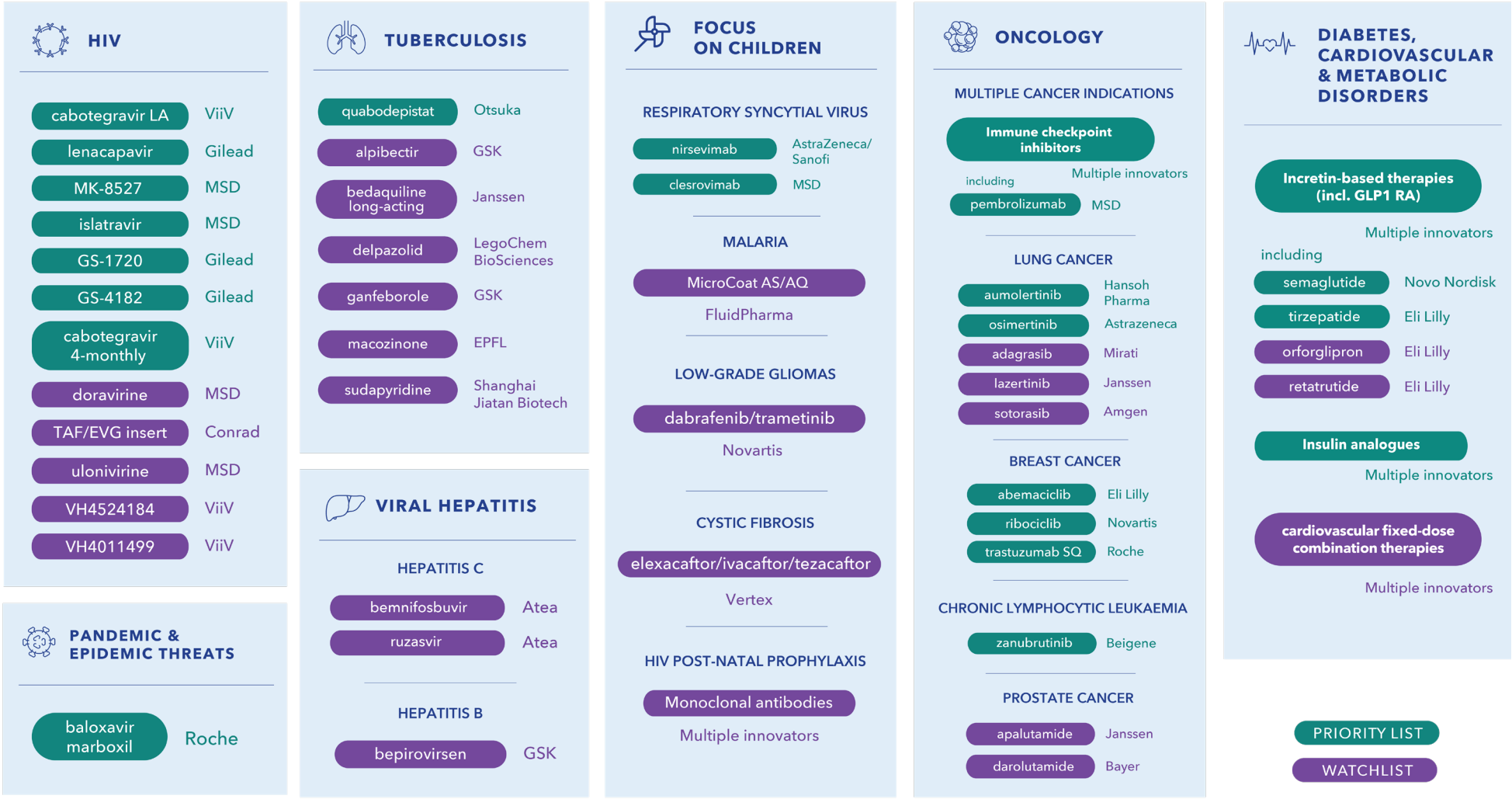

Figure 2: MPP prioritised and watchlist products 2025

What is new in 2025 list?

The following figure 3 and table 1 summarise the main changes in the list compared to 2024 prioritisation.
There were additions, changes in classification, and we have de-prioritised some candidates and removed others from the list.

Additions and changes

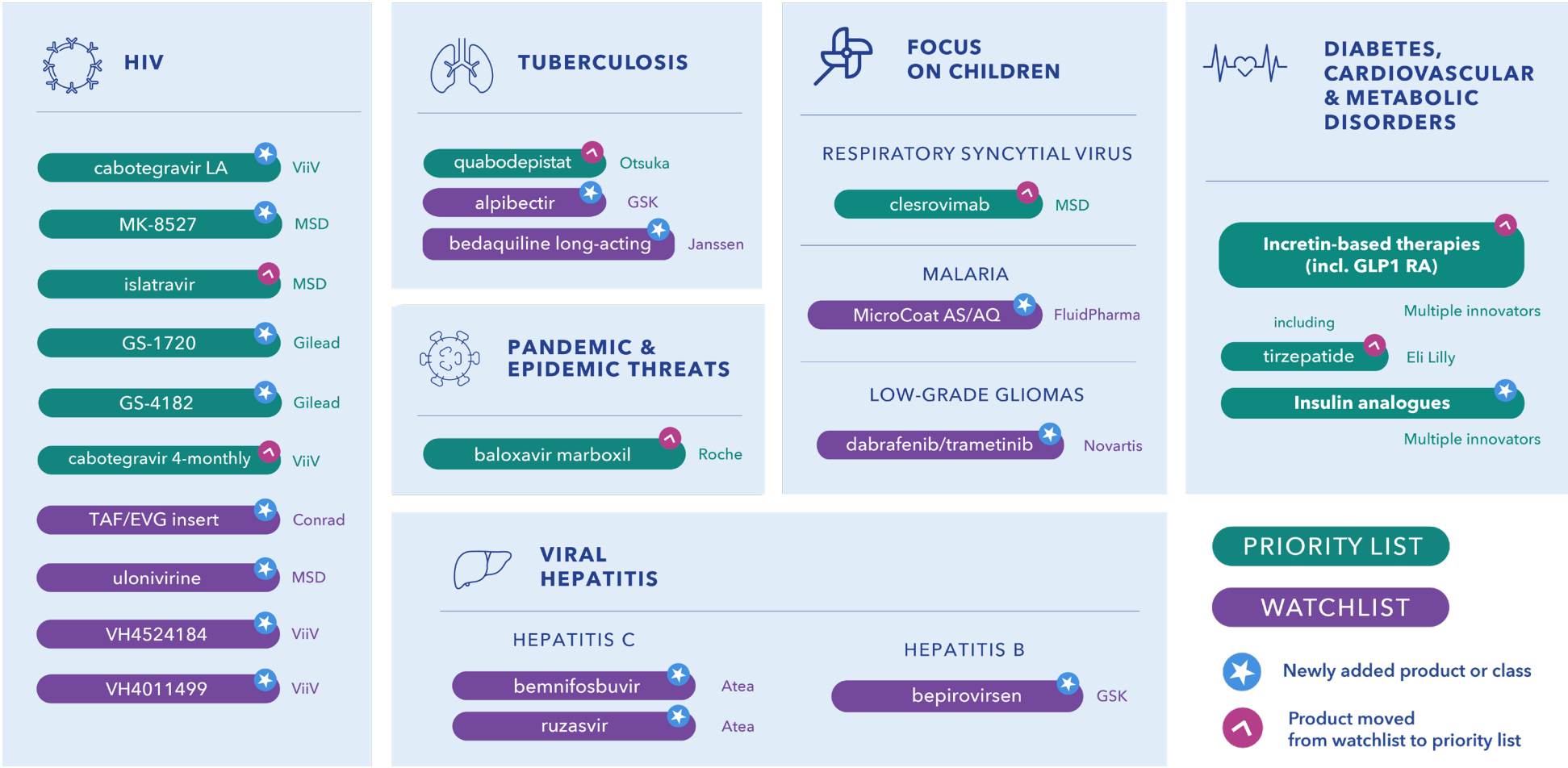

Figure 3: Additions and changes to MPP annual prioritisation list

Removals

Table 1: Removals from Prioritisation list in 2025 (in comparison to 2024 list)

Health Area	Indication	Product	Originator	Rationale for removal
HIV		rilpivirine	Janssen	No patent barrier in LMICs
TUBERCULOSIS		BTZ-043	University of Munich and DZIF	Impending patent expiry
VIRAL HEPATITIS		bulevirtide	Gilead	Limited patent scope
CHILDHOOD ONSET DISEASES	SICKLE CELL DISEASE	voxelotor	Pfizer	Clinical data showed that benefits no longer outweighed the risks
ONCOLOGY	CHRONIC LYMPHOCYTIC LEUKEMIA	ibrutinib	Janssen	Impending patent expiry
	MULTIPLE CANCER INDICATIONS	oral paclitaxel/encequidar	Athenex	Development discontinuation
OTHER INFECTIOUS DISEASES		gepotidacin	GSK	Limited patent scope

Access the searchable repository of MPP priorities and watchlist candidates

Overview of products by health area

HIV

In 2024, 39.9 million people were living with HIV worldwide, with only 30.7 million persons accessing antiretroviral therapy[10]. HIV paediatric care is improving, but still only 57% of children living with the virus had access to treatment, compared to 77% for adults. With 1.3 million people acquiring HIV annually, prevention is also key to tackle the transmission. Although pre-exposure prophylaxis (PrEP) has proven efficient in preventing HIV infection, its uptake is still slow.

Affordable and effective HIV medicines are imperative, especially for people living with HIV (PLHIV) in low- and middle-income countries (LMICs) where HIV is most prevalent. Medicines must also be available in the right formulations. Fixed-dose combinations and long-acting formulations can contribute to improving adherence. Specially formulated treatments for children, appropriate for different weights and developmental stages, improve care.

Since 2010, we have worked with leading HIV drug manufacturers, governments, international organisations, civil society, and affected communities[11] to improve access to World Health Organization (WHO) prioritised and recommended medicines for people living with HIV in LMICs. We have also worked to increase access to HIV prevention tools and supported the diversification of prevention options. In 2022, MPP signed a voluntary licensing agreement with ViiV Healthcare for cabotegravir long-acting (LA) for HIV PrEP[12]. This is an important step in accelerating affordable and equitable access to the first approved injectable long-acting PrEP recommended by WHO in up to 142 countries[13] [14].

There is increasing interest in long-acting therapeutics for both PrEP and HIV treatment, given their potential benefits in terms of efficacy (including through support of improved adherence), and user experience (including convenience and discretion). Ongoing changes related to the impact of international funding cuts on the global health landscape will also require additional performance and further efficiencies from HIV programmes in LMICs, necessitating continued efforts for the development and rollout of HIV prevention and treatment innovations, with clear roles for long-acting and ARV-sparing regimens in reaching more people effectively and managing increasingly scarce resources more efficiently.

10 UNAIDS: Global HIV & AIDS statistics

11 Launch of MPP's Community Advisory Panel (CAP)

12 MPP Press Release - cabotegravir long-acting (LA) for HIV pre-exposure prohylaxis (PrEP)

13 There are 90 countries nominally listed in the MPP-ViiV CAB for PrEP voluntary licence + 47 countries that appear not to have patents on CAB-LA and where generic supply may be possible + 5 additional countries post 2026/2027 (sources: MPP interactive map and InfoJustice)

14 MedsPaL

In light of the R&D pipeline and the current landscape in the HIV space, MPP has identified 7 medicines as priorities for voluntary licensing and has included 5 in the watchlist for HIV prevention and/or treatment, in addition, monoclonal autibodies for post-natal prophylaxis are included in the watchlist of products addressing children's health. Relevant changes in the 2025 MPP prioritisation report in the context of HIV, compared to 2024 list are:

- Cabotegravir LA for HIV treatment moved from watchlist to priority
- Islatravir for HIV treatment moved from watchlist to priority
- Addition of cabotegravir 4-monthly for both treatment and PrEP as priority
- Addition of GS-1720 for treatment as priority
- Addition of GS-4182 for treatment as priority
- Addition of MK-8527 for PrEP as priority
- Addition of ulonivirine for treatment to watchlist
- Addition of VH4524184 for treatment to watchlist
- Addition of VH4011499 for treatment to watchlist
- Addition of tenofovir alafenamide/elvitegravir insert for HIV to watchlist

Cabotegravir LA *ViiV Healthcare*

Cabotegravir (CAB) is the only approved long-acting integrase strand transfer inhibitor (INSTI). In combination with the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine (RPV), it forms the only approved fully long-acting HIV treatment regimen[15]. This regimen is currently approved by several national regulatory authorities for use in virologically suppressed adults with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine, administered monthly or every 2 months[16]. Despite its benefits, including for use in LMICs, the injectable CAB+RPV regimen is currently not included in WHO guidelines for HIV treatment.

Compared to daily oral antiretroviral therapy (ART), CAB+RPV could support the improvement of adherence to treatment, achieve and maintain virologic suppression. However, there may be concerns about the suitability of the use of this regimen in specific populations with co-infections (see below). One key issue for implementation in resource-limited settings is that rilpivirine—not cabotegravir—requires a cold chain for storage. Additionally, rilpivirine's low barrier to resistance raises concerns about the long-term effectiveness of the NNRTI class in case of clinical resistance to the drug.

For people living with both HIV and hepatitis B (HBV), switching from a tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF)-containing regimen—such as the widely used oral tenofovir/lamivudine/dolutegravir (TLD)—to dual regimens, including CAB+RPV, would remove the HBV-suppressive effects of TDF or TAF, potentially worsening HBV management in people living with both HIV and HBV. Furthermore, drug-drug interactions between CAB+RPV and tuberculosis (TB) treatments, such as rifampicin and rifabutin, pose additional concerns for individuals living with both HIV and TB.

Data indicate that people facing adherence challenges to daily oral treatment, who switched to long-acting injectable CAB+RPV experienced greater viral load reductions than those remaining on daily oral ART[17]. More recently, findings from the CARES study in 3 countries in sub-Saharan Africa demonstrated that switching to CAB+RPV was non-inferior to continuing oral ART, with high rates of HIV-1 RNA suppression at week 96. This study marks an important milestone, highlighting the potential clinical feasibility and effectiveness of long-acting injectable HIV treatment in LMICs[18].

15 CABENUVA; U.S. Food & Drug Administration Prescribing Information.

16 Global approvals of CAB+RPV long acting injectable for HIV treatment (LAPaL)

17 Kityo C, Mambule IK, Musaazi J, Sokhela S, Mugerwa H, Ategeka G, Cresswell F, Siika A, Kosgei J, Shah R, Naidoo L, Opiyo K, Otike C, Möller K, Kaimal A, Wambui C, Van Eygen V, Mohammed P, Addo Boateng F, Paton NI; CARES trial team. Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial. Lancet Infect Dis. 2024 Oct;24(10):1083-1092. doi: 10.1016/S1473-3099(24)00289-5. Epub 2024 May 28. PMID: 38821073.

18 CROI 2025 - Randomized trial of Cabotegravir and Rilpivirine Long-acting in Africa (CARES):Week 96 Result

With RPV patents expected to expire in 2027, and the formulation of cabotegravir being the same for PrEP and for treatment indications, in least developed countries, the expansion of the ViiV-MPP licence for cabotegravir long-acting for PrEP to also cover the treatment indication, could open the possibility for generic CAB+RPV LAI in LMICs, and potentially in the future, to other cabotegravir-based long-acting regimens for HIV treatment, if companion drugs also benefit from appropriate access programs.

Lenacapavir *Gilead*

Lenacapavir is a capsid inhibitor[19] with a novel mechanism of action, distinguishable from other currently approved classes of antiviral agents, as it inhibits HIV at multiple stages of its lifecycle and has no known cross resistance exhibited in vitro to other existing drug classes. Lenacapavir has received regulatory approvals in Europe and 10 high-income countries as a treatment for adults with multi-drug resistant HIV, intended for use in combination with other antiretroviral medications[20]. It is also awaiting approval for use in the context of HIV prevention.
Lenacapavir primary patents have been filed or granted in several LMICs and are expected to expire between 2034 and 2037. Gilead also holds secondary patents that may provide exclusivity until 2038 in many LMICs[21 22]. Gilead has signed bilateral voluntary licence agreements with six generic manufacturers, allowing for sales of lenacapavir for HIV prevention and treatment of heavily treatment-experienced adults with multi-drug-resistant HIV in 120 countries[23]. LMICs beyond the licence territory will not have access to the generic products via these agreements[24].

An approved long-acting companion medicine allowing for a fully long-acting lenacapavir-based treatment regimen is still missing, and lenacapavir is being evaluated as a long-acting option in multiple ongoing and planned early and late-stage clinical studies of potential fully long-acting HIV treatment regimens. Of notice, the current voluntary licence does not cover a broad treatment indication. Given the prominent role such regimens could play in the future, and remaining uncertainties surrounding lenacapavir's future accessibility and affordability in LMICs for both treatment and prevention indications, including the possibility of expanding the geographical scope and indication of the licensing agreements, lenacapavir remains a priority for MPP. Two potential HIV treatment regimens currently stand out as priorities for MPP licensing: lenacapavir with either cabotegravir or islatravir, based on relevant data as it is being generated. The possibility of the addition of a regional manufacturer for lenacapavir in countries with high HIV prevalence in sub-Saharan Africa would also be worth exploring.

Lenacapavir for PrEP: Lenacapavir is a candidate for long-acting pre-exposure prophylaxis (PrEP) through a twice-yearly subcutaneous injection, following an initial oral loading phase. Gilead has submitted marketing authorisation applications to EMA (for both EU MAA and EU-M4all)[25] and to the FDA[26]. Results from the PURPOSE 1 and PURPOSE 2 phase III trials have demonstrated high effectiveness in preventing HIV, with mostly mild injection site reactions such as pain, nodules, and indurations[27 28]. Additionally, recent data confirm lenacapavir's safety and efficacy in adolescents[29], broadening its potential impact on containing the HIV epidemic if rolled out extensively.
At CROI 2025, groundbreaking findings on new intramuscular formulations of lenacapavir were presented, featuring two single-dose injections designed

19 Dvory-Sobol H, Shaik N, Callebaut C, Rhee MS. Lenacapavir: a first-in-class HIV-1 capsid inhibitor. Curr Opin HIV AIDS. 2022;17(1):15-21. doi:10.1097/COH.0000000000000713
20 Global regulatory approvals of lenacapavir for treatment (LAPaL)
21 www.medspal.org: report on lenacapavir oral formulation
22 www.medspal.org: report on lenacapavir subcutaneous formulation
23 Gilead Signs Royalty-Free Voluntary Licensing Agreements with Six Generic Manufacturers to Increase Access to Lenacapavir for HIV Prevention in High-Incidence, Resource-Limited Countries (October 2, 2024)
24 Gray, G.E. and Venter, F.W.D., Working at Cross-PURPOSEs to Ending HIV, Published April 2, 2025N Engl J Med 2025;392:1344-1345DOI: 10.1056/NEJMe2414709
25 European Medicines Agency Validates Gilead's Marketing Authorization Application and EU-Medicines for All Application for Twice-Yearly Lenacapavir for HIV Prevention
26 U.S. FDA Accepts Gilead's New Drug Applications for Twice-Yearly Lenacapavir for HIV Prevention Under Priority Review
27 Kelley CF, et all. PURPOSE 2 Study Team. Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons. N Engl J Med. 2024 Nov 27. doi: 10.1056/NEJMoa2411858. Epub ahead of print. PMID: 39602624.
28 Bekker LG, et all. PURPOSE 1 Study Team. Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women. N Engl J Med. 2024 Oct 3;391(13):1179-1192. doi: 10.1056/NEJMoa2407001. Epub 2024 Jul 24. PMID: 39046157.
29 CROI 2025 - Lenacapavir Pharmacokinetics, Safety, and Efficacy in Adolescents and Adults in PURPOSE 1

for annual administration[30]. These formulations were safe and tolerable in the study participants, and maintained plasma drug concentrations above the 95% effective threshold for at least 56 weeks, highlighting the feasibility of extending dosing intervals even further. If successful in follow-up trials, adjusted yearly injections could represent a significant shift in HIV prevention strategies. If affordable and accessible, this candidate could represent a very powerful tool to contain the global HIV epidemic. It is not known whether this formulation is captured under the Gilead voluntary licence for lenacapavir.

Lenacapavir for treatment: Lenacapavir is currently approved by several stringent regulatory authorities for the treatment of HIV-1 infection in heavily treatment-experienced adults whose current antiretroviral regimen is failing due to resistance, intolerance, or safety concerns[31]. Lenacapavir's low administration frequency and long-acting nature could offer a paradigm shift also in treatment.
A phase II clinical study investigated the efficacy of a weekly oral combination of lenacapavir and islatravir. The study demonstrated strong virologic suppression without negatively affecting lymphocyte counts[32]. These results have prompted the initiation of two phase III trials[33] [34], which are evaluating a weekly oral fixed dose combination of islatravir and lenacapavir in virologically suppressed persons living with HIV. The research supports broader efforts to develop more convenient, decentralized HIV treatment options that could improve access while supporting increased adherence.
Lenacapavir is also under investigation in combination with cabotegravir (with or without rilpivirine) for individuals with NNRTI resistance. A small case-series showed high rates of virologic suppression in people with HIV on a LEN+CAB regimen, highlighting its potential as a long-acting injectable option for people with limited treatment choices[35]. However, additional research is needed to confirm safety, efficacy, durability, and resistance barriers. A multicentric clinical trial assessing the use of LEN+CAB for HIV treatment in comparison to standard of care is in planning stages.
Additionally, lenacapavir is being explored in combination with once-daily bictegravir as a possible simplified regimen for people with HIV who require complex treatment due to previous resistance or treatment failures[36].
However, accessibility remains a challenge—lenacapavir is not yet registered for the treatment indication in LMICs[37], limiting its availability to those who may benefit most from this alternative in a treatment regimen.

MK-8527 *MSD*

MK-8527 is an investigational nucleoside reverse transcriptase translocation inhibitor (NRTTI) being developed for the prevention of HIV. MK-8527 shares mechanistic similarities with islatravir, offering the potential for high potency and a strong genetic barrier to resistance[38]. MK-8527 is a promising clinical candidate for HIV PrEP, being evaluated for once-monthly oral dosing. The phase IIa study to assess safety, tolerability, and pharmacokinetics of oral MK-8527 once monthly was just completed[39], while a larger PK/PD study has just started[40]. Of notice, a specific trial is also planned, evaluating the drug PK in breast milk and blood of breastfeeding individuals[41]. MK-8527 primary patents with an expected expiry in 2034 have been granted to MSD in at least 35 LMICs and are pending in another 13 countries. Secondary patent filings are anticipated.

30 CROI 2025 -Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1 open-label study
31 SUNLENCA; U.S. Food & Drug Administration Prescribing Information
32 Week 48 Results of a Phase 2 Study Evaluating Once-weekly Oral Islatravir Plus Lenacapavir
33 NCT06630286: Study to Compare an Oral Weekly Islatravir/Lenacapavir Regimen With Bictegravir/Emtricitabine/Tenofovir Alafenamide in Virologically Suppressed People With HIV-1 (ISLEND-1)
34 NCT06630299: Study to Compare an Oral Weekly Islatravir/Lenacapavir Regimen With Standard of Care in Virologically Suppressed People With HIV-1 (ISLEND-2)
35 Gandhi M, Hill L, Grochowski J, Nelson A, Koss CA, Mayorga-Munoz F, Oskarsson J, Shiels M, Avery A, Bamford L, Baron J, Short WR, Hileman CO. Case Series of People With HIV on the Long-Acting Combination of Lenacapavir and Cabotegravir: Call for a Trial.
36 Study to Compare Bictegravir/Lenacapavir Versus Current Therapy in People With HIV-1 Who Are Successfully Treated With a Complicated Regimen (ARTISTRY-1)
37 Global regulatory approvals of Sunlenca® (lenacapavir) injection and tablets for the treatment of HIV infection, in combination with other antiretroviral(s), in adults with multi-drug resistant HIV
38 MK-8527 profile on LAPaL
39 Safety and Pharmacokinetic Study of Oral MK-8527 QM in Participants at Low-Risk for HIV-1 Infection (MK-8527-007)
40 A Study of MK-8527 in Healthy Adult Participants (MK-8527-013)
41 A Study of MK-8527 in Healthy Lactating Female Participants (MK-8527-009)

Islatravir *MSD*

Islatravir is a first-in-class nucleoside reverse transcriptase translocation inhibitor (NRTTI) that is not yet approved[42]. After a temporary pause in clinical development due to safety concerns, Merck has resumed selected islatravir programs with close safety monitoring[43].
Recent phase III studies have demonstrated that islatravir, when administered as a once-daily oral treatment in combination with doravirine (DOR/ISL 100 mg/0.25 mg), is both safe and non-inferior to commonly used antiretroviral therapy (ART) regimens in virologically suppressed individuals with HIV-1[44].
Additionally, islatravir is being investigated as a fixed dose combination with lenacapavir as weekly oral treatment (see also above in the lenacapavir section)[45]. If successful, an oral long-acting HIV treatment could provide an important alternative, particularly in settings focused on decentralized service delivery.
Patents on islatravir compound and its use for treating HIV – owned by Yamasa corporation and licensed exclusively to MSD – were mainly filed in HICs and Mexico and were expected to expire on 24.03.2025. A patent family covering the use of Islatravir for the treatment or prophylaxis of HIV (dosing regimen less frequent than once-daily) owned by MSD includes patent applications filed in several LMICs countries/regions with an expected expiry in February 2037[46].

GS-1720 *Gilead*

GS-1720 is an investigational once-weekly oral INSTI being evaluated for treatment in both treatment-naïve and switch populations of people living with HIV. GS-1720 is studied in combination with GS-4182, a new oral lenacapavir prodrug with improved bioavailability (see below). Phase II/III WONDERS trials are currently underway using the GS-1720+GS-4182 combination[47]. Gilead primary patent applications on GS-1720 have been filed in about 47 LMICs with an expected expiry in 2042. Further secondary patent filings are anticipated.

GS-4182 *Gilead*

GS-4182 is an investigational lenacapavir prodrug with improved bioavailability and potential for oral weekly administration. GS-4182 is studied in combination with GS-1720, a new oral INSTI[48]. Phase II/III WONDERS trials are currently underway using the GS-4182+GS-1720 combination[49]. In December 2022, Gilead filed three international patent applications covering lenacapavir prodrugs, which may include GS-4182. Confirmation will be possible once the chemical structure of GS-4182 is available in the public domain. The expected expiry of the compound patents is 2042, and additional secondary patent filings are anticipated. If successful, a weekly oral HIV treatment could provide a valuable alternative for PLHIV.

42 Islatravir profile on LAPaL
43 modeling to optimize islatravir QW dose in virologically supressed PWHIV
44 Merck announces topline results from pivotal phase 3 trials evaluating investigational once daily oral two drug single tablet regimen of doravirine and islatravir for the treatment of HIV in adults.
45 MK-8591D : islatravir and lenacapavir fixed dose combination for treatment with weekly oral dosing
46 www.medspal.org: report on islatravir
47 Study of Oral Weekly GS-1720 and GS-4182 Compared With Biktarvy in People With HIV-1 Who Have Not Been Treated
48 Safety and pharmacokinetic profile of single and multiple ascending doses of GS-4182, an oral prodrug of lenacapavir, in participants without HIV-1 (WEPEB117)
49 Phase 2:To evaluate the efficacy of oral weekly GS-1720 coadministered with GS-4182 versus Biktarvy®(BVY; bictegravir/emtricitabine/tenofovir alafenamide, coformulated) in treatment-naive PWH at Week 24 Phase 3:To evaluate the efficacy of oral weekly GS-1

Cabotegravir 4-monthly

ViiV Healthcare

Cabotegravir 4-monthly, also called CAB-ULA (ultra long-acting) is an investigational longer-acting formulation of cabotegravir that demonstrates a pharmacokinetic (PK) profile supporting dosing intervals of approximately four months[50]. This extended dosing schedule has the potential to reduce clinic visits and improve adherence. Early data suggest a favourable safety profile, with intramuscular (IM) administration being better tolerated than subcutaneous (SQ) injection. As a result, CAB-ULA IM dosed every four months is advancing into late-stage studies investigating its use for both HIV-1 PrEP and treatment[51].

For PrEP, the EXTEND 4M registration trial is evaluating a single IM injection of CAB-ULA at 1600 mg/3mL[52]. The FDA has approved this registration strategy, based on PK bridging studies, without requiring an additional efficacy study[53]. The trial was launched in December 2024 and is expected to reach its primary endpoints by Q3 2026.

For HIV treatment, a phase III registration trial is evaluating CAB-ULA combined with rilpivirine (RPV) at Q4M dosing, following the completion of phase I studies on multiple formulations[54].

Primary patents on cabotegravir have been granted in many LMICs and are expected to expire in 2026. A secondary patent on the 4-monthly formulation was published in March 2025[55]. The corresponding international patent application is pending, and geographical coverage in LMICs is expected to be available by March 2026, with patents anticipated to expire in 2043.

50 CROI 2024: Phase 1 Study of Cabotegravir Long-Acting Injectable Formulations Supports ≥4-Monthly Dose Interval

51 Cabotegravir 4-monthly on LAPaL

52 A Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of a New Formulation of Cabotegravir Long-Acting Administered Intramuscularly in a 4-month Dosing Interval (Q4M)

53 Presented by ViiV at the LEAP Long-Acting/Extended Release (LA/ER) Antiretroviral Research Resource Program (LEAP) Investigator Meeting and Annual Workshop, 8 March 2025

54 A Study to Investigate Pharmacokinetics, Safety and Tolerability of Long-Acting Cabotegravir Plus Recombinant Human Hyaluronidase PH20 in Healthy Adult Participants

55 Patent for cabotegravir 4-monthly

Doravirine *MSD*

Doravirine (DOR) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) approved for use in combination with other antiretroviral agents for the treatment of HIV-1 in adult patients with no prior antiretroviral treatment history[56]. It is being investigated for HIV treatment in combination with islatravir as once daily oral treatment[57]. However, the evidence of clinical benefits over the standard of care is still unclear.

Primary patents on doravirine compound and its combinations with other anti-HIV agents have been filed in many LMICs and are expected to expire in 2031[58]. In few countries, the patent term may be extended by another five years, until 2036. While bilateral voluntary licences have been granted to generic manufacturer for 86 countries, public information on such licences is limited[59]. The existing licence for DOR may enable access to generics of DOR+3TC in 86 LMICs; however, the development status for licensed generic DOR versions is unknown.

VH4524184 *ViiV Healthcare*

VH4524184 is a phase II third-generation integrase strand transfer inhibitor (INSTI) administered by injection, with a superior resistance profile compared to second-generation INSTIs[60]. It could be important in case of increasing DTG resistance. The chemical structure of VH4524184 is not available in the public domain. Similarly, no patent information is available yet, however patent filings are to be expected.

VH4011499 *ViiV Healthcare*

ViiV's new capsid inhibitor demonstrated promising phase IIa data, with oral doses ranging from 25 mg to 250 mg every five days in ART-naïve individuals. By day 11, virologic suppression was observed. The drug is planned for development as an injectable long-acting (LA) therapy[61]. The chemical structure of VH4011499 is not available in the public domain. Similarly, no patent information is available yet, however patent filings are to be expected.

56 PIFELTRO; U.S. Food & Drug Administration Prescribing Information

57 A Study of Doravirine/Islatravir (DOR/ISL, MK-8591A) for the Treatment of Human Immunodeficiency Virus 1 (HIV-1) Infection in Participants Who Previously Received DOR/ISL (MK-8591A-054)

58 www.medspal.org: report on doravirine

59 Merck enters into voluntary licensing agreements for doravirine to expand patient access in resource limited settings

60 CROI 2025: Proof-of-Concept Phase 2a Trial of VH4524184 (VH-184), a Third-Generation Integrase Strand Transfer Inhibitor

61 CROI 2025 - Proof-of-Concept Trial of Oral VH4011499 (VH-499), a New HIV-1 Capsid Inhibitor

Tenofovir alafenamide/elvitegravir (TAF/EVG) insert

CONRAD

This insert is a candidate Tenofovir alafenamide/elvitegravir (TAF/EVG) insert fast-dissolving, bullet-shaped tablet for vaginal or rectal administration for on-demand HIV prophylaxis (both PrEP and post-exposure prophylaxis, PEP). The insert contains a coformulation of antiretroviral drugs that dissolve upon insertion, preventing HIV replication locally. This candidate passed several phase I studies[62] [63] [64] [65] and is currently collecting more data on safety and PK for both administration routes[66] [67]. It is awaiting to enter phase II to continue assessing safety and effectiveness. As this phase II study was planned in the context of the USAID-funded MATRIX project, the progress of this promising prevention candidate that could complement other existing tools is currently paused.

CONRAD have filed for patents on their TAF/EVG sustained release formulation for vaginal or rectal use in 7 LMICs, including South Africa. If granted, these would likely expire in 2039. If successful, this product could complement other PrEP and PEP options, serving clients of any gender for whom a discreet, user-initiated, event-driven HIV prevention method would be appealing. The manufacturing prospects indicate a potential low-price for quality assured generic versions if a voluntary licence agreement is reached.

Ulonivirine

MSD

Ulonivirine (previously known as MK 8507) is an orally-administered investigational non-nucleoside reverse transcriptase inhibitor (NNRTI) being developed by MSD for the treatment of HIV-1 infection[68]. Its pharmacokinetic profile supports once-weekly oral administration, which could improve adherence. It is currently being studied in combination with islatravir in once-weekly regimens for maintaining viral suppression[69]. Its potential for less frequent dosing and use in combination therapy makes it a promising candidate for HIV treatment. Ulonivirine compound patents are granted in many LMICs, including India, with an expiry date expected by 2033.

62 Safety, PK, and PD Study of a Vaginal Insert Containing TAF and EVG

63 A phase I study to assess safety, pharmacokinetics, and pharmacodynamics of a vaginal insert containing tenofovir alafenamide and elvitegravir

64 Riddler SA, Kelly CW, Hoesley CJ, et al. A Phase 1 Clinical Trial to Assess the Safety and Pharmacokinetics of a Tenofovir Alafenamide/Elvitegravir Insert Administered Rectally for HIV Prevention. J Infect Dis. 2024;230(3):696-705. doi:10.1093/infdis/jiae

65 Thurman AR, Ouattara LA, Yousefieh N, Anderson PL, Bushman LR, Fang X, Hanif H, Clark M, Singh O, Doncel GF. A phase I study to assess safety, pharmacokinetics, and pharmacodynamics of a vaginal insert containing tenofovir alafenamide and elvitegravir. Front Cell Infect Microbiol. 2023 Apr 19;13:1130101. doi: 10.3389/fcimb.2023.1130101. PMID: 37153145; PMCID: PMC10154607

66 Safety and PK Multi-dose Study of TAF/EVG Vaginal Insert

67 Rectal Insert TAF/EVG Pre-Exposure Prophylaxis (RITE PrEP) Study (RITE PrEP)

68 Ulonivirine on LAPaL

69 NCT06891066 : A Study of Islatravir (ISL) and Ulonivirine (ULO) Once Weekly (QW) in Virologically Suppressed Adults With Human Immunodeficiency Virus Type 1 (HIV-1) (MK-8591B-060)

TUBERCULOSIS

An estimated global total of 10.8 million people fell ill with tuberculosis (TB) in 2023, most in low- and middle-income countries[70]. TB is the leading cause of death for people with HIV and a major contributor to antimicrobial resistance. In 2023, 1.25 million people died from TB, including 161 000 people with HIV.

Globally, there were an estimated 410 000 incident cases of multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB) in 2022. The World Health Organization's End TB Strategy sets ambitious targets at reducing TB deaths by 95% between 2015 and 2035, and to end TB[71]. To meet these targets, better therapies to treat TB are urgently needed, including shorter treatment regimens, particularly for MDR-TB[72].

Given the current situation in the TB space, MPP has identified one medicine as a priority and has included 6 in the watchlist. Relevant changes in the 2025 MPP prioritisation report compared to the previous year are:

- Addition of alpibectir to watchlist
- Addition of bedaquiline long-acting to watchlist
- Removal of BTZ-043, since the patents will expire in 2026.

70 WHO - Global tuberculosis report 2024

71 WHO - The end TB strategy

72 Saluzzo F, Adepoju VA, Duarte R, Lange C, Phillips PPJ. Treatment-shortening regimens for tuberculosis: updates and future priorities. Breathe (Sheff). 2023 Sep;19(3):230028. doi: 10.1183/20734735.0028-2023. Epub 2023 Oct 10. Erratum in: Breathe (Sheff). 2024 Jul 16;20(2):1. doi: 10.1183/20734735.5028-2023. PMID: 37830101; PMCID: PMC10567072.

Quabodepistat *Otsuka*

Quabodepistat is a medicine with a new mechanism of action that has potent antituberculosis activity and a favourable safety profile[73]. Despite premature termination of PAN-TB Consortium trials including quabodepistat - since the trial does not support the investigational regimens being able to achieve the trial objective of identifying a new regimen to treat tuberculosis in 3 months or less[74] - Otsuka plans to study the drug with bedaquiline and delamanid in phase III trials. The primary patent on quabodepistat has been granted in more than 50 LMICs and is expected to expire in 2035. There are secondary patents on intermediates and combinations that may provide exclusivity until 2037-2039 in many LMICs[75].

Sudapyridine *Shanghai Jiatan Biotech*

Sudapyridine is a new agent being studied for TB with a mechanism of action similar to bedaquiline, functioning as an ATP synthase inhibitor. It could be important for MDR-TB, which remains a major global health challenge[76]. Sudapyridine has the potential to reduce some of the side effects observed with bedaquiline (such as cardiac issues with prolonged QT intervals, or liver toxicity and gastrointestinal issues)[77]. It is currently in phase III of development in patients with rifampicin-resistant pulmonary tuberculosis[78]. Primary patents on sudapyridine are present in key countries of manufacture such as India, China and South Africa and are expected to expire in 2035. Secondary patents covering manufacturing processes and intermediates with an expected expiry date in 2037 are present in a few LMICs[79].

73 Otsuka Pharmaceutical Co., Ltd; Corporate website

74 Efficacy and Safety Evaluation of Two to Four Months of Treatment With the Combination Regimens of DBOS and PBOS in Adults With Pulmonary Tuberculosis

75 www.medspal.org : report on quabodepistat

76 Yao R, Wang B, Fu L, et al. Sudapyridine (WX-081), a Novel Compound against Mycobacterium tuberculosis. Microbiol Spectr. 2022;10(1):e0247721. doi:10.1128/spectrum.02477-21.

77 Evaluation of Early Bactericidal Activity and Safety in Pulmonary Tuberculosis With WX-081 (WX-081) - NCT04608955

78 A Phase III Study of Oral Sudapyridine (WX-081) Tablets in Rifampicin-Resistant Pulmonary Tuberculosis Patients (SURE-TB)

79 www.medspal.org: report on sudapyridine

Delpazolid *LegoChem BioSciences*

Delpazolid is an investigational antitubercular agent. It is being studied in combination with delamanid and bedaquiline. Delpazolid is a promising oxazolidinone antibiotic being developed for the treatment of TB[80] [81]. Currently in phase II clinical trials, delpazolid has demonstrated improved efficacy and safety compared to linezolid. The recently completed DECODE phase IIb trial evaluated different doses of delpazolid (up to 1200mg once daily) in combination with a backbone regimen of bedaquiline, delamanid, and moxifloxacin for the treatment of pulmonary TB[82]. The study found that delpazolid was safe and well-tolerated, while promising signs of efficacy for drug-sensitive TB. However, the trial had limitations, including a small sample size that resulted in wide confidence intervals and the absence of a standard of care control arm for comparison. Despite these limitations, the trial results suggest delpazolid could be a strong candidate for treating drug-resistant TB. As the clinical data are still immature, the drug candidate remains in the watchlist. The primary patent on delpazolid is filed or granted in key countries of manufacture such as India, China and South Africa and is expected to expire in 2029. Secondary patents with an expected expiry date in 2031 are filed or granted in a few LMICs[83].

Ganfeborole *GSK*

Ganfeborole (GSK3036656) is an investigational agent, demonstrating early bactericidal activity with a low, once-daily oral dose after 14 days of treatment in participants with drug-susceptible pulmonary tuberculosis[84] [85]. While ganfeborole is highly potent and effective at low doses, it may pose a risk of teratogenicity[86] [87]. It is in phase II and data are still immature and therefore the drug candidate remains in the watchlist. Patents on the compound have been filed or granted in several LMICs and are expected to expire between 2031-2036[88]. Additional secondary patents may be filed.

Macozinone *EPFL*

Macozinone (PBTZ-169) is a tuberculosis drug candidate that has demonstrated high potency against drug-susceptible and drug-resistant TB in preclinical studies[89]. Macozinone has additive effects with many TB therapeutic agents, both marketed and in development, and has synergic effects with bedaquiline and clofazimine in preclinical studies[90] [91]. Moreover, a long-acting injectable version of macozinone is being investigated[92]. As macozinone is in phase II, data are still immature and the drug candidate remains in the watchlist. Primary patents on macozinone have been granted in key countries of manufacture such as India, China and South Africa and are expected to expire in 2031. Secondary patents may be filed.

80 Kim JS, Kim YH, Lee SH, et al. Early Bactericidal Activity of Delpazolid (LCB01-0371) in Patients with Pulmonary Tuberculosis. Antimicrob Agents Chemother. 2022;66(2):e0168421. doi:10.1128/AAC.01684-21.

81 PanACEA DElpazolid Dose-finding and COmbination DEvelopment (DECODE) - NCT04550832

82 Preprints The Lancet: A Prospective, Randomised, Open Label Phase 2b Dose-Finding Trial of Delpazolid in Combination with Bedaquiline, Delamanid and Moxifloxacin for Pulmonary Tuberculosis: DECODE. Posted on 10 Dec 2024

83 www.medspal.org: report on delpazolid

84 An Early Bactericidal Activity, Safety and Tolerability of GSK3036656 in Subjects With Drug- sensitive Pulmonary Tuberculosis - NCT03557281

85 GlaxoSmithKline Pharmaceuticals Ltd; Press release: GSK announces positive Phase IIa study results for a new first-in-class candidate medicine for patients with tuberculosis

86 GSK TB Pipeline Update -November 2023

87 Diacon, A.H., Barry, C.E., Carlton, A. et al. A first-in-class leucyl-tRNA synthetase inhibitor, ganfeborole, for rifampicin-susceptible tuberculosis: a phase 2a open-label, randomized trial. Nat Med 30, 896–904 (2024). https://doi.org/10.1038/s41591-024-

88 www.medspal.org: report on ganfeborole

89 Innovative Medicines for Tuberculosis Foundation

90 Study to Evaluate the Safety, Tolerability and Pharmacokinetics of PBTZ169 in Multiple Dosing - NCT03776500

91 Phase 1 Study of PBTZ169 - NCT03036163

92 Medincell and iM4TB Initiate Development of a Long-Acting Injectable Version of Macozinone, a Promising Investigational Tuberculosis Treatment, Medincell website, visited April 22, 2025.

Alpibectir *GSK*

Alpibectir functions through a unique mechanism that targets bacterial transcriptional regulators, activating novel bioactivation pathways for ethionamide (Eto). Eto is an older, well-known anti-TB drug, but its use at high concentrations is limited due to significant side effects. By enhancing Eto's efficacy, alpibectir enables its use at lower, non-toxic concentrations, potentially improving its safety profile while maintaining therapeutic effectiveness[93]. Alpibectir is in phase II[94]. Primary patents on alpibectir have been filed in many LMICs and are expected to expire in 2038.

Bedaquiline long-acting *Janssen*

Bedaquiline is a crucial antibiotic for treating TB, particularly MDR-TB. It significantly improves treatment outcomes by reducing mortality and shortening therapy duration compared to older, less effective, often injectable, regimens. A long-acting formulation of bedaquiline could be useful as a new modality to increase adherence in the treatment of latent TB infection (LTBI, also known as TB preventive treatment, TPT), which is recommended by WHO for people living with HIV, household contacts of people with TB, and other risk groups. Bedaquiline long-acting is in phase I and data on safety and efficacy are still immature[95]. Although the compound patent expired in 2023, Janssen owns several patents in LMICs on long-acting formulations of bedaquiline expiring between 2038 and 2041[96].

93 ALPIBECTIR (BVL-GSK098) WGND Annual Meeting

94 A Study of the Early Effects, Safety, and Acceptability of Oral Alpibectir in Combination with Ethionamide (ENABLE)

95 A Single Ascending Dose, Single-Centre Study, to Assess Pharmacokinetics, Safety and Tolerability of a Single Intramuscular Dose of Bedaquiline Long-Acting Injection Formulation in Healthy Participants

96 Long-acting bedaquiline on LAPaL

VIRAL HEPATITIS

In 2022, viral hepatitis claimed approximately 1.3 million lives, of which 83% were attributed to hepatitis B and 17% to hepatitis C. New infections decreased from 3 million in 2019 to 2.2 million in 2022 (1.2 million hepatitis B, 1.0 million hepatitis C). Despite this progress, the global burden remains substantial with 304 million people living with viral hepatitis in 2022 (254 million with hepatitis B, 50 million with hepatitis C)[97].

Children represent 12% of the hepatitis burden, primarily affecting those with hepatitis B. Significant regional disparities persist, with the WHO African Region accounting for 63% of new hepatitis B infections, yet only 18% of newborns in this region receive the hepatitis B birth-dose vaccine. The Western Pacific Region reports 47% of hepatitis B deaths, with inadequate treatment coverage.

Although hepatitis C is curable, identifying populations living with the virus remains challenging due to limited awareness and screening programs. High-cost diagnostic tools and the requirement for confirmatory molecular diagnostics represent key barriers to treatment access. There is an urgent need for well-tolerated, highly effective pangenotypic cure regimens requiring less frequent administration.

Hepatitis B, while preventable through vaccination, maintains high prevalence rates. Beyond improved diagnostics, treatments that could provide a functional cure for hepatitis B are essential to reduce long-term disease burden, management costs, and complications. Expanded prevention, screening, and treatment initiatives are critical to address the global hepatitis crisis. Currently, few LMICs have committed to hepatitis elimination goals, and additional funding for effective diagnostic and care implementation is urgently needed.

MPP collaborates with diverse stakeholders—including originator and generic companies, governments, WHO, civil society, communities, procurement agencies, and clinical experts—to accelerate development and distribution of new treatments for eliminating HCV through shorter, more effective therapies in LMICs with high viral hepatitis burden. MPP's multilateral engagements increase awareness of WHO-recommended treatment options available through MPP licenses (including TDF, TAF, DAC, and DAC/SOF combinations) and support increased uptake of quality-assured, affordable treatments in LMICs.

97 World Health Organization - Elimination of hepatitis by 2030

Notably, MPP's work also addresses HBV through licensed TDF and TAF treatments, benefiting people living with HIV who receive TDF and TAF-based regimens with diagnosed or undiagnosed HBV, as well as individuals using oral PrEP containing TDF or TAF. Through these licenses, MPP supports the WHO strategy for triple elimination of vertical transmission of HIV, syphilis, and hepatitis B[98].

MPP closely monitors the evolving viral hepatitis therapeutics R&D pipeline (for hepatitis B, C, and D)[99] [100], in collaboration with leading experts to assess potential MPP interventions for leading candidates. Currently, three medicines (including investigational medicines) are included in the watchlist. With the currently available data, no viral hepatitis therapies have been identified as priority candidates for which an MPP agreement would achieve significant impact.

Relevant changes in the 2025 MPP prioritisation report compared to the previous year are:

- Addition of Bepirovirsen for hepatitis B to watchlist
- Addition of Bemnifosbuvir for hepatitis C to watchlist
- Addition of Ruzasvir for hepatitis C to watchlist
- Removal of Bulevirtide for hepatitis D from watchlist, since the primary patents will expire in January 2028 and no secondary patents were identified in LMICs.

98 Triple elimination initiative

99 Hepatitis B Foundation Drug Watch

100 Long-acting therapies trials tracker for hepatitis C, opioid use and overdose prevention therapy and malaria, July 2024, Treatment Action Group

Bepirovirsen for hepatitis B

GSK

Bepirovirsen is an investigational antisense oligonucleotide (ASO) therapy being developed for chronic hepatitis B. It targets all HBV messenger RNAs through a triple-action mechanism: (1) by reducing HBV replication, (2) by suppressing hepatitis B surface antigen (HBsAg) levels, and (3) by stimulating the immune system to potentially achieve a functional cure.

In the Phase IIb B-Clear trial, approximately 10% of participants achieved sustained HBsAg and HBV DNA loss after 24 weeks of treatment. Efficacy was observed in both nucleos(t)ide analogue (NA)-treated and untreated patients[101]. The ongoing Phase III B-Well program aims to further evaluate bepirovirsen's potential, focusing on patients with HBsAg ≤3,000 IU/mL. HBV cure occurs rarely with monotherapy, and combination therapies are being evaluated. Cure rates are significantly higher in persons with lower HBsAg levels. The FDA has recognized bepirovirsen with fast-track designation, highlighting its status as the only single agent in Phase III showing promise for finite-duration therapy for HBV, with the possibility of functional cure in some patients. This represents a potential breakthrough in chronic viral hepatitis B treatment.

GSK in-licensed bepirovirsen from Ionis (formerly Isis) Pharmaceuticals in 2019[102]. Ionis holds the primary patent on bepirovirsen, which has been filed in many low- and middle-income countries (LMICs) and is expected to expire in 2032.

Bemnifosbuvir for hepatitis C

Atea

Bemnifosbuvir is a nucleotide analog polymerase inhibitor designed to inhibit viral replication by impairing viral RNA polymerase. It has demonstrated potent pan-genotypic antiviral activity against HCV and has shown approximately 10-fold higher activity than sofosbuvir in vitro, while retaining efficacy against sofosbuvir-resistant strains[103]. Bemnifosbuvir's safety profile has been favorable, with a low risk of drug-drug interactions and no food effect reported. When combined with ruzasvir, an oral NS5A inhibitor, the two compounds have shown synergistic antiviral effects in vitro. The combination of bemnifosbuvir and ruzasvir has demonstrated a high sustained virologic response rate of 98% (208/213) at 12 weeks post-treatment (SVR12) after just eight weeks of treatment in a phase II study[104]. This regimen offers potential advantages over existing treatments, including a short treatment duration (8 weeks), low risk of drug-drug interactions, and efficacy across HCV genotypes 1-4, positioning it as a promising new option for HCV therapy[105]. Atea's primary patents on bemnifosbuvir, expected to expire in 2036, have been granted in 35 LMICs and are pending in another 14 LMICs. Atea owns several secondary patents on salts and polymorphs that may provide exclusivity until 2038-2042, as well as combinations with ruzasvir until 2039-2042 in many LMICs.

Ruzasvir for hepatitis C

Atea

Ruzasvir is an oral NS5A inhibitor that also exhibits potent pan-genotypic antiviral activity against HCV. When combined with bemnifosbuvir, the regimen showed a high sustained virologic response after a short treatment duration, with minimal drug interactions and broad efficacy across multiple HCV genotypes, making it a promising therapy option (see also above in the bemnifosbuvir section)[106]. Ruzasvir was first developed by MSD and exclusively licensed to Atea in 2021. Primary patents, expected to expire between 2031 and 2033, have been widely withdrawn and kept in force only in a few European countries. Atea filed two combination patents for bemnifosbuvir + ruzasvir. The second combination patent, expiring in 2042, is pending in 17 LMICs.

101 Cremer J, Elston R, Campbell FM, Kendrick S, Paff M, Quinn G, Theodore D. B-Clear Phase 2b Study Design: Establishing the Efficacy and Safety of Bepirovirsen in Patients with Chronic Hepatitis B Virus Infection. Adv Ther. 2023 Sep;40(9):4101-4110. doi: 10.1007/s12325-023-02531-z. Epub 2023 Jul 1. PMID: 37393402; PMCID: PMC10427703.

102 https://www.gsk.com/en-gb/media/press-releases/gsk-presents-promising-new-data-for-bepirovirsen-an-investigational-treatment-for-chronic-hepatitis-b/

103 https://www.tandfonline.com/doi/full/10.1080/13543784.2024.2305137

104 Atea Pharmaceuticals Announces Positive Results from Phase 2 Study of Bemnifosbuvir and Ruzasvir Regimen for Treatment of Hepatitis C Virus (HCV)

105 Atea: on bemnifosbuvir-ruzasvir

106 Atea Pharmaceuticals Announces Positive Results from Phase 2 Study of Bemnifosbuvir and Ruzasvir Regimen for Treatment of Hepatitis C Virus (HCV)

PANDEMIC & EPIDEMIC THREATS

The COVID-19 pandemic highlighted the urgent need for robust pandemic preparedness, including swift response strategies, global cooperation, and resilient healthcare systems. Strengthening surveillance, early detection, and rapid vaccine and other medical interventions development are essential to mitigate future public health crises.

MPP is building on the experience and lessons learned from its work on licensing and technology transfer during the COVID-19 pandemic to enhance its contribution to pandemic preparedness and response (PPR)[107]. The goal is two-fold: timely and equitable access to affordable, quality-assured health products, and security of supply during future emergencies. By actively engaging in pandemic preparedness, MPP aims to contribute to the resilience of healthcare systems and help mitigate the impact of future health crises[108].

Along with Unitaid, MPP participates in key global efforts such as the Global Therapeutics Development Coalition [109] to ensure that access is considered early in the product development lifecycle. Among several priority pathogens, influenza viruses have been identified as contributing to substantial illness and death each year, with highly pathogenic strains like H5N1 continuing to emerge and presenting a significant pandemic risk.

Seasonal influenza circulates in all parts of the world, with a year-round disease burden. It causes illnesses that range in severity and sometimes lead to hospitalisation and death. Worldwide, influenza epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290,000 to 650,000 deaths annually[110]. Given its potential role as a treatment option during an eventual influenza pandemic, MPP has added baloxavir marboxil as a priority product for in-licensing.

107 Intellectual property licensing of therapeutics during the COVID-19 crisis: lessons learnt for pandemic preparedness and response

108 MPP ON PANDEMIC PREPAREDNESS AND RESPONSE

109 Machingaidze S, Pérez Casas C, Mburu S, Draghia-Akli R, Mowbray C, Rosen J, et al. (2024) The case for a global therapeutics development coalition: Building a therapeutics pipeline for pandemic and endemic diseases. PLOS Glob Public Health 4(8): e0003654.

110 WHO Influenza fact-sheet

Baloxavir marboxil *Roche*

Baloxavir marboxil is an FDA-approved oral antiviral for both the treatment and prevention of influenza. An oral one-dose, one-time treatment for influenza, could serve, in addition to its use in seasonal influenza, as a valuable tool in pandemic preparedness in the event of an outbreak with a highly virulent influenza strain[111]. Single oral administration, with no requirement for companion drugs, would support simplified treatment delivery. As a drug in a new class of antiviral treatment for influenza, it could provide an additional layer of protection. WHO has included baloxavir marboxil in its 2024 revised influenza guidelines[112]. A conditional recommendation was made for administering baloxavir marboxil to asymptomatic individuals exposed to zoonotic influenza viruses, such as H5N1, that are associated with high mortality. Baloxavir marboxil has also the potential to reduce influenza transmission due to a rapid effect in decreasing viral shedding[113 114].

Primary patents on baloxavir marboxil have been filed or granted in several LMICs to Shionogi and they are expected to expire between 2030-2036. Secondary patents may provide exclusivity in few LMICs until 2039[115].

111 XOFLUZA; U.S. Food & Drug Administration Prescribing Information

112 WHO Clinical practice guidelines for influenza 2024

113 Ison MG, Portsmouth S, Yoshida Y, Shishido T, Mitchener M, Tsuchiya K, Uehara T, Hayden FG. Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial. Lancet Infect Dis. 2020 Oct;20(10):1204-1214. doi: 10.1016/S1473-3099(20)30004-9. Epub 2020 Jun 8. PMID: 32526195.

114 Monto AS, Kuhlbusch K, Bernasconi C, et al. Efficacy of Baloxavir Treatment in Preventing Transmission of Influenza. N Engl J Med. 2025;392(16):1582-1593. doi:10.1056/NEJMoa2413156

115 www.medspal.org: report on baloxavir marboxil

FOCUS ON CHILDREN

As part of our commitment to improving children's health, MPP is focusing on medicines for childhood-onset diseases—conditions that begin early in life and continue into adulthood, or are high in the public health agenda in relation to young ages. In most disease areas MPP works in, children often face delays in access to essential medicines compared to adults. Many important therapeutics are not yet available in child-friendly formulations. Since its creation, MPP has worked to close this gap by partnering with manufacturers to develop and accelerate access to paediatric formulations. This work increasingly takes place through our role in the Global Accelerator for Paediatric Formulations Network (GAP-f), a WHO-led initiative that MPP co-founded. Within GAP-f, we help prioritise and support the development of the most-needed paediatric medicines, with the goal of getting them to children faster.

This chapter outlines MPP's current priorities and watchlist products with added benefit to children's health. Key updates since the last report include the addition of nirsevimab and clesrovimab to the priority list for the prevention of RSV-related lower respiratory disease; the addition of dabrafenib/trametinib for low-grade glioma on the watchlist; the addition of microcoat artesunate and amodiaquine (AS/AQ) for malaria and the removal from the watch list of voxelotor for sickle cell disease, following Pfizer's decision to withdraw the product based on clinical data indicating that its benefits no longer outweighed the risks.

FOCUS ON CHILDREN

- **Respiratory syncytial virus**

Respiratory syncytial virus (RSV) is a leading cause of acute lower respiratory infections in children and severe respiratory disease in the elderly. Each year, RSV leads to over 3.6 million hospitalisations and around 100,000 deaths in children under 5, with 97% of paediatric deaths occurring in low- and middle-income countries due to limited medical care[116]. While most young children have mild symptoms, some, especially those with their first infection or underlying health conditions, develop severe diseases like pneumonia and bronchiolitis. Two immunisation options are available for infants: a monoclonal antibody and a maternal vaccine. Three vaccines also prevent severe RSV in elderly adults with certain health conditions. However, the high cost of these vaccines and under-recognition of RSV's impact in LMICs delay access to these potentially life-saving interventions[117]. Therefore, there is a delay in introducing these potentially life-saving interventions for RSV prevention into the countries where they are most needed.

116 WHO - Respiratory syncytial virus (RSV)

117 Zar HJ, Piccolis M, Terstappen J, Mazur NI, Gaayeb L, Morin S, Bont L. Access to highly effective long-acting RSV-monoclonal antibodies for children in LMICs-reducing global inequity. Lancet Glob Health. 2024 Oct;12(10):e1582-e1583. doi: 10.1016/S2214-109X(24)00258-4. Epub 2024 Jul 24. PMID: 39067468.

Nirsevimab *AstraZeneca/Sanofi*

Nirsevimab is an approved monoclonal antibody (mAb) for the prevention of RSV in children[118]. It has shown high efficacy in preventing lower respiratory tract infections (LRTIs), hospitalisations and severe RSV when administered as a single intramuscular injection in infants ahead of/or during their first RSV season[119] [120]. The WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommended that all countries introduce passive immunization for the prevention of severe RSV disease in young infants, including nirsevimab[121]. Patents covering nirsevimab have been filed or granted in several LMICs and they are expected to expire between 2028 and 2035. Secondary patents covering a formulation and a treatment regimen with expiry dates in 2038 and 2040 were filed in several LMICs[122].

Clesrovimab *MSD*

Clesrovimab is an investigational mAb, which in phase III trials was shown to be very effective in preventing RSV-associated hospitalisations and LRTI when administered as a single dose to infants of all weights from birth to 1 year, and entering their first season of RSV[123]. Clesrovimab is not approved yet[124]. Since clesrovimab's efficacy and safety data appear similar to nirsevimab's, it is likely that SAGE may evaluate it positively in the future, following its approval. Patents covering clesrovimab have been filed or granted in more than fifty LMICs and they are expected to expire in 2036. Secondary patents covering a formulation expected to expire 2039 were filed in few LMICs. Other secondary patents may be filed[125].

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118 BEYFORTUS; U.S. Food & Drug Administration Prescribing Information

119 Simões EAF, et al. Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomised controlled trials. Lancet Child Adolesc Health. 2023 Mar;7(3):180-189. doi: 10.1016/S2352-4642(22)00321-2. Epub 2023 Jan 9. PMID: 36634694; PMCID: PMC9940918.

120 Mallah N, Pardo-Seco J, Pérez-Martínez O, Durán-Parrondo C, Martinón-Torres F; NIRSE-GAL study group. Full 2023-24 season results of universal prophylaxis with nirsevimab in Galicia, Spain: the NIRSE-GAL study. Lancet Infect Dis. 2025;25(2):e62-e63. doi:10.1016/S1473-3099(24)00811-9

121 Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization - September 2024

122 www.medspal.org: report on nirsevimab

123 Clesrovimab (MK-1654): Pediatric Clinical Program – MSD 2024

124 Merck announced the U.S. Food and Drug Administration (FDA) has accepted the Biologics License Application (BLA) for clesrovimab (MK-1654) to protect infants from respiratory syncytial virus (RSV) disease during their first RSV season. The FDA has set a Prescription Drug User Fee Act (PDUFA), or target action, date of June 10, 2025 (source: Merck update at JP Morgan Healthcare Conference, Jan. 13, 2025)

125 www.medspal.org: report on clesrovimab

FOCUS ON CHILDREN

- **Malaria**

Malaria incidence increased in the last years, reaching nearly 263 million cases globally in 2023, and close to 600 thousand malaria-related deaths, with children under five years old accounting for 80% of those casualties in sub-Saharan Africa[126] [127]. Significant efforts are being made to further prevent new infections, including through the development and approval of malaria vaccines and antibody therapies[128] [129] [130] [131]. It is crucial to continue improving the safety and efficacy of malaria treatments and prevention products while also enhancing the palatability of paediatric formulations to ensure rapid and widespread uptake of malaria medicines among children.

MPP included one paediatric formulation in the watchlist for malaria. This formulation has benefited from Unitaid funding for development[132], and its role in paediatric malaria will soon be evaluated as of an upcoming Paediatric Drug Optimization (PADO) exercise led by GAP-f and WHO technical departments, which is planned for mid-2025.

126 World malaria report 2024

127 Global Malaria Progress Stalled With Nearly 600,000 Deaths in 2023

128 Ali MS, Stockdale L, Sagara I, et al. The anti-circumsporozoite antibody response to repeated, seasonal booster doses of the malaria vaccine RTS,S/AS01E. NPJ Vaccines. 2025;10(1):26. Published 2025 Feb 6. doi:10.1038/s41541-025-01078-0

129 A Single-Dose Breakthrough: PfSPZ-LARC Vaccines Offer Transformative Protection Against Malaria

130 Berry AA, Richie TL, Church LWP, et al. Safety, tolerability and immunogenicity of a condensed, multi-dose prime regimen of PfSPZ Vaccine for the prevention of Plasmodium falciparum malaria infection. Malar J. 2025;24(1):88. Published 2025 Mar 17. doi:10.

131 Cherrelle Dacon et al. ,Protective antibodies target cryptic epitope unmasked by cleavage of malaria sporozoite protein. Science387,eadr0510(2025).DOI:10.1126/science.adr0510

132 Innovations in paediatric medicines delivery awarded UnitaidExplore funding

MicroCoat artesunate and amodiaquine (AS/AQ)

FluidPharma

The MicroCoat platform technology employs a fluid bed coating process to produce individually coated drug micropellets, that regulate the rate of drug release, enabling taste masking and extended release as relevant[133]. The technology is investigated for an application to a malaria treatment for paediatric populations in LMICs through the support of a UnitaidExplore grant[134] [135]. MicroCoat AS/AQ combines into a fixed-dose combination of taste-masked anti-malarial drugs artesunate and amodiaquine[136], offering ease of administration and improved palatability for children compared to marketed products (especially for amodiaquine, which is very bitter and thereby challenging for use in children), while maintaining the same efficacy and safety[137]. The formulation has been designed to be suitable for infants and young children for the treatment of uncomplicated *P. falciparum* malaria in LMICs, by ensuring not only palatability, but also easier swallowing and more flexible dosing than standard of care. The product is stable at accelerated and long-term conditions and is in early clinical development.

133 Taste Masked Artesunate/Amodiaquine Micropellets in the Fight Against Malaria

134 Mikart and Fluid Pharma enter into a collaboration agreement to manufacture clinical trial materials using proprietary MicroCoat™ technology to advance new therapies

135 Innovative delivery systems for paediatric medicines: technology landscape. Geneva: World Health Organization;2020. Licence: CC BY-NC-SA 3.0 IGO.

136 Ngasala B, Bushukatale S, Chiduo M, et al. Efficacy of artesunate-amodiaquine for treatment of uncomplicated Plasmodium falciparum malaria in mainland Tanzania. Malar J. 2024;23(1):90. Published 2024 Mar 29. doi:10.1186/s12936-024-04923-0

137 FluidPharma Technology

FOCUS ON CHILDREN

- **Low-grade gliomas**

Low-grade gliomas (LGGs)[138] are primary brain tumours that develop from glial cells, which support and protect neurons. They are the most common brain tumours in children and young adults, accounting for around 30% of all paediatric central nervous system CNS tumours[139]. In approximately 15–20% of LGGs, a BRAF V600E mutation is found. This mutation activates a key signaling pathway that drives tumour growth and affects response to chemotherapy[140].

Dabrafenib/trametinib *Novartis*

A targeted combination of dabrafenib (a BRAF inhibitor) and trametinib (a MEK inhibitor) has shown significantly improved response rates, progression-free survival, and safety compared to traditional chemotherapy for the management of low-grade gliomas. Both drugs are FDA-approved for use in children, with age-appropriate formulations available[141] [142], and each may also be used as monotherapy for other MAPK pathway-driven tumours. However, the use of these medicines requires BRAF mutation testing, which may limit access in LMICs. Of notice, these agents have a broader indication, such as for melanoma, and have a large use in adult diseases. The primary patents on dabrafenib and trametinib (owned by Novartis) expire in 2025 and 2029 respectively. Secondary patents on the combination extend to 2030, and additional formulation patents may last until 2033–2038. The primary dabrafenib patent is present in over 30 LMICs, with secondary patents on the combination in 25 LMICs. As part of the PADO–cancer process, the MPP was asked to explore licensing options for this combination[143].

138 Aiman W, Gasalberti DP, Rayi A. Low-Grade Gliomas. [Updated 2023 May 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-

139 St. Jude Car & Treatment; Low-Grade Glioma Treatment

140 Lassaletta A et al. Therapeutic and Prognostic Implications of BRAF V600E in Pediatric Low-Grade Gliomas. J Clin Oncol. 2017 Sep 1;35(25):2934-2941. doi: 10.1200/JCO.2016.71.8726. Epub 2017 Jul 20. PMID: 28727518; PMCID: PMC5791837.

141 TAFINLAR; U.S. Food & Drug Administration Prescribing Information

142 MEKINIST; U.S. Food & Drug Administration Prescribing Information

143 Paediatric drug optimization for cancer medicines: meeting report, World Health Organizazion, January 2024

FOCUS ON CHILDREN

- **Cystic fibrosis**

Cystic fibrosis is a rare, progressive, life-threatening disease, caused by mutations in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene that results in the formation of thick mucus that builds up in the lungs, digestive tract, and other parts of the body. Cystic fibrosis leads to severe respiratory and digestive problems as well as other complications including diabetes, meningitis, osteomyelitis as well as skin and soft tissues infections[144 145 146]. There is currently no cure for the condition and people with cystic fibrosis need daily treatments depending on the severity of their symptoms. There are no global annual deaths estimates for cystic fibrosis and related life expectancy, but it is generally assumed that in the absence of CFTR modulators, the median life expectancy for cystic fibrosis would be around 25 years (compared to 46 in presence of CFTR modulators)[147 148 149].

144 Singh, J., Hunt, S., Simonds, S. et al. The changing epidemiology of pulmonary infection in children and adolescents with cystic fibrosis: an 18-year experience. Sci Rep 14, 9056 (2024). https://doi.org/10.1038/s41598-024-59658-4

145 Coderre L, Debieche L, Plourde J, Rabasa-Lhoret R, Lesage S. The Potential Causes of Cystic Fibrosis-Related Diabetes. Front Endocrinol (Lausanne). 2021 Jul 30;12:702823. doi: 10.3389/fendo.2021.702823. PMID: 34394004; PMCID: PMC8361832.

146 Kiedrowski MR, Bomberger JM. Viral-Bacterial Co-infections in the Cystic Fibrosis Respiratory Tract. Front Immunol. 2018 Dec 20;9:3067. doi: 10.3389/fimmu.2018.03067. PMID: 30619379; PMCID: PMC6306490.

147 Guo J., Garratt A., Hill A., Worldwide rates of diagnosis and effective treatment for cystic fibrosis, Journal of Cystic Fibrosis, Volume 21, Issue 3, 2022, Pages 456-462, ISSN 1569-1993

148 McBennett KA, Davis PB, Konstan MW. Increasing life expectancy in cystic fibrosis: Advances and challenges. Pediatr Pulmonol. 2022 Feb;57 Suppl 1(Suppl 1):S5-S12. doi: 10.1002/ppul.25733. Epub 2021 Nov 11. PMID: 34672432; PMCID: PMC9004282.

149 Balfour-Lynn I.M., King J.A., CFTR modulator therapies – Effect on life expectancy in people with cystic fibrosis, Paediatric Respiratory Reviews, Volume 42, 2022, Pages 3-8, ISSN 1526-0542

Elexacaftor/ivacaftor/tezacaftor *Vertex*

The combination of elexacaftor, tezacaftor and ivacaftor represents the first triple therapy available for the treatment of cystic fibrosis (CF) in patients with the most common CFTR mutation, F508del[150]. Approved for individuals aged 2 years and older[151] who have at least one copy of this mutation, the therapy is potentially suitable for approximately 90% of people living with CF. Its oral formulation and lack of cold chain requirements further enhance its suitability for wider use, including in LMICs. However, several barriers limit access to this treatment in LMICs. Diagnosis of CF relies on a sweat test, which is often unavailable in these settings, and genetic testing is essential to determine eligibility for CFTR-modulator therapy. Newborn screening programmes for CF are limited, and access to both diagnostic tests remain constrained. Additionally, there is a lack of established CF patient registries in most LMICs – currently, only Egypt and South Africa have such systems in place on the African continent. Building capacity among healthcare workers to recognise CF and developing patient registries are critical steps to support equitable access to this transformative therapy in LMICs. Ivacaftor and tezacaftor primary patents owned by Vertex are expected to expire between 2025 and 2028. Elexacaftor primary patents including its combination with tezacaftor and ivacaftor have been filed or granted in more than seventy LMICs with an expected expiry in 2037. Numerous secondary patents covering polymorphic forms, formulations and treatment regimens are present in many LMICs with an expected expiry dated between 2026 and 2039.

150 Middleton PG et al, Elexacaftor-Tezacaftor-Ivacaftor for Cystic Fibrosis with a Single Phe508del Allele. N Engl J Med. 2019 Nov 7;381(19):1809-1819. doi: 10.1056/NEJMoa1908639. Epub 2019 Oct 31. PMID: 31697873; PMCID: PMC7282384.

151 TRIKAFTA; U.S. Food & Drug Administration Prescribing Information

FOCUS ON CHILDREN

- **HIV post-natal prophylaxis**

Monoclonal antibodies for HIV post-natal prophylaxis

Multiple innovators

These laboratory-made proteins emulate the immune system's ability to counteract harmful pathogens, including HIV. Although still in the early stages of development, broadly-neutralising antibodies demonstrate significant potential for use as HIV post-natal prophylaxis (PNP), due to their favourable safety profile and the convenience they may offer through a single administration covering the peri-natal and breastfeeding period via intramuscular injection[152],[153],[154]. Despite potential benefits, crucial clinical data on the efficacy of monoclonal antibodies for PNP remain lacking[155]. Specifically, there is a notable gap in understanding whether a single monoclonal antibody could suffice for prevention. If multiple mAbs are necessary, the cost could become a significant concern, especially when compared to cheaper small molecules.

Beyond their use in postnatal prophylaxis, broadly neutralizing antibodies (bNAbs) are also being investigated for HIV cure strategies. The RIO study explored the use of two antibodies that can complementarily neutralize HIV through distinct mechanisms of action (3BNC117 and 10-1074, also known as teropavimab and zinlirvimab) in cis-gender men participants who accepted to stop their HIV-antiretroviral treatment, indicating that a one-time infusion of this antibodies combination could sustain viral suppression for over a year in some participants[156] [157] [158]. While these findings remain preliminary, they highlight the broader therapeutic potential of bNAbs beyond postnatal prophylaxis.

152 Accelerating bnAbs for peri- and post-natal HIV prophylaxis: An Action Plan

153 Press Release: IAVI and partners kick-start CELEBRATE study to explore acceptability and feasibility of bnAbs for infant HIV prevention

154 CROI 2023: The promise of bnAbs for infant post-natal prophylaxis to end paediatric HIV: the path forward

155 Accelerating bnAbs for peri- and post-natal HIV prophylaxis: An Action Plan

156 The RIO trial: A Randomised Placebo-Controlled Study of 2 LS-bNAbs (3BNC-117-LS & 10-1074-LS) in People Treated in Early HIV

157 Gilead Sciences Licenses Portfolio of HIV Antibodies From The Rockefeller University

158 Teropavimab and zinlirvimab on LAPaL

ONCOLOGY

Cancer is one of the leading causes of death worldwide, accounting for nearly 10 million deaths in 2022[159] [160] or about one in six deaths. Cancers of the breast, lung, colon and rectum, prostate, stomach, liver, cervix and skin are among the most common. In people living with HIV, some cancers are particularly prevalent due to their increased vulnerability to oncogenic infections[161] [162] [163] [164]. Thanks to antiretroviral treatments, people living with HIV now have a longer life expectancy and can manage their virological condition as a chronic disease. However, this improvement is accompanied by a change in the epidemiological profile: cancer has become one of the main causes of morbidity and mortality in this population, following the trends observed in the general population.

While many cancers can be cured when detected early and treated effectively, access to timely diagnosis and quality treatment remains a major challenge in low- and middle-income countries. This context fully justifies the MPP's commitment in this area, in order to facilitate access to innovations in oncology for the populations that need them most.

This chapter provides a summary of MPP priorities and watchlist in the field of oncology. Seven oncology medicines and a drug class are identified as priorities and are included in the watchlist. In this report, we removed oral paclitaxel + encequidar, which was previously in the watchlist, following the discontinuation of its development. The FDA had issued a Complete Response Letter (CRL), indicating the application was not ready for approval in its current form, and the originator has since filed for bankruptcy. We also removed ibrutinib which was listed as priority for chronic lymphocytic leukaemia (CLL), as the primary patent expires in 2026.

159 World Health Organization, Cancer Factsheet, 2025

160 Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer

161 Omar, A., Marques, N., & Crawford, N. (2024). Cancer and HIV: The Molecular Mechanisms of the Deadly Duo. Cancers, 16(3), 546. https://doi.org/10.3390/cancers16030546

162 Marino A, Pavone G, Martorana F, et al. Navigating the Nexus: HIV and Breast Cancer-A Critical Review. Int J Mol Sci. 2024;25(6):3222. Published 2024 Mar 12. doi:10.3390/ijms25063222

163 Engels EA, Shiels MS, Barnabas RV, et al. State of the science and future directions for research on HIV and cancer: Summary of a joint workshop sponsored by IARC and NCI. Int J Cancer. 2024;154(4):596-606. doi:10.1002/ijc.34727

164 Mathoma A, Sartorius B, Mahomed S. The Trends and Risk Factors of AIDS-Defining Cancers and Non-AIDS-Defining Cancers in Adults Living with and without HIV: A Narrative Review. J Cancer Epidemiol. 2024;2024:7588928. Published 2024 Mar 21. doi:10.1155/2024

ONCOLOGY

- **Multiple cancer indications**

Immune checkpoint inhibitors *Multiple innovators*

including **Pembrolizumab** *MSD*

Immune checkpoint inhibitors (ICIs) have revolutionised oncology, opening new possibilities for cancer treatment through immunotherapy[165]. These monoclonal antibodies block proteins that would otherwise prevent the immune system from attacking cancer cells. The most well-known in this class are PD-1 and PD-L1 inhibitors. Their versatility has led to approval for a wide range of cancers, with a robust and promising pipeline of new ICIs. The WHO EML Committee has recognised their therapeutic value by including certain ICIs for the treatment of cutaneous melanoma, underscoring their effectiveness and potential for broader application.

Notably, ICIs have shown promise in addressing some of the most pressing global cancer challenges, including breast and cervical cancers—the most commonly diagnosed and deadliest cancers among women in LMICs. Among people living with HIV, many cancers occur more frequently due to infectious origins, such as Kaposi's sarcoma (linked to human herpesvirus 8), non-Hodgkin lymphoma (linked to Epstein–Barr virus), and cervical cancer (linked to human papillomavirus, HPV)[166]. People living with HIV who are on antiretroviral therapy and virally suppressed can live longer, managing HIV as a chronic condition, and face similar health issues as the general population. As a result, cancer has emerged as a leading cause of death in this population, posing new clinical challenges. Despite the paucity of safety and efficacy data of ICIs in the HIV population, emerging studies suggest that ICIs treatments do not interfere with HIV management, reinforcing the value of these therapies for this population[167].

However, ensuring broad access to ICIs remains a challenge. Recognising this, the WHO EML Committee has recommended further efforts to improve the affordability of ICIs, including consideration of voluntary licensing through MPP. In addition to voluntary licensing of intellectual property, MPP's support for hands-on technology transfer could help accelerate development and lower the costs of quality-assured biosimilar versions of ICIs for use in LMICs. In line with this, MPP has strategically prioritised ICIs as a class, with pembrolizumab, approved for 18 types of cancer, including certain early-stage and advanced cancers, identified as a flagship product for this class.

Pembrolizumab is presented in the lung cancer section.

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165 Sharma P et al; Immune checkpoint therapy-current perspectives and future directions. Cell. 2023 Apr 13;186(8):1652-1669. doi: 10.1016/j.cell.2023.03.006. PMID: 37059068.

166 Grulich AE and al. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet. 2007 Jul 7;370(9581):59-67. doi: 10.1016/S0140-6736(07)61050-2. PMID: 17617273.

167 Assoumou L and al. Safety and tolerability of immune checkpoint inhibitors in people with HIV infection and cancer: insights from the national prospective real-world OncoVIHAC ANRS CO24 cohort study. J Immunother Cancer. 2024 Aug 22;12(8):e009728. doi: 10.1136/jitc-2024-009728. PMID: 39179255; PMCID: PMC11344510.

ONCOLOGY

- **Lung cancer**

Lung cancer arises from the rapid and unregulated proliferation of abnormal cells in the lungs, posing a significant threat to health and carrying a high risk of fatality. In 2022, globally, lung cancer was responsible for 2.48 million new cases and 1.8 million deaths[168].

The two most common forms of lung cancer are: non-small cell lung carcinoma (NSCLC), which is prevalent and tends to develop at a gradual pace, and small cell lung carcinoma (SCLC), which is rarer but usually exhibits a rapid growth rate and disease progression. In LMICs, there were 1.4 million incident cases of NSCLC in 2022[169]. Unfortunately, around 70% of NSCLC cases are diagnosed in advanced stages, such as locally advanced or metastatic[170].

Aumolertinib *Hansoh Pharma*

Aumolertinib is a third-generation molecular targeted drug that acts as an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) with antineoplastic activity. It inhibits mutant forms of EGFR, including the T790M mutation. Aumolertinib has demonstrated significant benefits over standard first- and second-generation treatments included in the WHO Essential Medicines List for NSCLC. It is currently under review for approval by the European Medicines Agency (EMA)[171] [172]. Aumolertinib compound patent is expected to expire in 2035, and it has been granted in key countries of manufacture such as India, China and South Africa. Secondary patents may provide exclusivity in few LMICs until 2036-2039[173].

168 Zhou J, Xu Y, Liu J, Feng L, Yu J, Chen D. Global burden of lung cancer in 2022 and projections to 2050: Incidence and mortality estimates from GLOBOCAN. Cancer Epidemiol. 2024 Dec;93:102693. doi: 10.1016/j.canep.2024.102693. Epub 2024 Nov 13. PMID: 39536404.

169 Globocan 2022

170 Casal-Mouriño A et al; Epidemiology of stage III lung cancer: frequency, diagnostic characteristics, and survival. Transl Lung Cancer Res. 2021 Jan;10(1):506-518. doi: 10.21037/tlcr.2020.03.40. PMID: 33569332; PMCID: PMC7867742.

171 Hansoh Pharma, Press Release.

172 Lu S et al; AENEAS: A Randomized Phase III Trial of Aumolertinib Versus Gefitinib as First-Line Therapy for Locally Advanced or MetastaticNon-Small-Cell Lung Cancer With EGFR Exon 19 Deletion or L858R Mutations. J Clin Oncol. 2022 Sep 20;40(27):3162-3171. doi: 10.1200/JCO.21.02641. Epub 2022 May 17. PMID: 35580297; PMCID: PMC9509093.

173 www.medspal.org: report on aumolertinib

Osimertinib *AstraZeneca*

Osimertinib is a third-generation molecular targeted drug that acts as an EGFR TKI, designed to target both EGFR-sensitising and EGFR T790M resistance mutations. It has demonstrated clinical activity against central nervous system (CNS) metastases and is approved by both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Osimertinib has shown significant benefits over standard first- and second-generation treatments included in the WHO EML for non-small cell lung cancer. The EML committee has called on MPP to explore licensing opportunities for osimertinib[174] [175]. The primary patent on osimertinib is expected to expire in 2032 and has been granted in more than 60 LMICs[176].

Pembrolizumab *MSD*

Pembrolizumab is an immune checkpoint inhibitor, specifically an anti-programmed death receptor-1 (PD-1) therapy, that enhances the body's immune response to detect and combat tumour cells. It is a humanised monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes, which can target both tumour and healthy cells. Pembrolizumab as a single agent reduces the risk of death in NSCLC patients by 40%, significantly extending survival by more than a year with fewer sides effects compared to traditional chemotherapy[177] [178]. First approved in 2014, pembrolizumab has since gained approval for 18 types of cancer, including lung cancer and certain early-stage and advanced cancers. MSD holds the exclusive patent rights on pembrolizumab until 2028 with patents filed or granted in at least 15 LMICs[179].

174 TAGRISSO; U.S. Food & Drug Administration Prescribing Information

175 Ramalingam SS et al; FLAURA Investigators. Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC. N Engl J Med. 2020 Jan 2;382(1):41-50. doi: 10.1056/NEJMoa1913662. Epub 2019 Nov 21. PMID: 31751012.

176 www.medspal.org: report on osimertinib

177 Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2016;375(19):1823-1833. doi:10.1056/NEJMoa1606774

178 Reck M, Rodríguez-Abreu D, Robinson AG, et al. Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non-Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50. J Clin Oncol. 2021;39(21):2339-2349.doi:10.1200/JCO.21.00174

179 www.medspal.org: report on pembrolizumab

Adagrasib *Mirati/BMS*

Adagrasib is an oral Kirsten Rat Sarcoma Virus (KRAS) inhibitor designed to potently and selectively target the KRAS G12C mutation. It received accelerated approval from the US FDA in 2022[180] for the treatment of NSCLC and has demonstrated durable clinical benefits, including improved progression-free survival[181] [182]. Notably, in 2024, the US FDA also granted accelerated approval for adagrasib in combination with immunotherapy for adults with KRAS G12C-mutated colorectal cancer, further reinforcing its potential across multiple tumour types[183]. Adagrasib primary patents have been filed in many LMICs and are expected to expire in 2038.

Lazertinib *Janssen*

Lazertinib is an oral, potent, and irreversible EGFR TKI that is highly selective for activating (EGFRm) and T790M resistance mutations. In 2024, the US FDA approved the combination of lazertinib and immunotherapy for first-line treatment of NSCLC harbouring the mutation[184]. Research on lazertinib monotherapy is ongoing, highlighting its potential as an alternative treatment option for lung cancer[185]. The primary patent on lazertinib has been granted in many LMICs including India and is expected to expire in 2034. There are secondary patents that may provide further exclusivity until 2038-2041 in many LMICs.

Sotorasib *Amgen*

Sotorasib is an oral Kirsten Rat Sarcoma Virus (KRAS inhibitor designed to potently and selectively target the KRAS G12C mutation. It received accelerated approval from the US FDA in 2021 for the treatment of NSCLC[186]. Notably, in January 2025, the FDA granted accelerated approval for sotorasib in combination with immunotherapy for adults with KRAS G12C-mutated colorectal cancer, further reinforcing its potential across multiple tumour types[187]. The primary patent on sotorasib has been granted in many LMICs and is expected to expire in 2038. Several secondary patents on crystalline forms and processes are expected to expire between 2039 and 2040.

180 KRAZATI; U.S. Food & Drug Administration Prescribing Information

181 Jänne PA, Riely GJ, Gadgeel SM, et al. Adagrasib in Non-Small-Cell Lung Cancer Harboring a KRASG12C Mutation. N Engl J Med. 2022;387(2):120-131. doi:10.1056/NEJMoa2204619

182 Bristol Myers Squibb, Press Release, March 2024.

183 Bristol Myers Squibb, Press Release, June 2024.

184 U.S. Food & Drug Administration Press Release, August 2024.

185 Cho BC et al. Lazertinib Versus Gefitinib as First-Line Treatment in Patients With EGFR-Mutated Advanced Non-Small-Cell Lung Cancer: Results From LASER301. J Clin Oncol. 2023 Sep 10;41(26):4208-4217. doi: 10.1200/JCO.23.00515. Epub 2023 Jun 28. PMID: 37379502.

186 LUMAKRAS; U.S. Food & Drug Administration Prescribing Information.

187 Amgen, Press Release, January 2025.

ONCOLOGY

- **Breast cancer**

Breast cancer is the most common cancer in women and the second most common cancer worldwide[188]. In 2022, there were over 2.29 million new cases of breast cancer in women[189]. There are four main subtypes of female breast cancer, ranked by prevalence: HR+/HER2-, HR-/HER2-, HR+/HER2+, and HR-/HER2+. Hormone receptor (HR) status indicates whether tumour cells have receptors for the hormones oestrogen or progesterone; HR+ tumours grow in response to these hormones. Human epidermal growth factor receptor 2 (HER2) status refers to the presence of the HER2/neu protein, which is linked to more aggressive forms of breast cancer when overexpressed (HER2+)[190]. This classification is crucial for guiding treatment decisions and predicting disease progression.

188 Global Cancer Observatory: Cancer Today; 2024.

189 Ferlay J et al, Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer; 2024.

190 National Institutes of Health – National Cancer Institute – Cancer Stat Facts: Female Breast Cancer Subtypes

Abemaciclib *Eli Lilly*

Abemaciclib is an oral cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitor, approved by the US FDA for treating HR+/HER2- advanced breast cancer[191] [192]. CDK 4/6 inhibitors are the preferred treatment option for HR+/HER2- advanced breast cancer. The EML expert committee recognised its potential for future inclusion and recommended that MPP explore licensing opportunities to support affordable access. Abemaciclib primary patents have been granted in more than 40 LMICs and are expected to expire in 2029 in most countries[193].

Ribociclib *Novartis*

Ribociclib is an oral CDK 4/6 inhibitor, approved by the US FDA for treating HR+/HER2- advanced breast cancer[194] [195]. CDK 4/6 inhibitors are the preferred treatment option for HR+/HER2- advanced breast cancer. The EML expert committee recognised its potential for future inclusion and recommended that MPP explore licensing opportunities to support affordable access. Ribociclib and abemaciclib are similar alternative treatment options. Ribociclib primary patents have been filed or granted in many LMICs and are expected to expire between 2027 and 2029. Secondary patents may provide exclusivity until 2031-2036 in many LMICs[196].

Trastuzumab subcutaneous *Roche*

Trastuzumab, a humanised IgG1 monoclonal antibody used to treat HER2-overexpressing metastatic breast cancer, has been developed (from infusion initially) into a subcutaneous formulation using recombinant human hyaluronidase to enhance delivery by temporarily breaking down hyaluronan, a barrier-forming substance in the tissues beneath the skin. Approved in 2019[197], the subcutaneous formulation follows a fixed-dose regimen, making it easier and quicker to administer than the original intravenous version[198]. Trastuzumab primary patents expired in 2012. Secondary patents on the subcutaneous formulation have been filed and granted widely in LMICs and are expected to expire in 2030[199].

191 VERNEZIO; U.S. Food & Drug Administration Prescribing Information

192 Johnston S, Martin M, Di Leo A, et al. MONARCH 3 final PFS: a randomized study of abemaciclib as initial therapy for advanced breast cancer. NPJ Breast Cancer. 2019;5:5. Published 2019 Jan 17. doi:10.1038/s41523-018-0097-z

193 www.medspal.org: report on abemaciclib

194 Lu YS et al. Updated Overall Survival of Ribociclib plus Endocrine Therapy versus Endocrine Therapy Alone in Pre- and Perimenopausal Patients with HR+/HER2- Advanced Breast Cancer in MONALEESA-7: A Phase III Randomized Clinical Trial. Clin Cancer Res. 2022;28(5):851-859. doi:10.1158/1078-0432.CCR-21-3032

195 KISAQLI; U.S. Food & Drug Administration Prescribing Information

196 www.medspal.org: report on ribocicib

197 HERCEPTIN HYLECTA; U.S. Food & Drug Administration Prescribing Information

198 Pivot X, Gligorov J, Müller V, et al. Preference for subcutaneous or intravenous administration of trastuzumab in patients with HER2-positive early breast cancer (PrefHer): an open-label randomised study. Lancet Oncol. 2013;14(10):962-970. doi:10.1016/S1470-2045(13)70383-8

199 www.medspal.org: report on trastuzumab subcutaneous

ONCOLOGY

- **Chronic Lymphocytic Leukaemia**

Chronic Lymphocytic Leukaemia (CLL) is the most common type of leukaemia, accounting for approximately 25% to 30% of all cases. While it is generally considered a disease of older adults, its burden is shifting, with mortality rates rising rapidly in some regions. In particular, Central Sub-Saharan Africa has seen the biggest rise in death rates and overall health burden (taking into account both illness and early death), increasing by about 2.8% and 2.7% per year, respectively. The burden has risen sharply in LMICs highlighting the growing impact of CLL in resource-limited settings[200].

Zanubrutinib *Beigene*

Zanubrutinib is a BTKi approved by the FDA in 2023[201] for the treatment of CLL[202]. Recognizing the important emerging role of BTKi as a therapeutic class in the treatment of CLL, the EML Committee advised that it would consider an application for zanubrutinib as therapeutic alternative for inclusion and recommended that MPP explore licensing opportunities to support affordable access. The primary patent on zanubrutinib was granted in few LMICs, including India, where it is expected to expire in 2034. Secondary patents on crystalline forms are expected to expire in 2037[203].

200 Ou Y et al. Trends in Disease Burden of Chronic Lymphocytic Leukemia at the Global, Regional, and National Levels From 1990 to 2019, and Projections Until 2030: A Population-Based Epidemiologic Study. Front Oncol. 2022 Mar 10;12:840616. doi: 10.3389/fonc.2022.840616. PMID: 35359356; PMCID: PMC8961301.

201 BRUKINSA; U.S. Food & Drug Administration Prescribing Information.

202 Tam CS et al. Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. Lancet Oncol. 2022 Aug;23(8):1031-1043. doi: 10.1016/S1470-2045(22)00293-5. Epub 2022 Jul 7. Erratum in: Lancet Oncol. 2023 Mar;24(3):e106. doi: 10.1016/S1470-2045(23)00073-6. PMID: 35810754.

203 www.medspal.org: report on zanubrutinib

ONCOLOGY

- **Prostate cancer**

Prostate cancer was the fourth most common cancer globally in 2022[204], accounting for 14.2% of all new cancer diagnoses in men[205]. Notably, incidence rates have been rising in several Sub-Saharan African populations[206]. Men of African descent face nearly twice the risk of being diagnosed with prostate cancer before the age of 45 compared to Caucasian men[207]. Additionally, research suggests that higher overall and central body fat increases the risk of prostate cancer-related mortality[208].

204 Ferlay J et al (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer

205 Global Cancer Observatory, 2024.

206 Seraphin TP et al. Rising Prostate Cancer Incidence in Sub-Saharan Africa: A Trend Analysis of Data from the African Cancer Registry Network. Cancer Epidemiol Biomarkers Prev. 2021;30(1):158-165. doi:10.1158/1055-9965. EPI-20-1005

207 Metcalfe C, Evans S, Ibrahim F, et al. Pathways to diagnosis for Black men and White men found to have prostate cancer: the PROCESS cohort study. Br J Cancer. 2008;99(7):1040-1045. doi:10.1038/sj.bjc.6604670

208 Perez-Cornago A, Dunneram Y, Watts EL, Key TJ, Travis RC. Adiposity and risk of prostate cancer death: a prospective analysis in UK Biobank and meta-analysis of published studies. BMC Med. 2022;20(1):143. Published 2022 May 5. doi:10.1186/s12916-022-02336-x

Apalutamide *Janssen*

Apalutamide is an oral second-generation androgen receptor antagonist approved by the US FDA in 2018[209] [210]. For the treatment of non-metastatic castration-resistant and metastatic castration-sensitive prostate cancer, clinical guidelines recommend androgen receptor antagonists, such as apalutamide, in combination with androgen-deprivation therapy as the standard of care. With approval for both of these advanced prostate cancer types, apalutamide emerges as a key therapeutic option. Apalutamide primary patents are expected to expire in 2027. Secondary patents may provide exclusivity until 2033-2038 in many LMICs.

Darolutamide *Bayer*

Darolutamide is an oral second-generation androgen receptor antagonist approved by the US FDA in 2019[211]. For the treatment of non-metastatic castration-resistant and metastatic castration-sensitive prostate cancer, clinical guidelines recommend androgen receptor antagonists, such as darolutamide, in combination with androgen-deprivation therapy as the standard of care. Unlike other second-generation androgen receptor antagonists, darolutamide has a distinct structure, which may offer advantages in tolerability and efficacy[212]. With approval for both of these advanced prostate cancer types, darolutamide stands out as a key therapeutic option. Darolutamide primary patent has been granted in many LMICs and is expected to expire in May 2030. The patent term has been extended in few LMICs until 2035. Secondary patents have not been identified in LMICs.

209 ERLEADA; U.S. Food & Drug Administration Prescribing Information.

210 Smith MR, Saad F, Chowdhury S, et al. Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. N Engl J Med. 2018;378(15):1408-1418. doi:10.1056/NEJMoa1715546

211 NUBEQUA; U.S. Food & Drug Administration Prescribing Information.

212 George D, Morgans A, Khan N, et al. Real-world use and outcomes of darolutamide (DARO), enzalutamide (ENZA), and apalutamide (APA) for nonmetastatic castration-resistant prostate cancer (nmCRPC): race subgroup analysis. J Clin Oncol. 2025;43(suppl 5):158. doi:10.1200/JCO.2025.43.5_suppl.158

DIABETES, CARDIOVASCULAR & METABOLIC DISORDERS

This chapter provides a summary of MPP priorities and watchlist in the diabetes, cardiovascular and metabolic disorders field. Incretin-based therapies have been prioritised as a class, with two products on the priority list and two products on the watchlist. Insulin analogues have also been prioritised as a class. Cardiovascular fixed-dose combination therapies are currently on the watchlist.

DIABETES, CARDIOVASCULAR & METABOLIC DISORDERS

- **Diabetes and obesity**

In 2021, 537 million adults (10.5% of the global population) are grappling with diabetes. Projections indicate that this number will climb to 643 million by 2030. Approximately 240 million individuals worldwide live with undiagnosed diabetes. Notably, 90% of these undiagnosed cases are concentrated in LMICs. Type 1 diabetes (T1DM) affects over 1.2 million children and adolescents, with 54% of them under the age of 15. Type 2 diabetes (T2DM) is the most common type of diabetes, accounting for over 90% of all diabetes worldwide[213]. Globally, the prevalence of type 2 diabetes is high and rising across all regions and has also become a concern in children and young people as a result of an increasing prevalence of obesity[214].

In 2022, one in eight people worldwide were living with obesity[215]. Obesity and type 2 diabetes are closely linked, driving cardiometabolic conditions such as cardiovascular and kidney diseases, which present major health challenges, particularly in LMICs. By 2035, 79% of individuals living with obesity are expected to be in LMICs[216]. Obesity trends and metabolic dysregulation are also rising among people living with HIV. With increased life expectancy, this population faces a growing burden of NCDs, including CVDs and diabetes. In South Africa, a recent study found that 63% of people living with HIV were overweight or obese, and 6% had diabetes[217]. Ensuring accessibility and affordability of effective treatments is crucial, as the high cost of current medications poses significant barriers, particularly in LMICs with a high HIV burden[218].

213 Ong, Kanyin Liane et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021, The Lancet, Volume 402, Issue 10397, 203 - 234

214 International Diabetes Federation - Diabetes Atlas 2021

215 World Health Organization – Obesity – Key Facts

216 World Obesity Atlas 2024

217 Gizamba JM and al. Prevalence of obesity, hypertension and diabetes among people living with HIV in South Africa: a systematic review and meta-analysis. BMC Infect Dis. 2023 Dec 7;23(1):861. doi: 10.1186/s12879-023-08736-5. PMID: 38062372; PMCID: PMC10704741.

218 Chandiwana N, Manne-Goehler J, Gaayeb L, Calmy A, Venter WDF. Novel anti-obesity drugs for people with HIV. Lancet HIV. 2024 Aug;11(8):e502-e503. doi: 10.1016/S2352-3018(24)00151-6. Epub 2024 Jul 14. PMID: 39009002.

Incretin-based therapies (incl. GLP1-RA)

Multiple innovators

Incretin hormones are gut hormones that amplify nutrient-induced insulin secretion in response to meal intake. Incretin peptides, principally Glucagon-like peptide-1 (GLP-1) and Gastric inhibitory polypeptide (GIP), regulate islet hormone secretion, glucose concentrations, lipid metabolism, gut motility, appetite, body weight, and immune function, providing a scientific basis for utilizing incretin-based therapies in the treatment of T2DM. GLP-1 receptor agonists (RAs) are attractive options for the treatment of T2DM as they effectively reduce glycaemia and promote weight loss while posing a low risk of hypoglycaemia. Some incretin mimetics also have documented beneficial effects on various health issues, including for the cardiovascular system, chronic kidney disease, and non-alcoholic fatty liver disease[219], with research ongoing into potential benefits in other areas as well[220 221].

Sub-cutaneous semaglutide

Novo Nordisk

Subcutaneous semaglutide, a once-weekly peptide-based GLP-1 RA, is highly effective in achieving and maintaining glycaemic targets in people with T2DM. It also promotes weight loss in adults with overweight or obesity and reduces the risk of major adverse cardiovascular events in this population[222 223]. Additionally, semaglutide has been shown to significantly reduce the risk of kidney disease progression in adults with T2DM and chronic kidney disease. A label extension for risk reduction of chronic kidney disease (CKD) related events has been filed based on these findings, with a regulatory decision expected in the first half of 2025[224]. Additional regulatory submissions are anticipated in 2025, following successful phase III trials investigating semaglutide's potential to reduce heart failure outcomes and improve metabolic dysfunction-associated steatohepatitis (MASH)[225]. To date, semaglutide remains the GLP-1 RA with the most advanced clinical profile. Primary patents on semaglutide expiring between 2024-2026 have been or granted in few LMICs. Patents on the sub-cutaneous formulation expired in 2024. Novo Nordisk owns many secondary patents that may extend exclusivity until 2040[226].

Oral semaglutide

Novo Nordisk

Oral semaglutide, a once daily peptide-based GLP-1 RA, is highly effective in achieving and maintaining glycaemic targets while also promoting weight loss in people with T2DM[227]. Clinical trials have demonstrated additional benefits, including a reduction in major adverse cardiovascular events (MACE) in those with T2DM and either cardiovascular disease or chronic kidney disease. A label extension was submitted to the FDA for the prevention of major adverse cardiovascular events (MACE) in patients with type 2 diabetes (T2D) and established cardiovascular disease (CVD) and/or chronic kidney disease (CKD) at the end of 2024[228]. A higher-dose formulation of oral semaglutide has also been shown to support weight management in adults with obesity or overweight[229]. As a result, regulatory filing for an obesity indication may take place in 2025, which would make it the first oral GLP-1 therapy approved for

219 Drucker DJ. Mechanisms of Action and Therapeutic Application of Glucagon-like Peptide-1. Cell Metab. 2018 Apr 3;27(4):740-756. doi: 10.1016/j.cmet.2018.03.001. PMID: 29617641.

220 Nowell J, Blunt E, Edison P. Incretin and insulin signaling as novel therapeutic targets for Alzheimer's and Parkinson's disease. Mol Psychiatry. 2023 Jan;28(1):217-229. doi: 10.1038/s41380-022-01792-4. Epub 2022 Oct 18. PMID: 36258018; PMCID: PMC9812772.

221 Hendershot CS, Bremmer MP, Paladino MB, et al. Once-Weekly Semaglutide in Adults With Alcohol Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. Published online February 12, 2025. doi:10.1001/jamapsychiatry.2024.4789

222 OZEMPIC; U.S. Food & Drug Administration Prescribing Information.

223 WEGOVY; U.S. Food & Drug Administration Prescribing Information.

224 Novo Nordisk, Press Release, December 2024.

225 Novo Nordisk, Annual Report 2024.

226 www.medspal.org: semaglutide sub-cutaneous formulation

227 RYBELSUS; U.S. Food & Drug Administration Prescribing Information.

228 Novo Nordisk, Press Release, December 2024.

229 Novo Nordisk, Press Release, May 2023.

this use. The oral formulation of semaglutide may make it appropriate for use in resource limited settings as it is heat stable. Primary patents on semaglutide expiring between 2024-2026 have been or granted in few LMICs. Secondary patents on semaglutide solid compositions with salcaprozate sodium, an important excipient of the finished product, have been filed in about seventeen LMICs, including major manufacturing countries such as India, South Africa, China and Brazil where they are expected to expire in 2031. Novo Nordisk owns many secondary patents that may extend exclusivity until 2040[230].

Tirzepatide *Eli Lilly*

Tirzepatide, a once weekly sub-cutaneous dual GLP-1 / GIP RA, is highly effective in achieving and maintaining glycaemic targets in people with T2DM and promoting weight loss in adults with obesity or overweight. It has also been approved for the reduction of the severity of sleep-apnea in adults with obesity[231] [232]. Successful clinical trials demonstrated benefits in adults with obesity and heart failure with preserved ejection fraction, with an application for approval submitted in 2024[233]. Ongoing phase III and phase II clinical trials are investigating its efficacy in major adverse cardiovascular events (MACE) in people living with T2DM and CKD in people with obesity with or without T2DM. The primary patent on tirzepatide has been granted so far in at least 37 LMICs, including India, and pending in another 14 with an expected expiry in 2036. Secondary patents on the subcutaneous formulation have been filed and granted widely in LMICs and are expected to expire in 2039[234].

Orforglipron *Eli Lilly*

Orforglipron, an investigational once-daily oral non-peptide GLP-1 RA, is currently in two phase III clinical trial programmes for T2DM and obesity[235], with results expected in 2025. Its oral formulation and fully synthetic nature make it a promising therapy. The patents on orfoglipron compound are granted in 32 LMICs and pending another 18 LMICs and is expected to expire is 2037[236].

Retatrutide *Eli Lilly*

Retatrutide, an investigational once-weekly subcutaneous GLP-1/GIP/glucagon agonist, has shown significant improvements in glycaemic control for people with T2DM and substantial weight reduction in those with obesity. Its safety profile is consistent with other incretin mimetics, making it a promising therapy[237]. The primary patent on retatrutide has been granted so far in at least 16 LMICs, including India, and pending in another 30 LMICs with an expected expiry in 2038[238].

230 www.medspal.org: report on oral semaglutide

231 MOUNJARO; U.S. Food & Drug Administration Prescribing Information.

232 ZEPBOUND; U.S. Food & Drug Administration Prescribing Information.

233 Eli Lilly, Press Release, August 2024.

234 www.medspal.org: report on tirzepatide **accessed on 24.03.2025**

235 Wharton S and al. Daily Oral GLP-1 Receptor Agonist Orforglipron for Adults with Obesity. N Engl J Med. 2023 Sep 7;389(10):877-888. doi: 10.1056/NEJMoa2302392. Epub 2023 Jun 23. PMID: 37351564.

236 www.medspal.org: report on orfoglipron **accessed on 24.03.2025**

237 Jastreboff AM and al; Retatrutide Phase 2 Obesity Trial Investigators. Triple-Hormone-Receptor Agonist Retatrutide for Obesity - A Phase 2 Trial. N Engl J Med. 2023 Aug 10;389(6):514-526. doi: 10.1056/NEJMoa2301972. Epub 2023 Jun 26. PMID: 37366315.

238 www.medspal.org: report on retatrutide **accessed on 24.03.2025**

Insulin analogues

Multiple innovators

MPP is exploring ways to improve access to long-acting insulin analogues in LMICs, where the burden of diabetes poses a profound challenge, and appropriate treatment options remain limited and/or non accessible[239]. Analogue formulations of insulin offer significant clinical advantages over traditional human insulins that are currently the most widely used insulins in LMICs. Their improved pharmacokinetic profiles support better glycaemic control, reduce the risk of hypoglycaemia and allow for more flexible dosing schedules[240 241 242 243 244]. The clinical advantages of insulin analogues over human insulin led to their inclusion in the WHO Model List of Essential Medicines in 2021[245], recognising their potential to improve diabetes management globally. Despite these benefits, the high cost of insulin analogues continues to limit their uptake in LMICs, where human insulins remain more affordable and widely used. MPP's engagement in this space seeks to address affordability challenges and contribute to broader access to newer, more effective diabetes treatments in underserved settings, while also monitoring progress in next-generation insulin formulations that offer sustained, longer-acting coverage with the potential to further reduce hypoglycaemia risk and ease the injection burden for people living with diabetes. Given the diversity within the class of insulin analogues, a snapshot card was not produced, as it would not adequately capture the specificities of the different products. While patents have expired for most insulin analogues (administered more often than weekly), technology transfer – including to strengthen regional manufacturing – could support an MPP intervention within this area.

239 Nathan DM; DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. Diabetes Care. 2014;37(1):9-16. doi: 10.2337/dc13-2112. PMID: 24356592; PMCID: PMC38679

240 Petersen, J.J., Juul, S., Kamp, C.B. et al. Regular human insulins versus rapid-acting insulin analogues in children and adolescents with type 1 diabetes: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis. Syst Rev 14, 5 (2025). https://doi.org/10.1186/s13643-024-02729-4

241 Rossetti P, Porcellati F, Fanelli CG, Perriello G, Torlone E, Bolli GB. Superiority of insulin analogues versus human insulin in the treatment of diabetes mellitus. Arch Physiol Biochem. 2008;114(1):3-10. doi:10.1080/13813450801900777

242 Melo, K.F.S., Bahia, L.R., Pasinato, B. et al. Short-acting insulin analogues versus regular human insulin on postprandial glucose and hypoglycemia in type 1 diabetes mellitus: a systematic review and meta-analysis. Diabetol Metab Syndr 11, 2 (2019).

243 Sebastian SA, Co EL, Mehendale M, Hameed M. Insulin analogs in the treatment of type II diabetes and future perspectives. Dis Mon. 2023;69(3):101417. doi:10.1016/j.disamonth.2022.101417

244 Besançon S, Haynes A, Togo AD, et al. Marked improvement in HbA1c following introduction of biosimilar insulin to treatment regimen of children and youth with type 1 diabetes in Mali: A randomised controlled trial. Diabet Med. Published online March 3, 2025

245 World Health Organization; The selection and use of essential medicines; 2021.

DIABETES, CARDIOVASCULAR & METABOLIC DISORDERS

- **Cardiovascular diseases**

Cardiovascular diseases (CVDs) stand as the leading global cause of death, accounting for 33% of all deaths in 2021, with an estimated 19.4 million lives lost. Over three-quarters of CVD deaths occur in LMICs[246]. These diseases were responsible for 38% of the 17 million premature deaths (those under 70 years old) attributed to NCDs in 2021[247]. Early detection of CVDs is paramount to initiate timely management through counselling and medication. Despite high-quality scientific evidence of the benefits of different classes of drugs in preventing and controlling CVDs, their current use remains low.

Cardiovascular fixed-dose combination therapies

Multiple innovators

Fixed-dose combination medicines for CVD, also known as polypills, have been shown to simplify treatment, improve adherence, and help manage key risk factors. These pills combine cholesterol-lowering medicines, blood pressure drugs, and, when appropriate, aspirin, to significantly reduce illness and death caused by atherosclerotic CVD. Their use is suggested for both primary and secondary prevention of CVD. The need for effective and accessible CVD prevention is especially important for people living with HIV, who face a higher risk of developing heart disease but have limited tailored prevention options. A recent study found that those who took a medicine that lowers cholesterol had fewer major heart problems than those who received a placebo over about five years, underscoring the importance of expanding prevention strategies in this group. The proven benefits and cost-effectiveness of fixed-dose combination therapies support their broader use and led to their inclusion on the WHO Essential Medicines List in 2023[248].

246 Wang Y and al; Results From the 2021 Global Burden of Disease Study. Cureus. 2024 Nov 24;16(11):e74333. doi: 10.7759/cureus.74333. PMID: 39720386; PMCID: PMC11668263.

247 World Health Organization – Cardiovascular diseases (CVD) - Key facts

248 World Health Organization Model List of Essential Medicines, 2023.

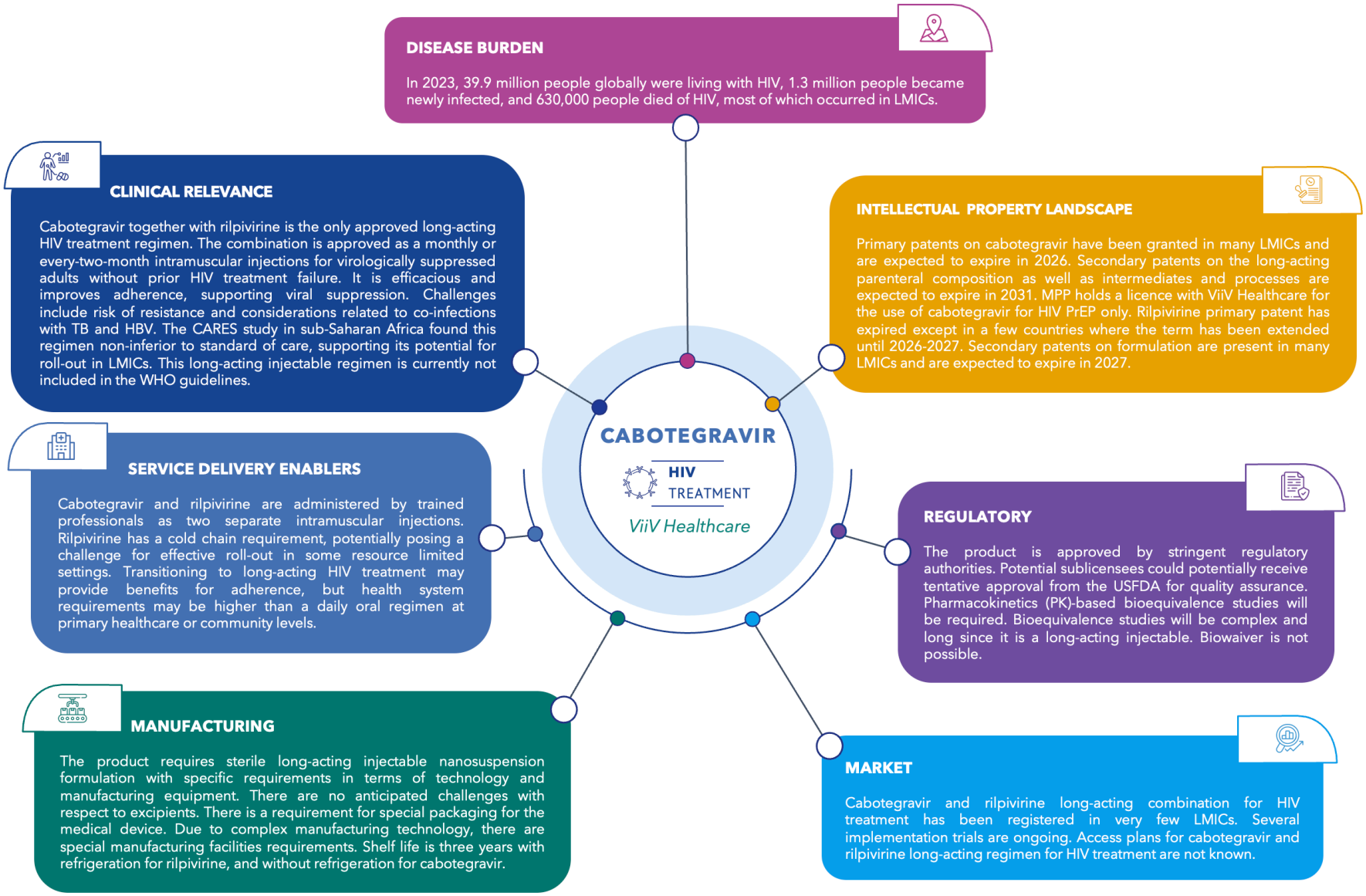
Products snapshots

In this chapter, we provide additional information on the priority medicines and health technologies listed previously.

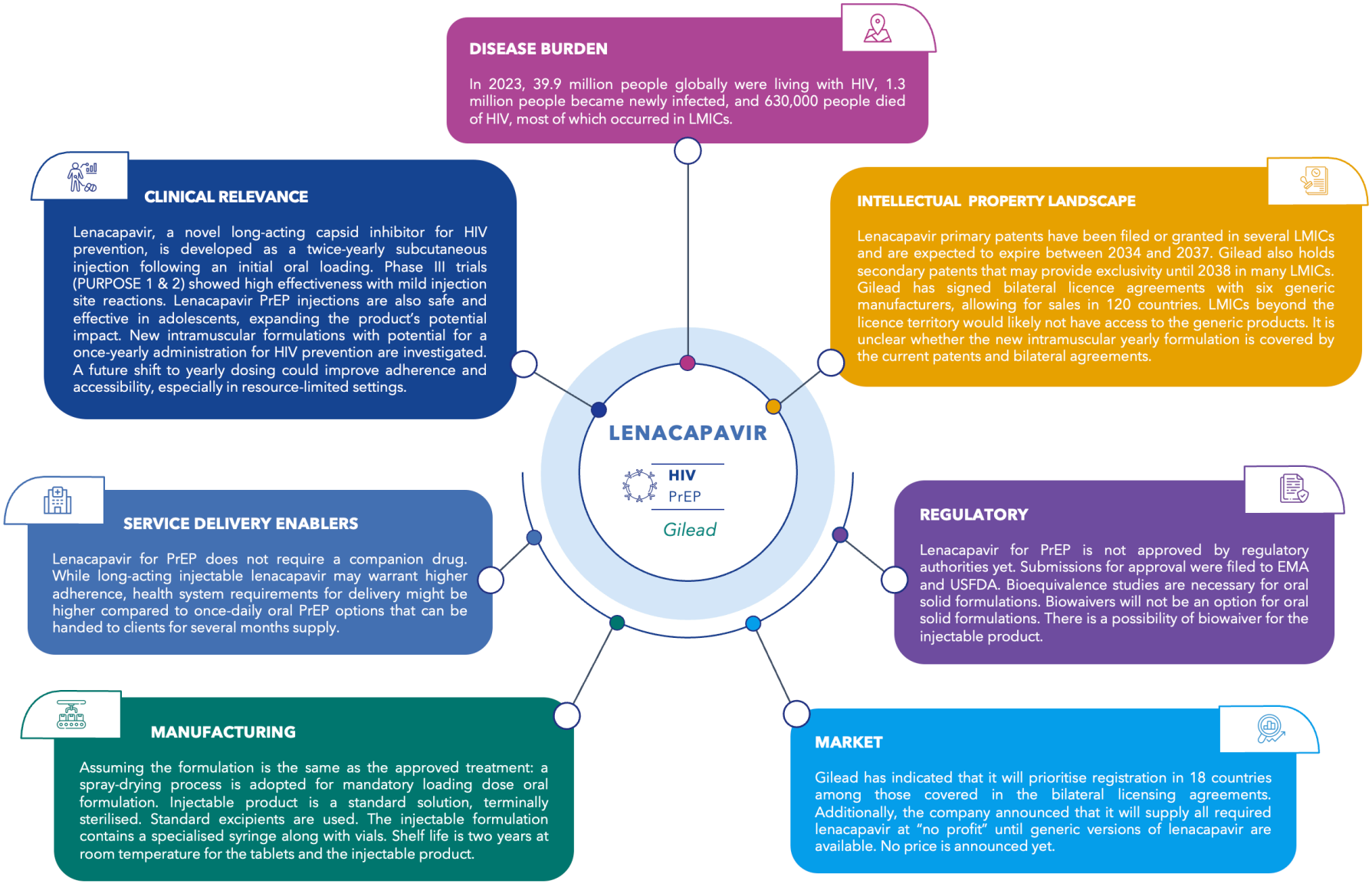
The detailed analysis is presented as a graphic snapshot following the prioritisation framework structure. Snapshots contain plain language key messages for each of the prioritisation criteria that MPP has evaluated.

For some products, there is not currently enough data available in the public domain to assess some of the criteria such as the manufacturing, regulatory, and market considerations. For these products, we have provided a partial assessment.

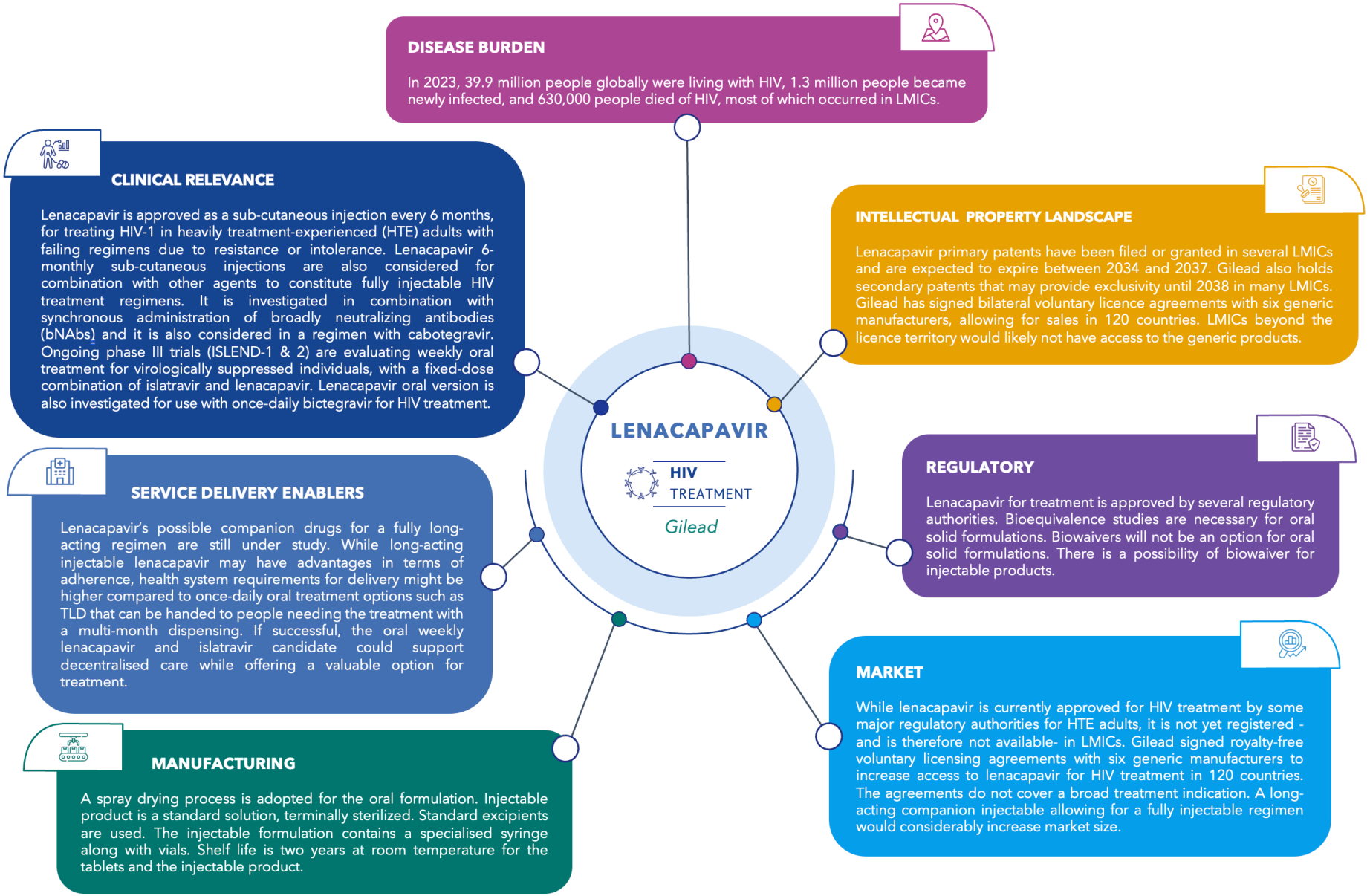
HIV



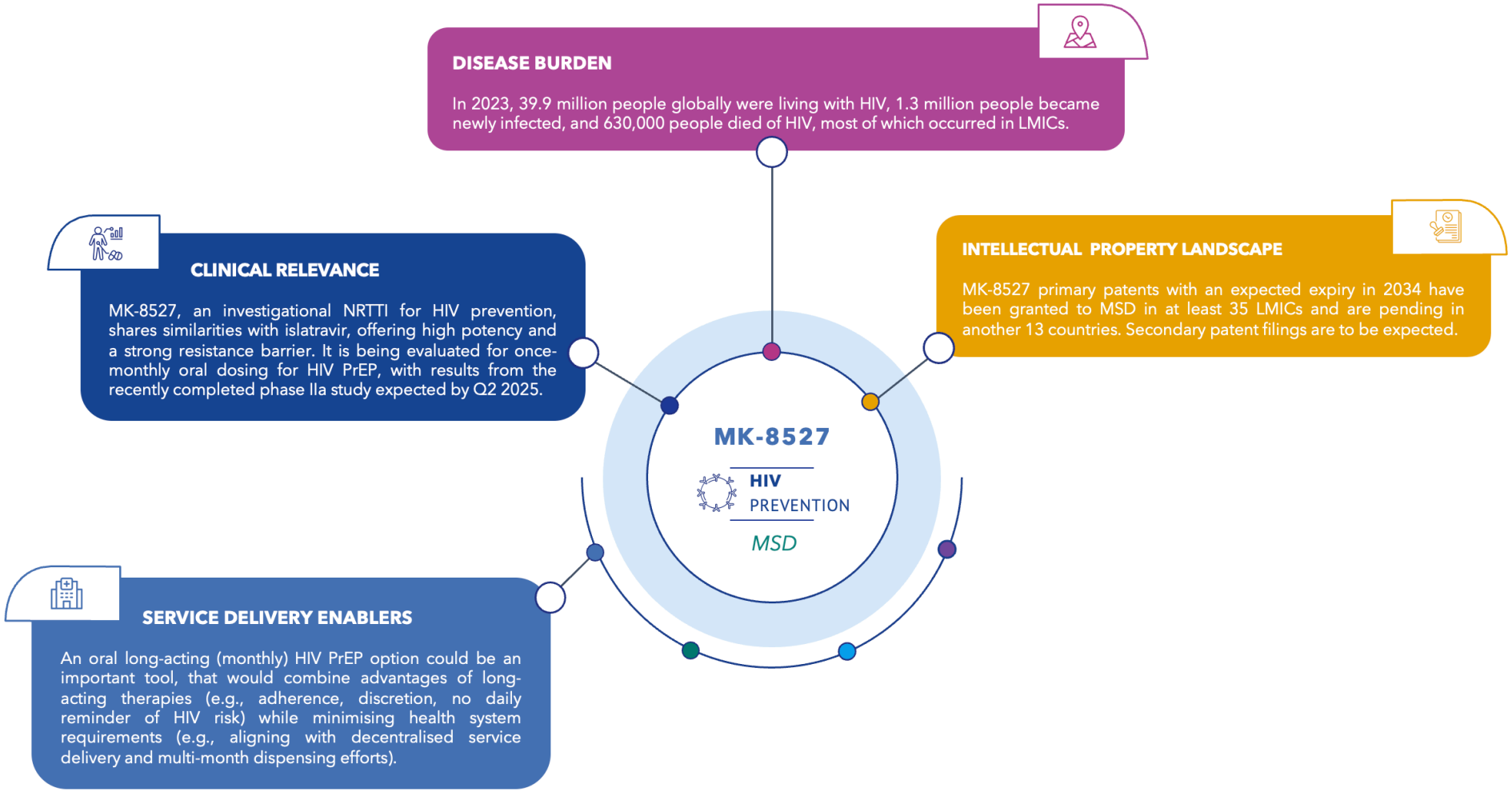
HBV: Viral hepatitis B; **HIV:** Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **MPP:** The Medicines Patent Pool; **PK:** pharmacokinetics; **PrEP:** Pre-Exposure Prophylaxis; **TB:** tuberculosis; **USFDA:** The United States Food and Drug Administration; **WHO:** The World Health Organization



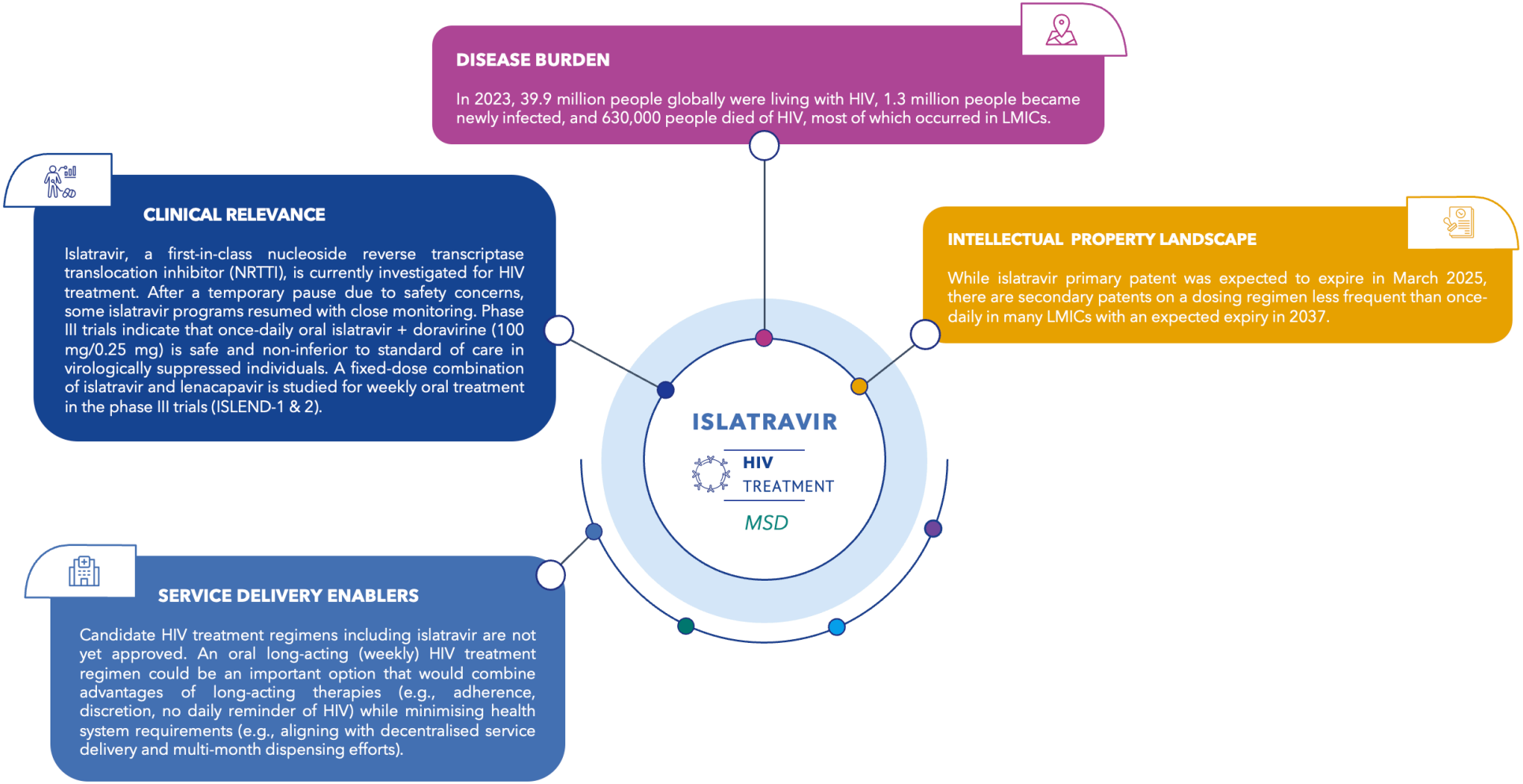
EMA: The European Medicines Agency; **HIV:** Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **PrEP:** Pre-Exposure Prophylaxis ; **USFDA:** The United States Food and Drug Administration



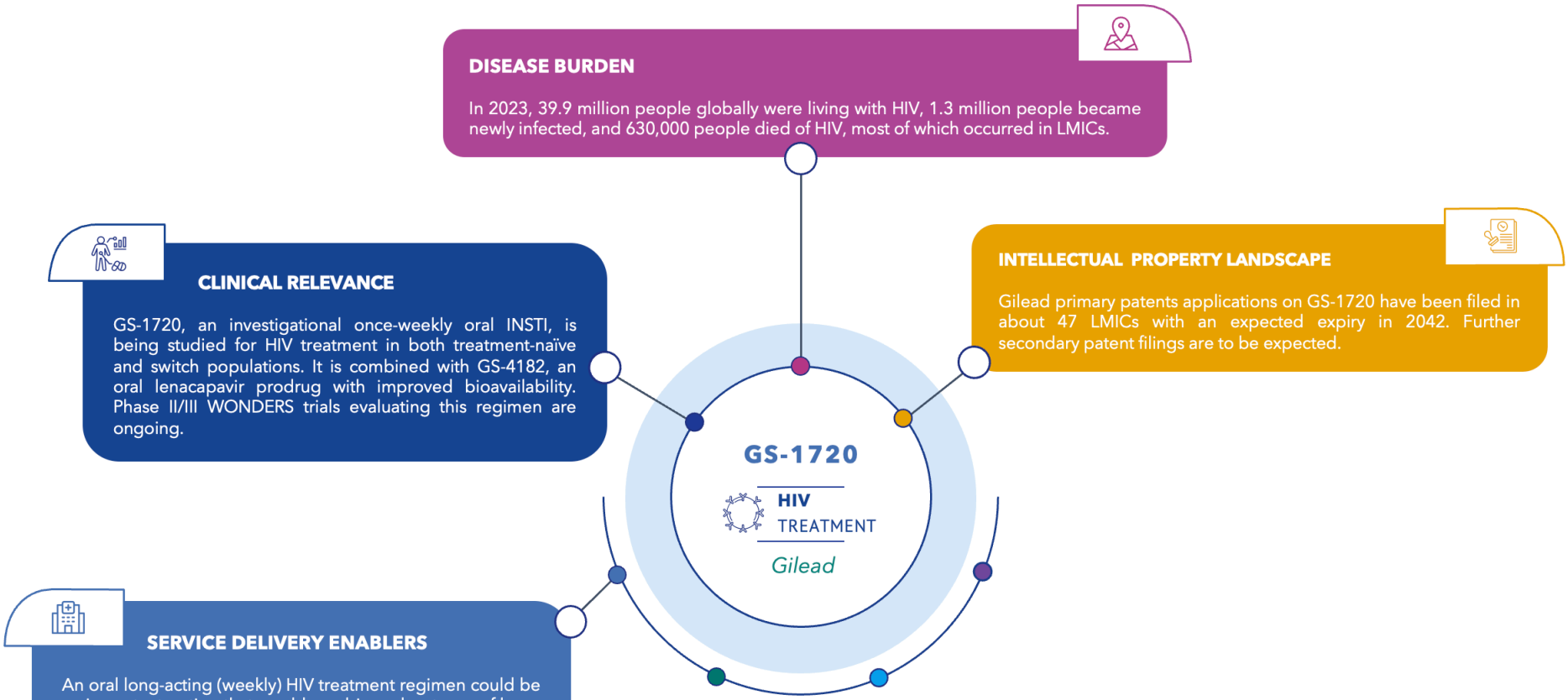
HIV: Human immunodeficiency virus; **HTE**: heavily treatment-experienced; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **TLD**: tenofovir, lamivudine and dolutegravir



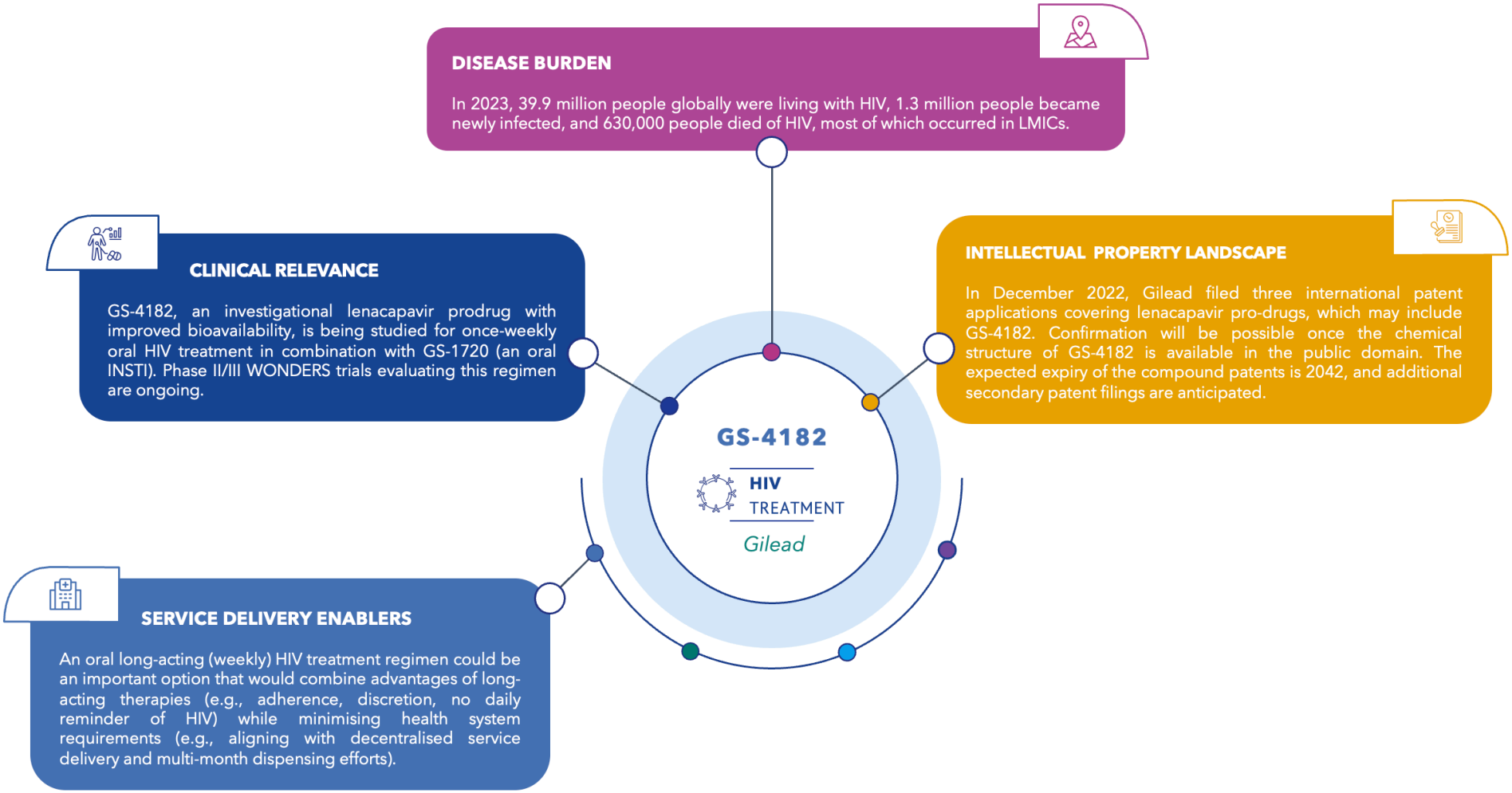
HIV: Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **PrEP:** Pre-Exposure Prophylaxis; **NRTTI:** nucleoside reverse transcriptase translocation inhibitor



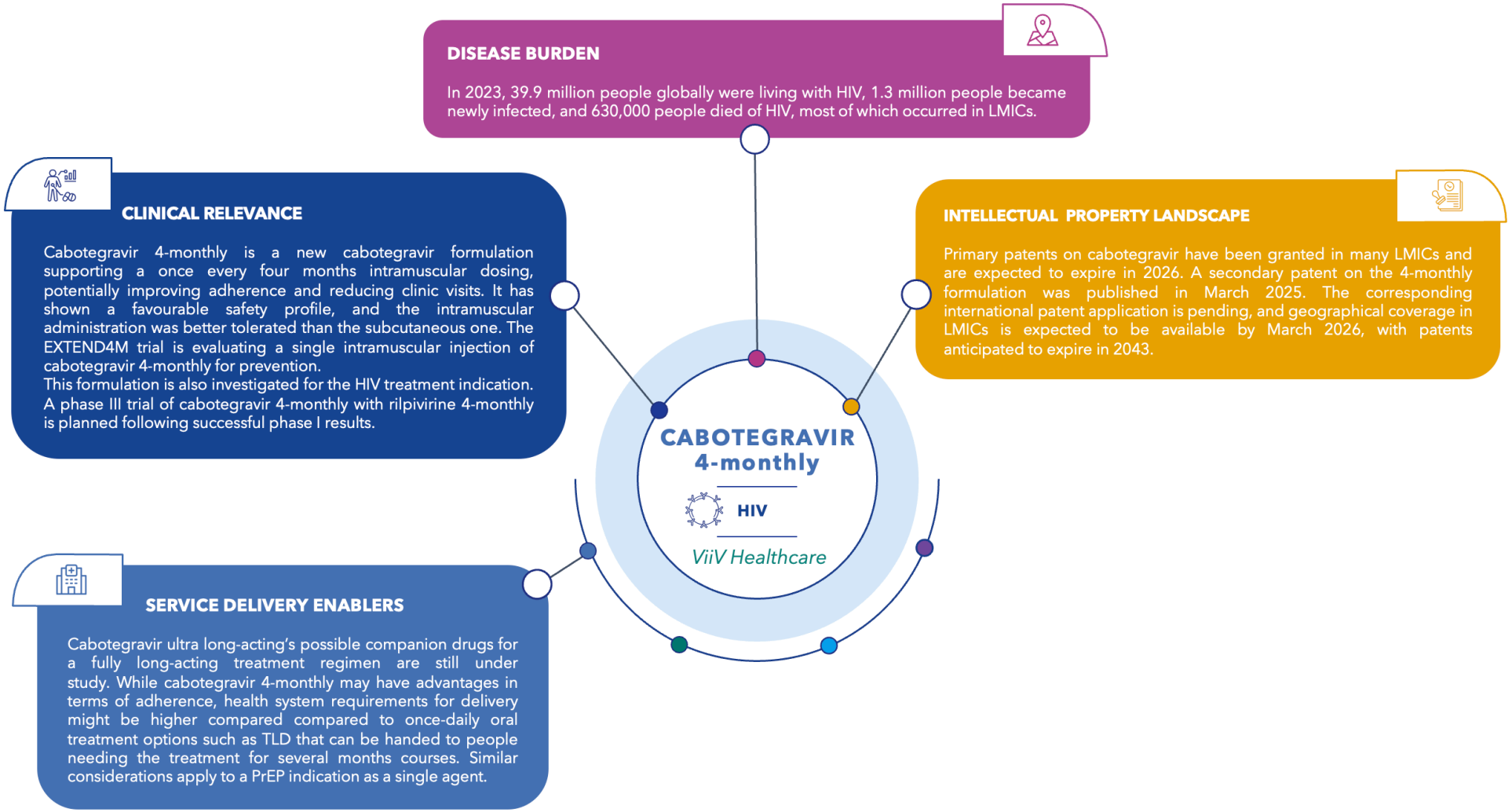
HIV: Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **NRTTI:** nucleoside reverse transcriptase translocation inhibitor; **WHO:** The World Health Organization



HIV: Human immunodeficiency virus; **INSTI:** Integrase strand transfer inhibitor; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification

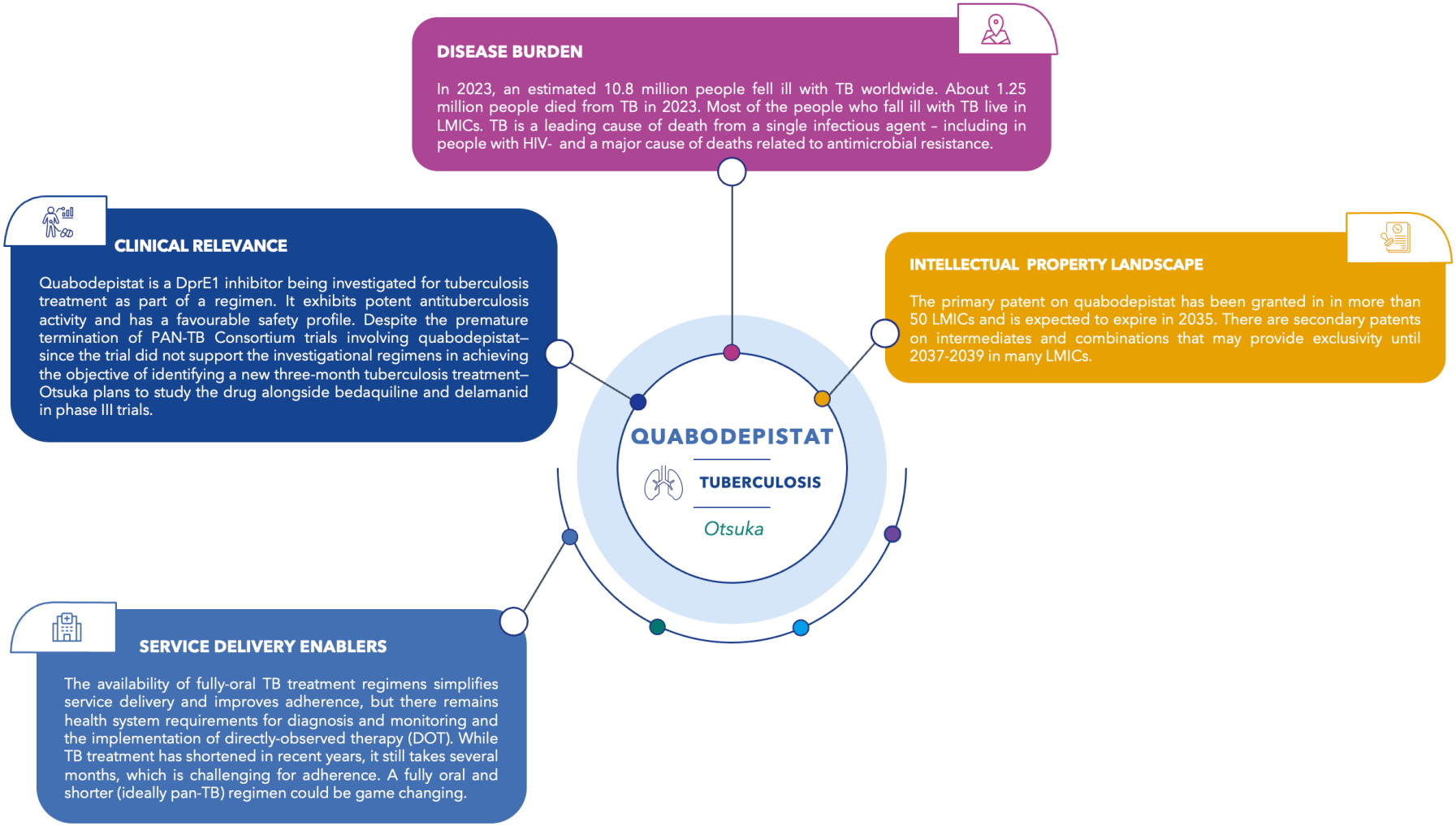


HIV: Human immunodeficiency virus; **INSTI:** Integrase strand transfer inhibitor; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification



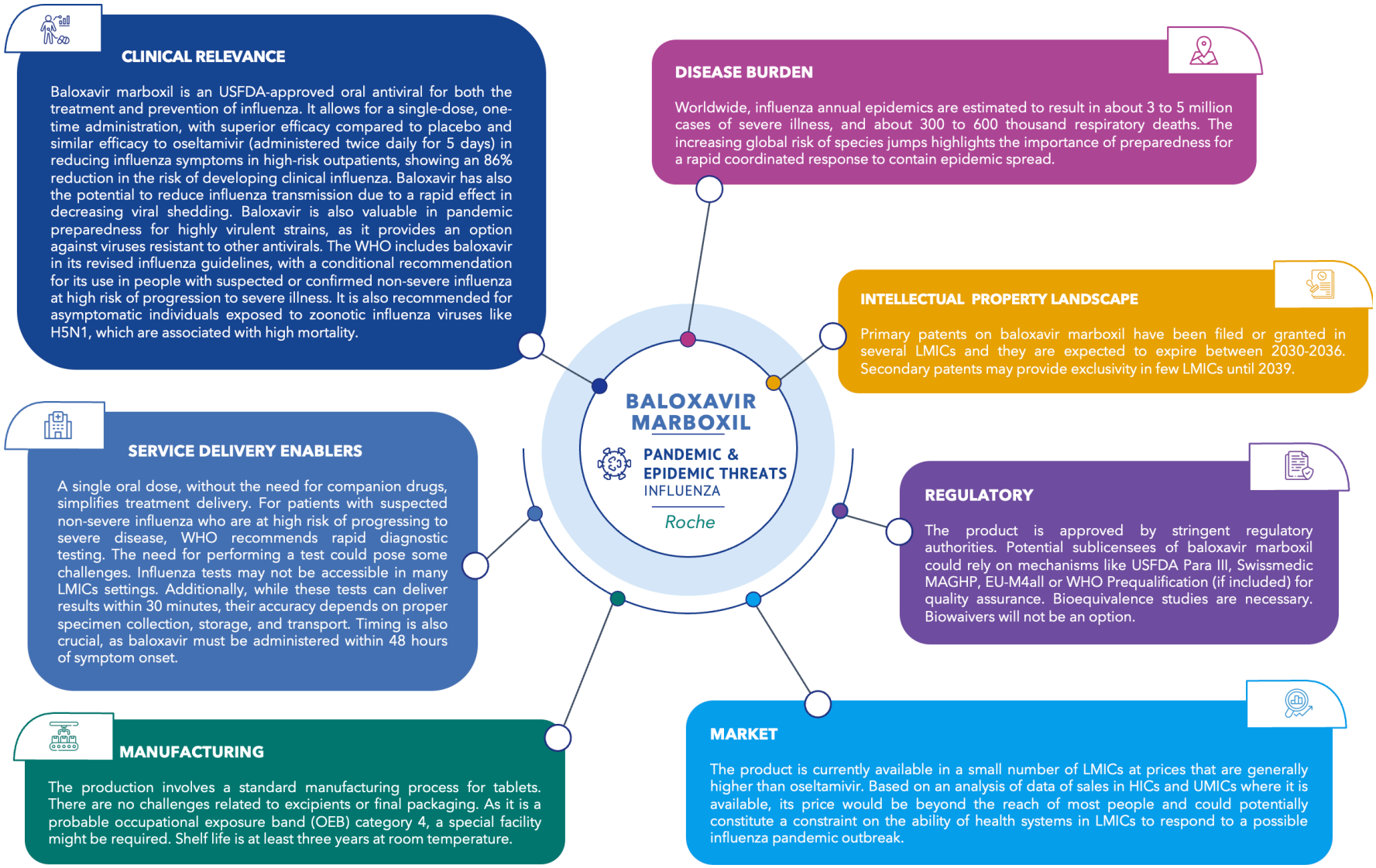
HIV: Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **PrEP:** Pre-Exposure Prophylaxis; **TLD**: tenofovir, lamivudine and dolutegravir

TUBERCULOSIS



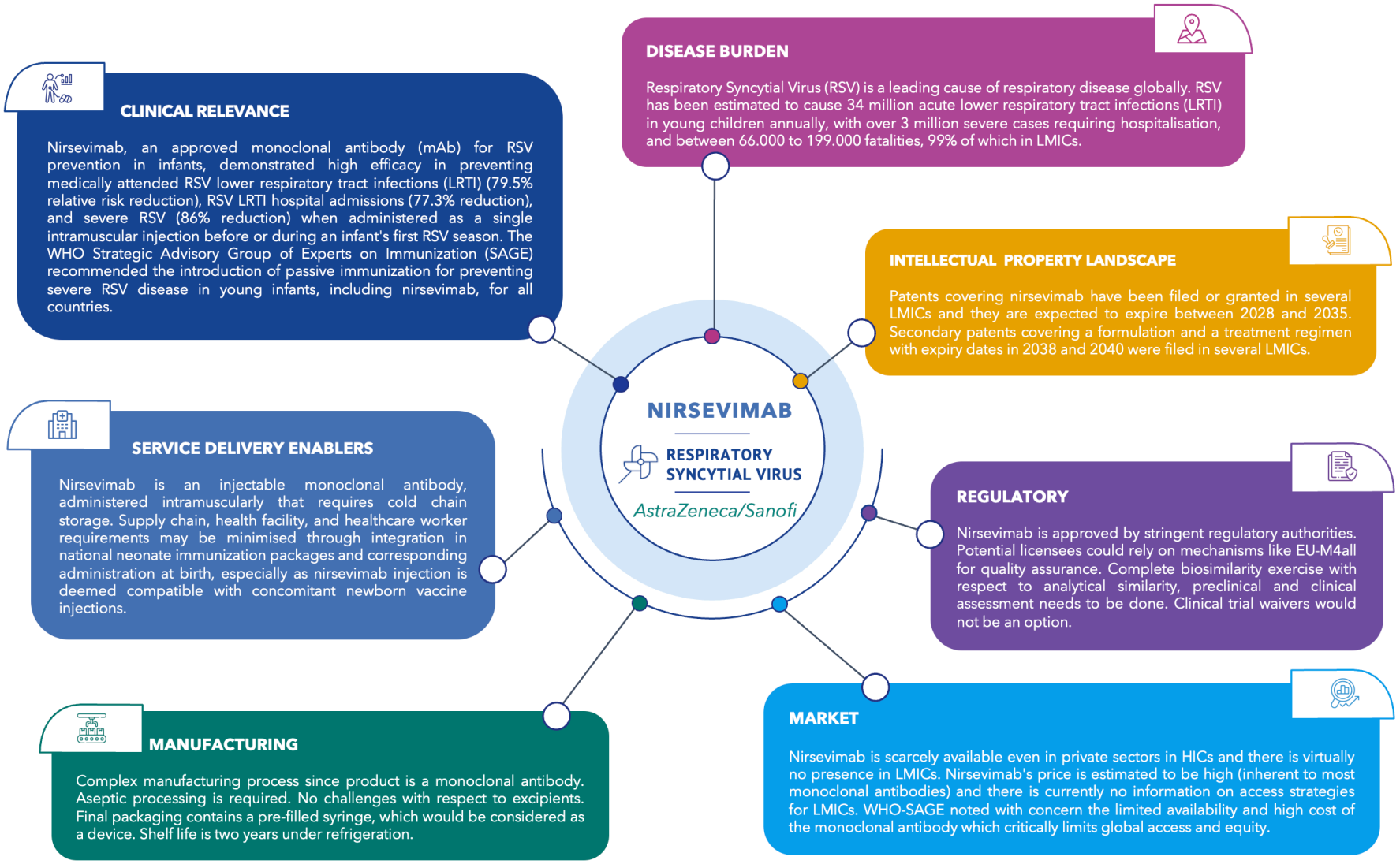
DOT: directly observed therapy; **HIV:** Human immunodeficiency virus; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **TB**: tuberculosis

PANDEMIC & EPIDEMIC THREATS

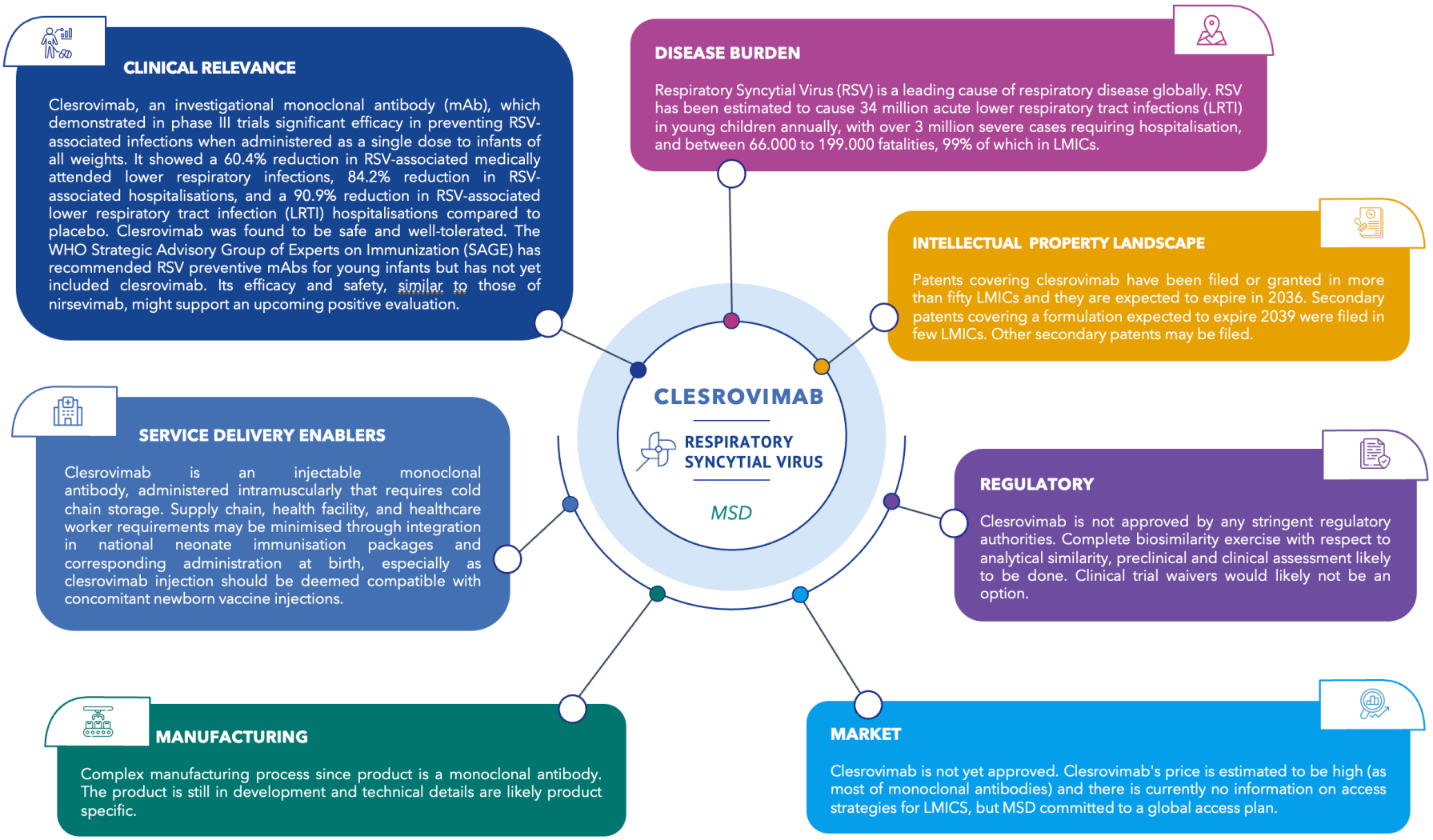


EU-M4all: The European Medicines Agency (EMA), in cooperation with the World Health Organization (WHO), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (EU). The procedure is called EU-Medicines for all or 'EU-M4all'; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **OEB:** occupational exposure band; **Swissmedic MAGHP:** Swissmedic procedure for scientific advice and Marketing Authorisation for Global Health Products; **USFDA:** The United States Food and Drug Administration; **WHO:** The World Health Organization

RESPIRATORY SYNCYTIAL VIRUS

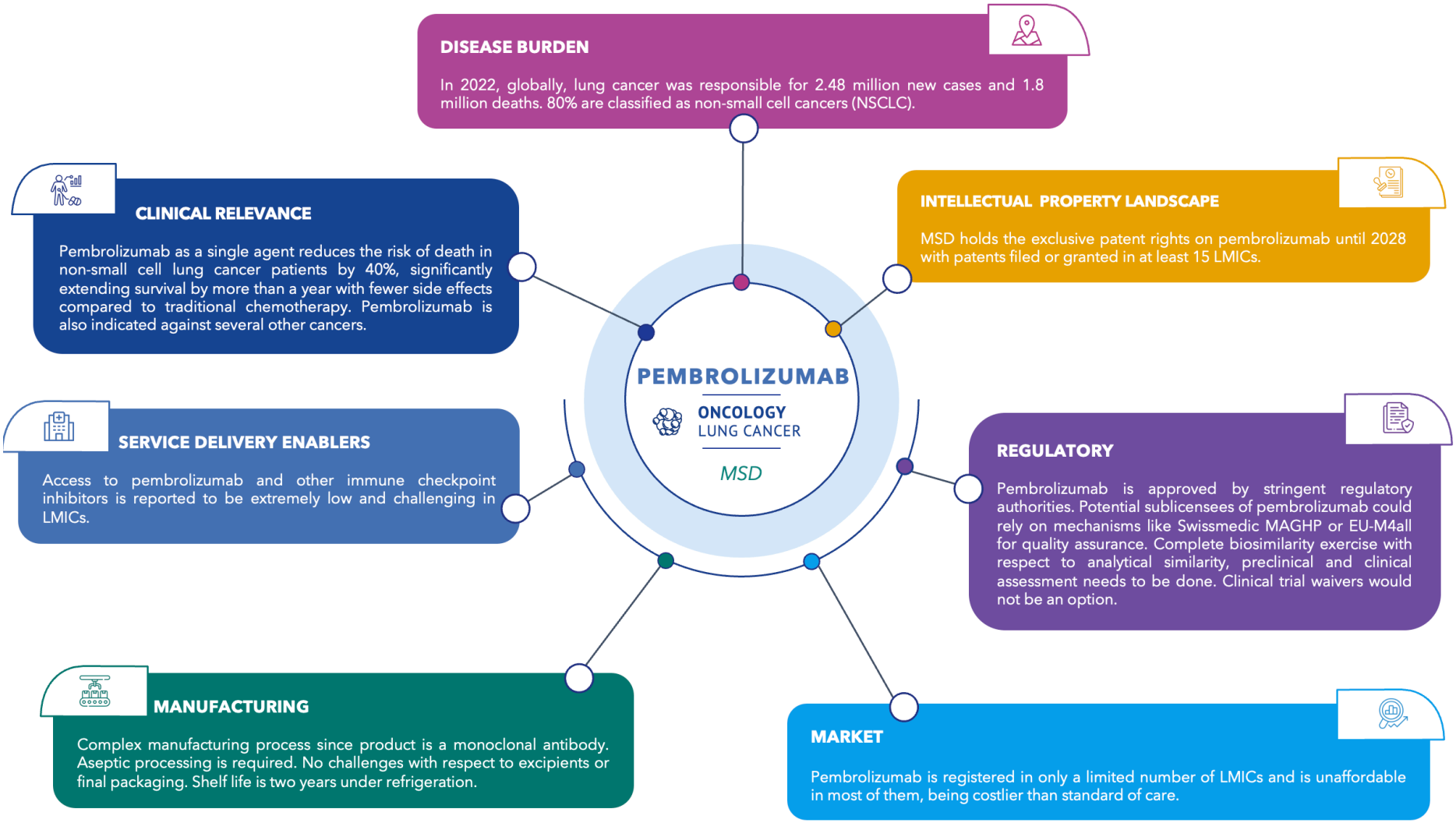


LMICs: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **LRTI**: lower respiratory tract infections ; **mAb:** monoclonal antibody; **RSV**: Respiratory Syncytial Virus; **SAGE**: The WHO Strategic Advisory Group of Experts on Immunization; **WHO:** The World Health Organization

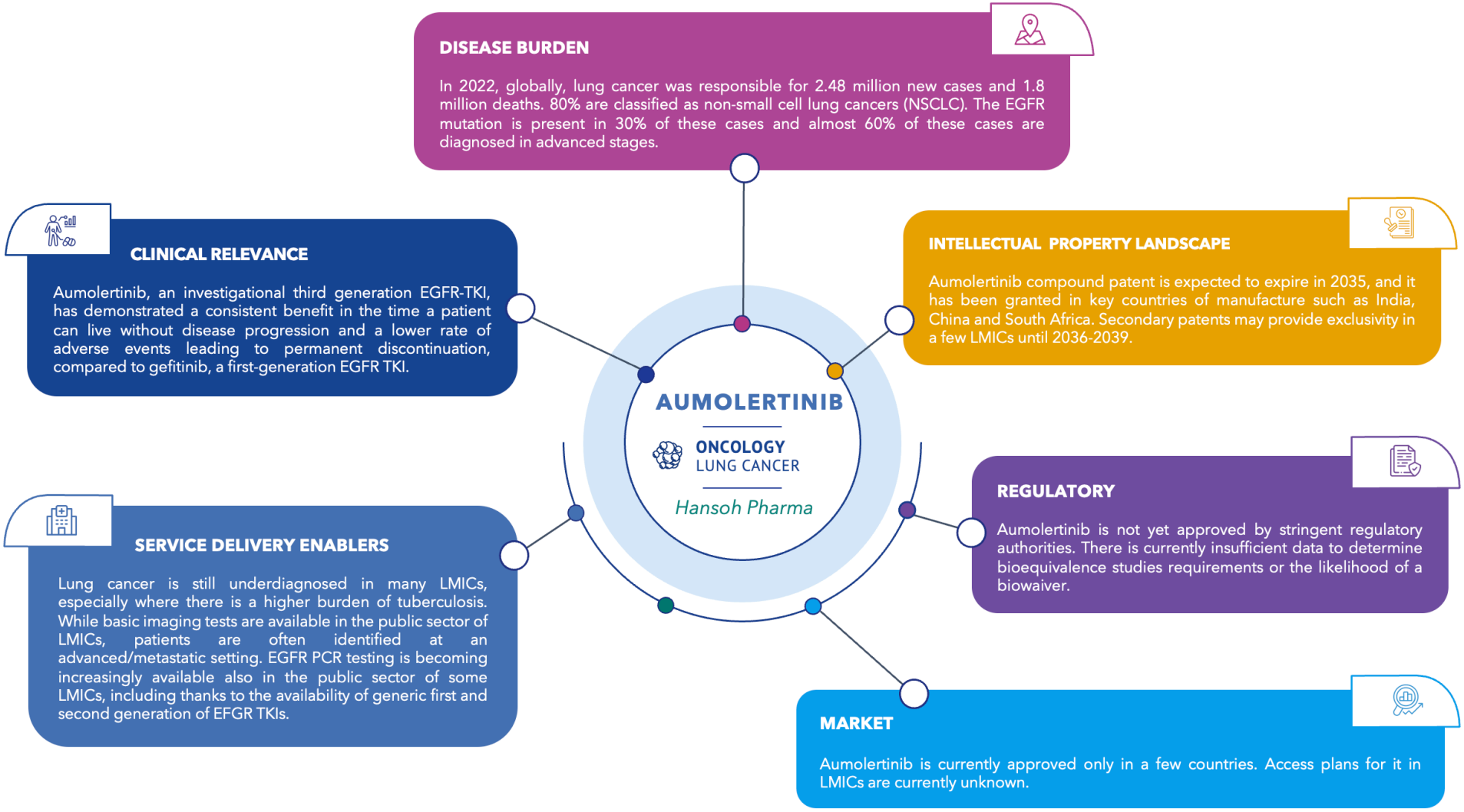


LMICs: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **LRTI**: lower respiratory tract infections ; **mAb:** monoclonal antibody; **RSV**: Respiratory Syncytial Virus; **SAGE**: The WHO Strategic Advisory Group of Experts on Immunization; **WHO:** The World Health Organization

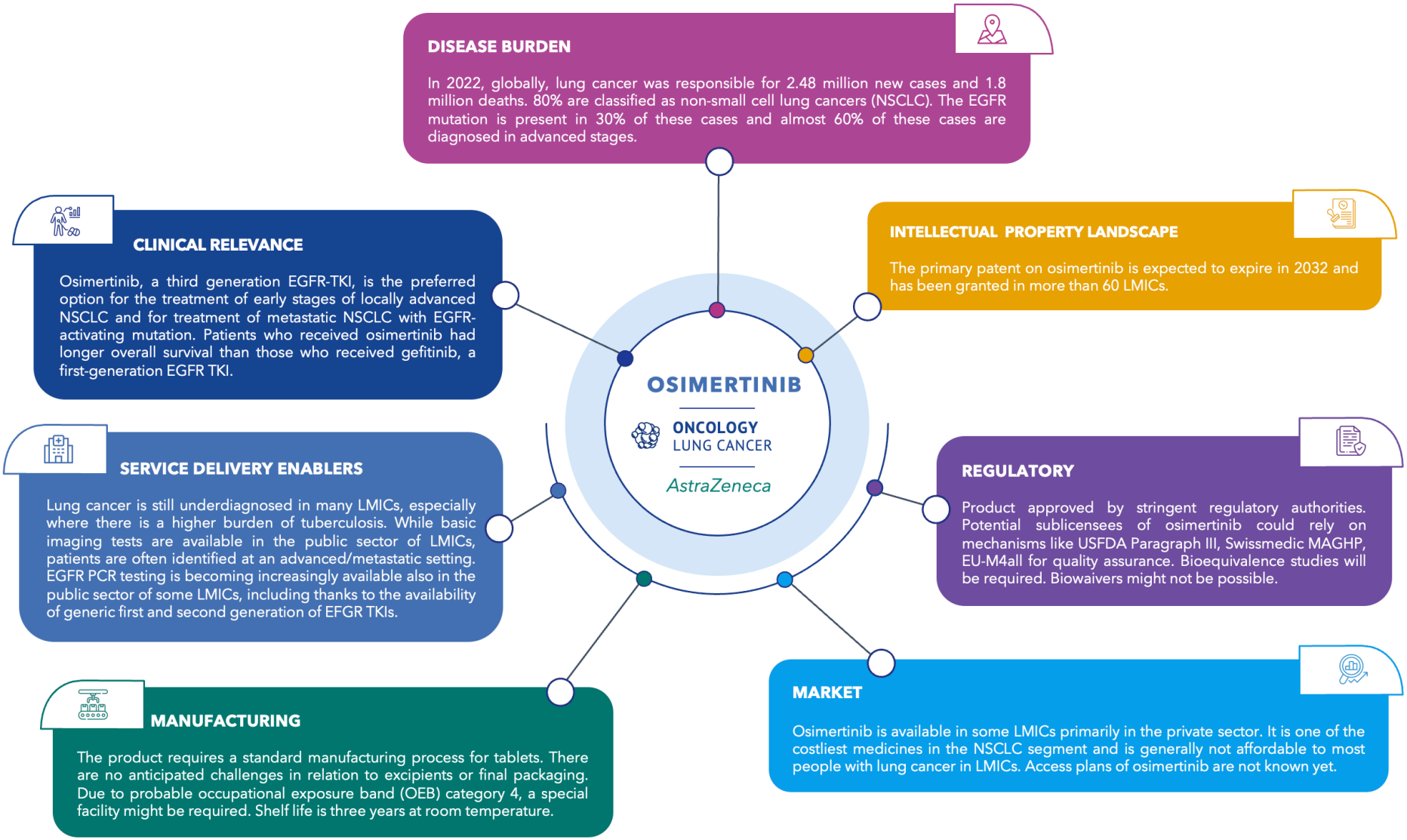
ONCOLOGY



EU-M4all: The European Medicines Agency (EMA), in cooperation with the World Health Organization (WHO), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (EU). The procedure is called EU-Medicines for all or 'EU-M4all'; **NSCLC:** non-small cell lung cancer; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **Swissmedic MAGHP:** Swissmedic procedure for scientific advice and Marketing Authorisation for Global Health Products



EGFR-TKI: Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor ; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **NSCLC:** non-small cell lung cancer; **PCR:** Polymerase Chain Reaction



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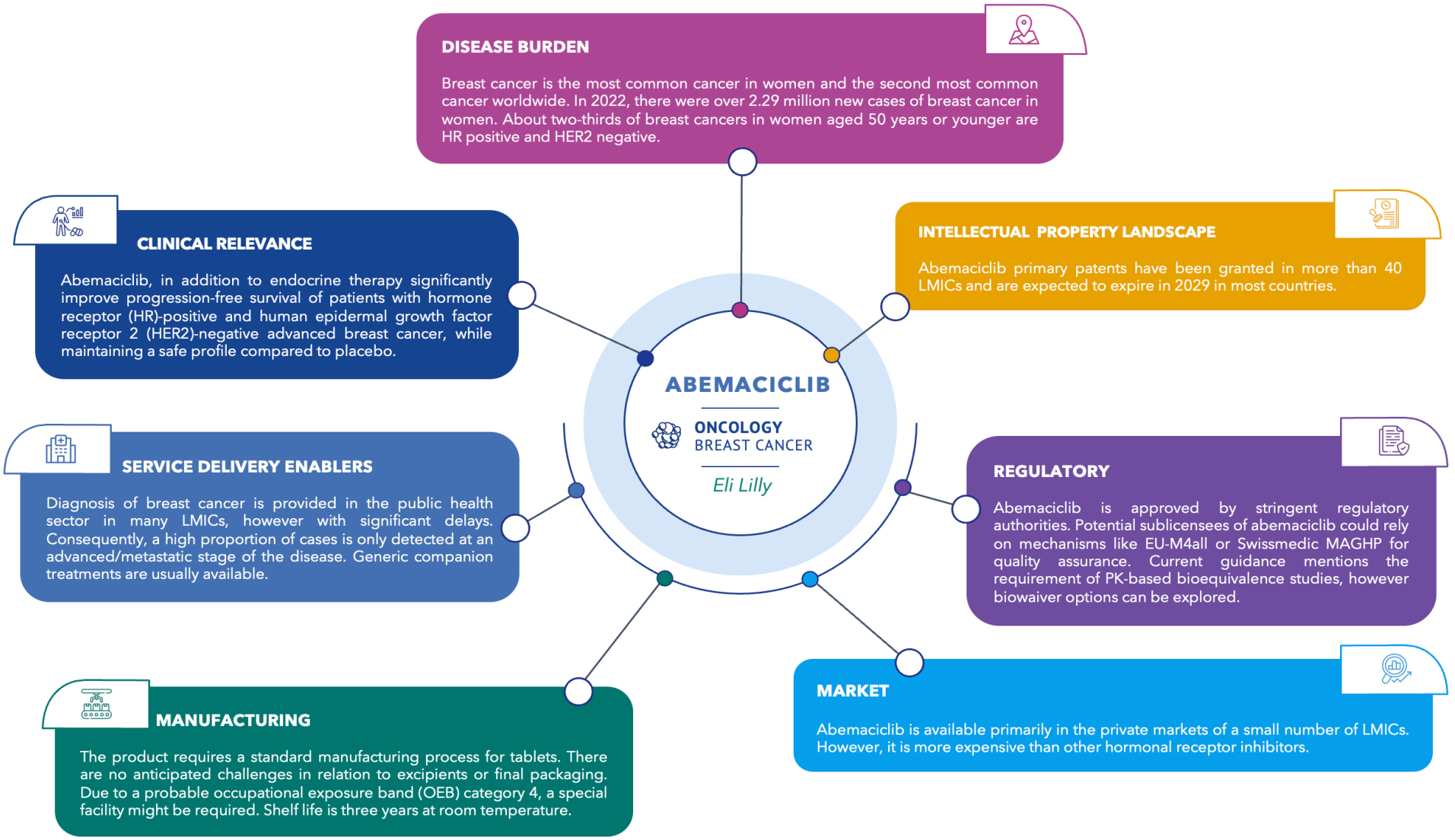

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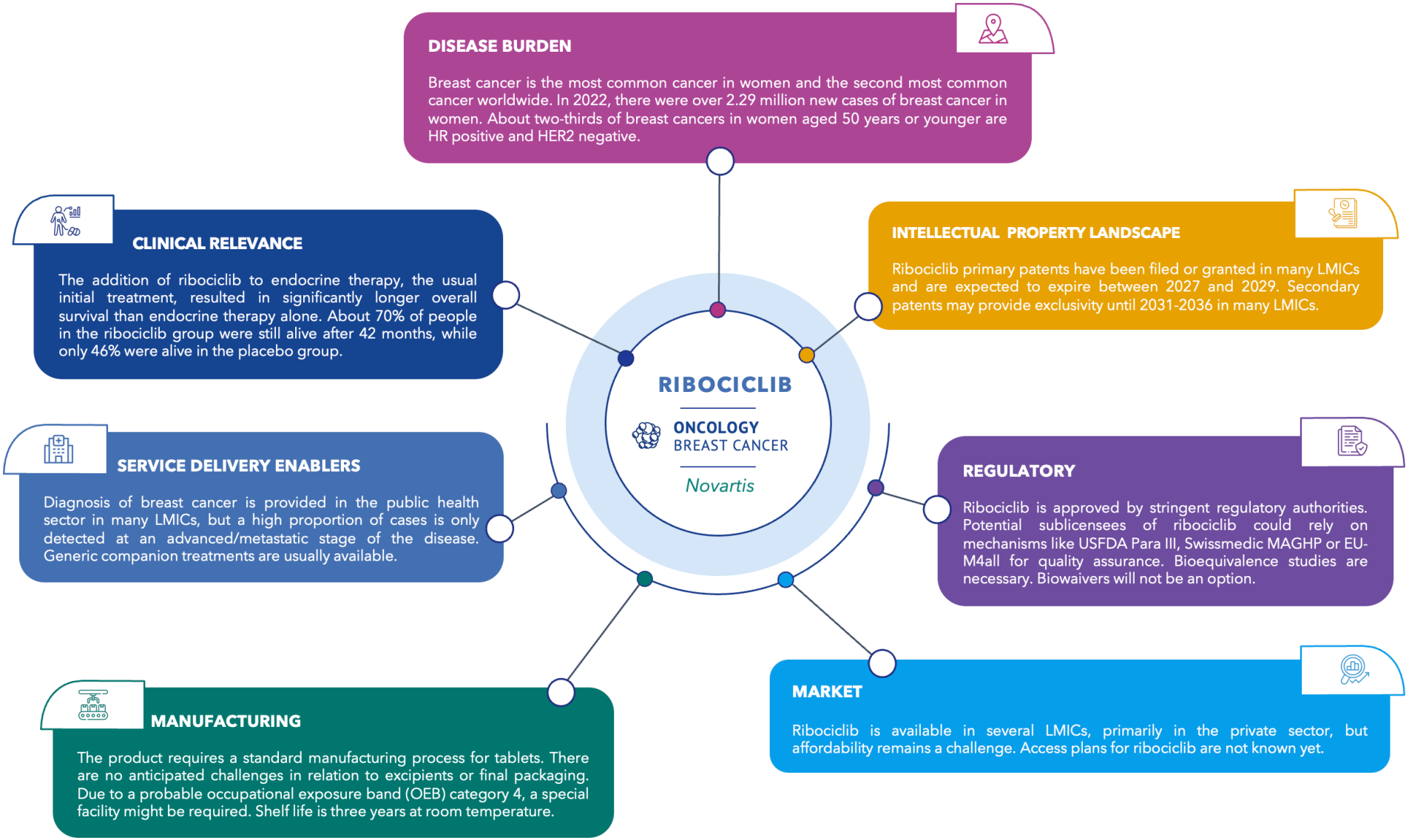

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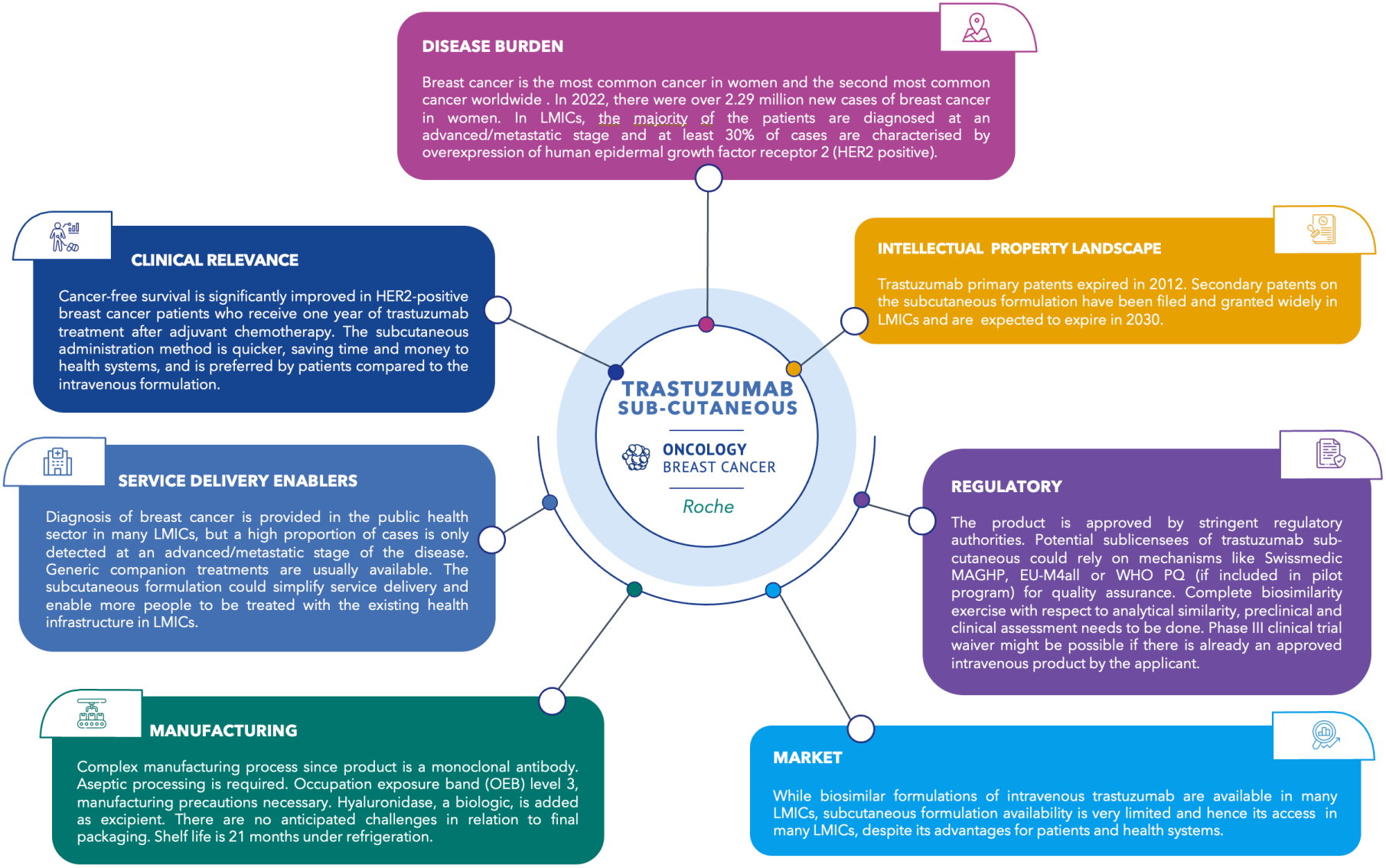

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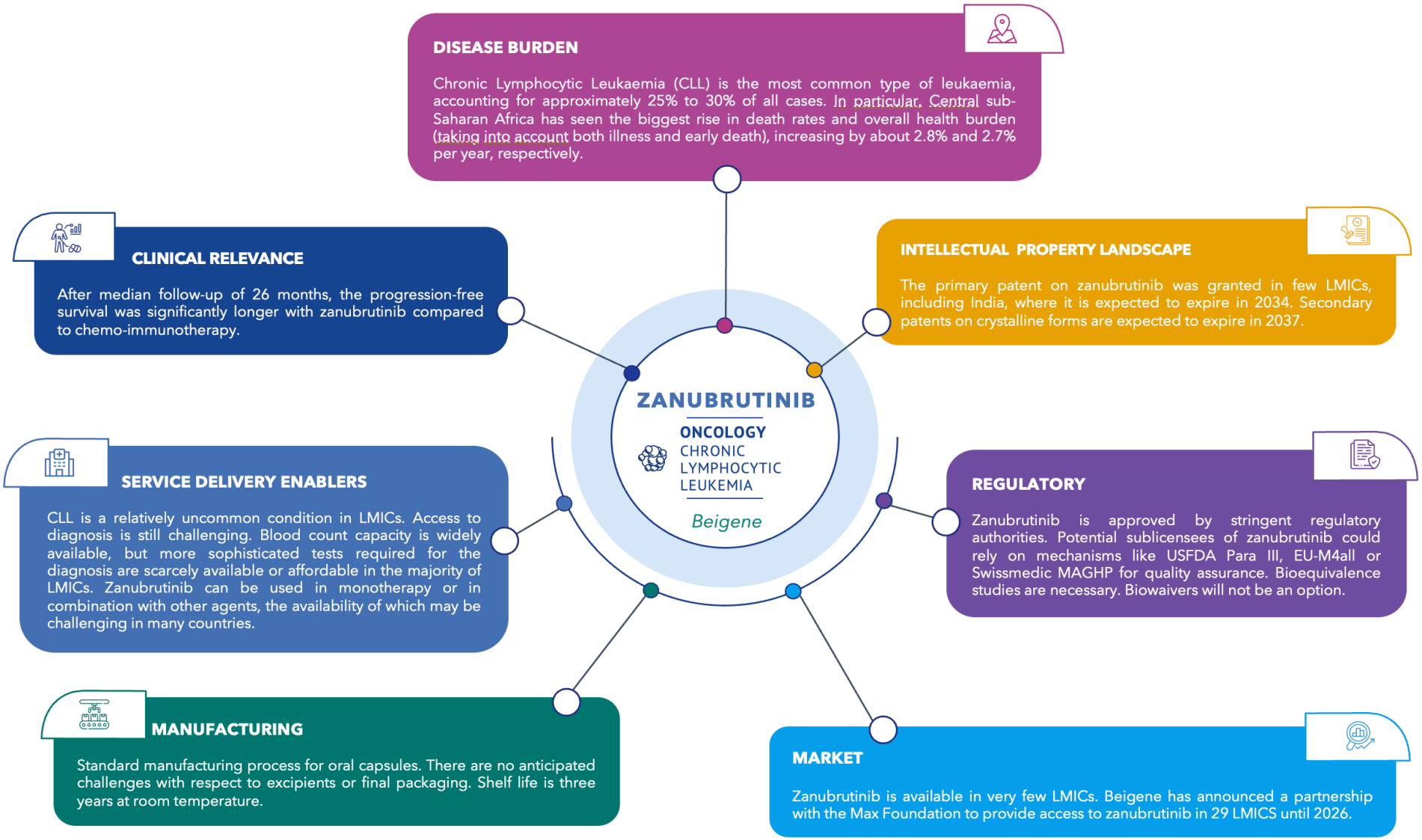
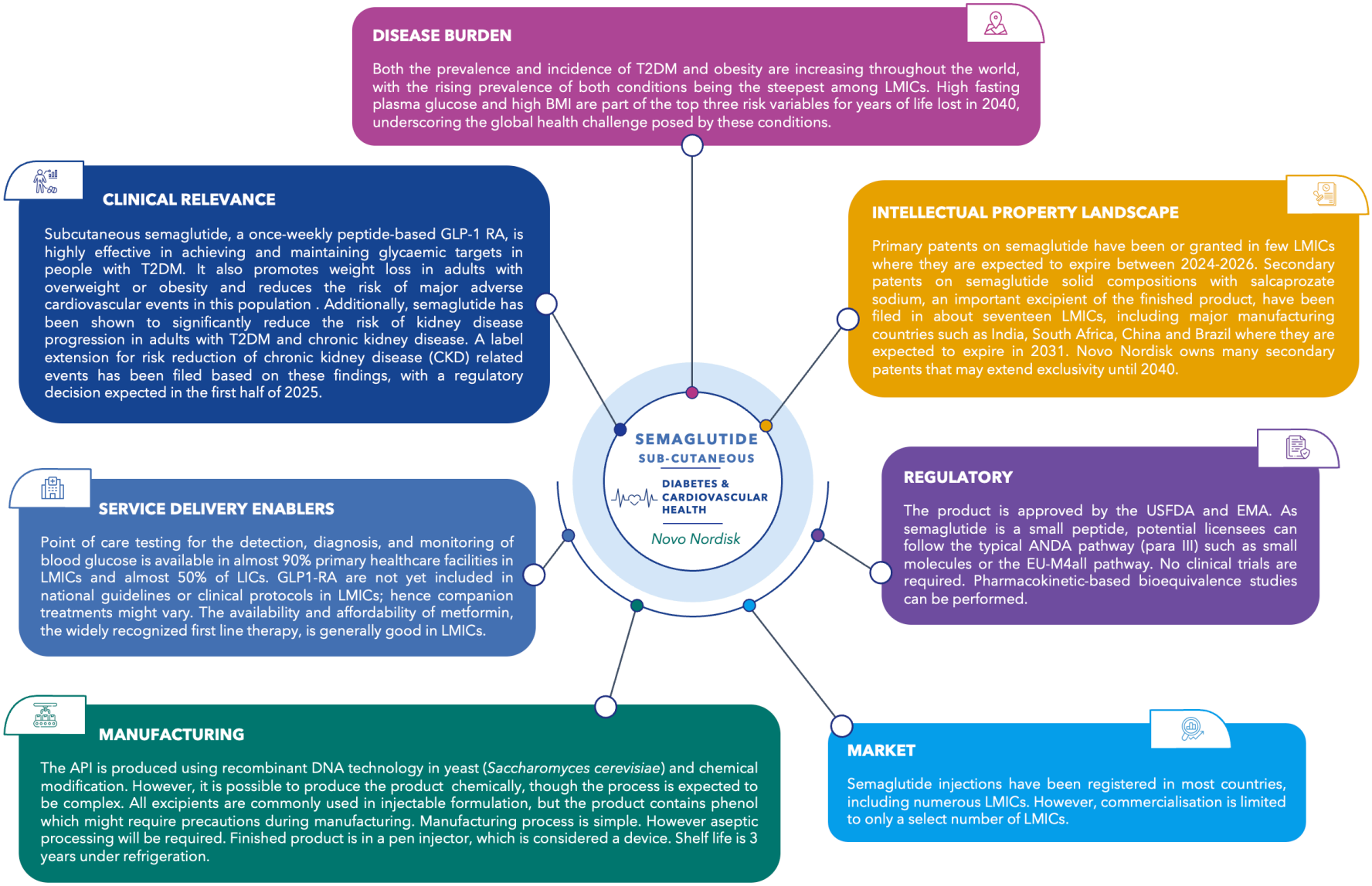
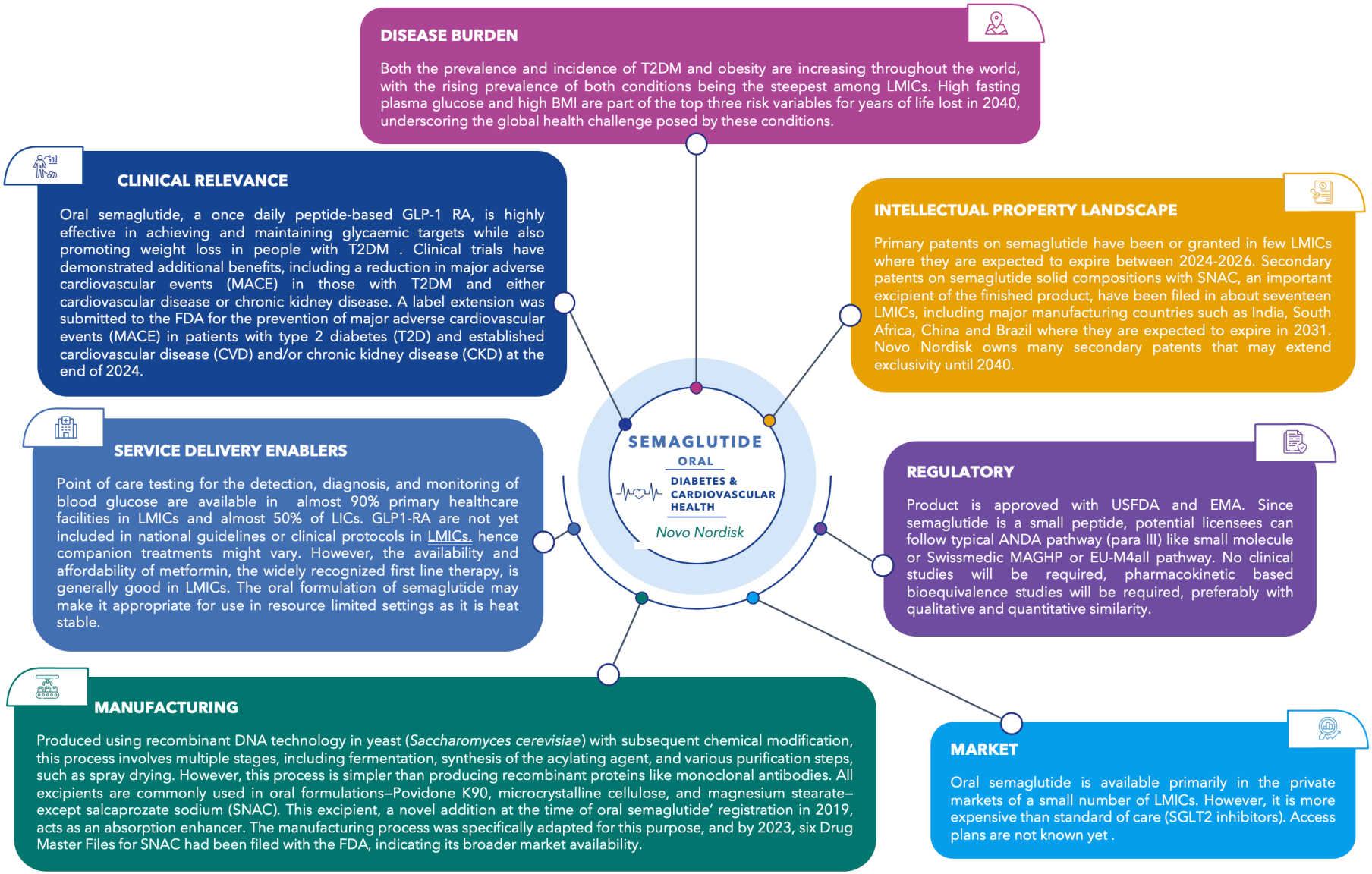


CLL: Chronic Lymphocytic Leukaemia**; EU-M4all**: The European Medicines Agency (EMA), in cooperation with the World Health Organization (WHO), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (EU). The procedure is called EU-Medicines for all or 'EU-M4all'; **LMICs**: low-income, lower middle-income and upper middle-income countries as per World Bank classification; **Swissmedic MAGHP:** Swissmedic procedure for scientific advice and Marketing Authorisation for Global Health Products; **USFDA:** The United States Food and Drug Administration

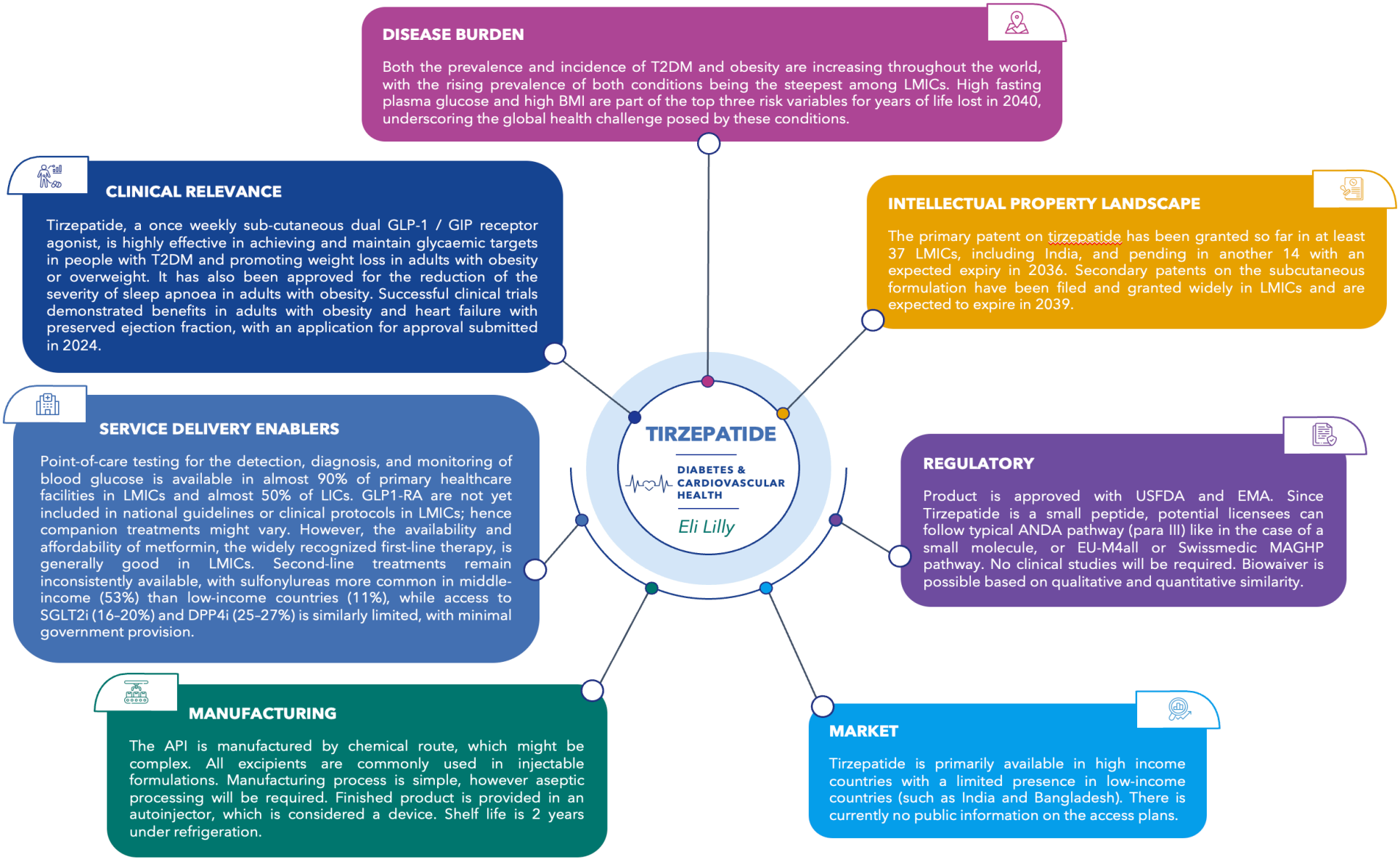
DIABETES, CARDIOVASCULAR & METABOLIC DISORDERS



ANDA: Abbreviated New Drug Application; **API**: Active Pharmaceutical Ingredient; **BMI**: Body Mass Index; **CKD**: chronic kidney disease; **DNA:** Deoxyribonucleic acid; **EU-M4All**: The European Medicines Agency (**EMA**), in cooperation with the World Health Organization (WHO), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (EU). The procedure is called EU-Medicines for all or 'EU-M4all'; **GLP-1 RA**: Glucagon-like peptide-1 receptor agonist; **LMICs**: low-income (**LICs**), lower middle-income and upper middle-income countries as per World Bank classification; **T2DM:** Type 2 diabetes mellitus.



ANDA: Abbreviated New Drug Application; **API**: Active Pharmaceutical Ingredient; **BMI**: Body Mass Index; **CKD**: chronic kidney disease; **CVD**: cardiovascular disease; **DNA:** Deoxyribonucleic acid; **EU-M4All**: The European Medicines Agency (**EMA**), in cooperation with the World Health Organization (WHO), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (EU). The procedure is called EU-Medicines for all or 'EU-M4all'; **GLP-1 RA**: Glucagon-like peptide-1 receptor agonist; **LMICs**: low-income (**LICs**), lower middle-income and upper middle-income countries as per World Bank classification; **MACE**: major adverse cardiovascular events; **SGLT2i:** Sodium-Glucose Transport Protein 2 (SGLT2) inhibitors also known as "gliflozins"; **SNAC**: Sodium N-(8-[2-hydroxylbenzoyl] amino) caprylate; **Swissmedic MAGHP:** Swissmedic procedure for scientific advice and Marketing Authorisation for Global Health Products; **T2DM:** Type 2 diabetes mellitus; **USFDA:** The United States Food and Drug Administration



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Annex: Prioritisation framework

PRODUCT ASSESSMENT FRAMEWORK TO GUIDE PRIORITISATION EXERCISE

The assessment framework proposed to be applied to each product has the following arborescence:

- Level 1 — PILLAR
- Level 2 — Sub pillar
- Level 3 — CRITERIA
- Level 4 — Sub criteria

Each sub-criteria is accompanied by an explanation of how the information gathered will likely be used in assessing the potential of an MPP intervention for the product in question. The final decision on product prioritisation is at the discretion of the prioritisation committee.

ASSESSMENT FRAMEWORK

1. PUBLIC HEALTH CONSIDERATIONS

1.1. Disease burden

- 1.1.2. Prevalence & incidence
- 1.1.3. Treatment options
- 1.1.4. Disease severity
- 1.1.5. Epidemic risk

1.2. Clinical relevance

- 1.2.1. Safety
- 1.2.2. Efficacy
- 1.2.3. Posology & method of administration
- 1.2.4. Cross-disease impact

2. ACCESS CONSIDERATIONS

2.1. Intellectual property landscape

- 2.1.1. Years to patent expiry of API
- 2.1.2. Geographical coverage of patents
- 2.1.3. Secondary patents
- 2.1.4. Multiple patent owners

2.2. Service delivery enablers

- 2.2.1. Diagnostic
- 2.2.2. Companion drugs
- 2.2.3. Health system requirements

2.3. Manufacturing

- 2.3.1. Manufacturing simplicity
- 2.3.2. Presentation & storage

2.4. Regulatory

- 2.4.1. Regulatory pathway
- 2.4.2. Regulatory cost & complexities
- 2.4.3. Probability of biowaiver /Clinical trial waiver

2.5. Market

- 2.5.1. Affordability & Availability of candidate
- 2.5.2. Commercial potential for MPP Generics' network
- 2.5.3. Impact

1. PUBLIC HEALTH CONSIDERATIONS

1.1. Disease burden

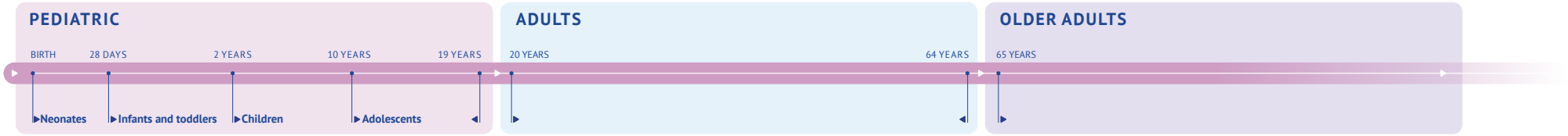
CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
1	Prevalence/incidence	**BURDEN OF DISEASE IN LMICS (GLOBAL OR LOCAL)**	The burden of the disease in LMICs (global) or in specific LMIC regions or countries (local).
2	Prevalence/incidence	**BURDEN OF DISEASE IN SPECIFIC POPULATIONS**	The burden of the condition in key populations (PLHIV, pregnant and lactating individuals, pediatric populations, and adolescents, people who inject drugs (PWID), incarcerated individuals, sex workers, and any other vulnerable groups).
3	Treatment options	**LACK OF ALTERNATIVE TREATMENTS**	Whether there is a lack of alternative treatment for the product-specific indication.
4	Disease severity	**DISABILITY-ADJUSTED LIFE YEARS (DALYs)**	Disability-adjusted life years (DALYs) as a measure of disease severity.
5	Disease severity	**NUMBER OF DEATHS**	Yearly estimated deaths linked directly or indirectly to the condition.
6	Epidemic risk	**EPIDEMIC/PANDEMIC RISK**	Whether there is a risk for imminent or future outbreaks of the disease.

1.2. Clinical relevance

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
7	Safety	**SAFETY/TOLERABILITY**	Overall safety and tolerability profile of the product.
8	Safety	**DRUG-DRUG INTERACTIONS (DDI) WITH HIGH-BURDEN DISEASES REGIMENS**	Drug-drug interactions (DDI) with standard of care (SoC) for high-burden infectious diseases such as HIV, TB, and Hepatitis C, and other DDIs.
9	Safety	**PRODUCT-INDUCED ADVERSE EVENTS**	Whether the product causes adverse events (e.g. hepatotoxicity, nephrotoxicity, weight gain, hypertension).

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
10	Safety	**SPECIAL ADMINISTRATION RESTRICTIONS**	Special administration restrictions such as fasting, or requirements for food intake.
11	Efficacy	**EFFICACY**	Overall efficacy compared to SoC. Efficacy should be ideally superior to the SoC. If the efficacy is comparable to SoC, then an additional advantage should be present. If the efficacy is inferior to the SoC, then product should be excluded from the evaluation.
12	Efficacy	**ADHERENCE**	Facilitated adherence to the product compared to SoC (from user/caregiver perspective).
13	Efficacy	**GENETIC BARRIER TO RESISTANCE**	When relevant. Whether there is a high genetic barrier to resistance, especially important for long/life treatment duration.
14	Efficacy	**KNOWN RESISTANCE MUTATIONS**	When relevant. Whether the product has known significant viral/bacterial resistance mutations of concern.
15	Efficacy	**SPECTRUM**	When relevant. Whether the product covers several diseases or all disease sub-types (e.g. Hepatitis C pan-genotypic treatment, multi-purpose technology, latent and active TB, several sexually transmitted infections (STIs), several cancers, etc.).
16	Efficacy	**INNOVATIVE PRODUCT**	Whether the product is innovative (such as a new promising mechanism of action, breakthrough therapy designation, orphan drug designation etc.).
17	Posology & method of administration	**DOSAGE**	Dosage for each indication (e.g. mg, mg/kg, mg/m2).
18	Posology & method of administration	**LENGTH OF THE TREATMENT**	Duration of the treatment for the main and secondary indications.
19	Posology & method of administration	**FREQUENCY OF ADMINISTRATION**	The frequency of dosing (e.g. once or twice daily or every 6 months).
20	Posology & method of administration	**AVAILABILITY OF A PEDIATRIC FORMULATION**	Whether a pediatric formulation/development program is available.
21	Posology & method of administration	**METHOD OF ADMINISTRATION**	Route of administration and concise instructions for correct administration and use.
22	Cross-disease impact	**CROSS-DISEASE IMPACT**	Synergies with other health areas i.e., whether the product could be used across several diseases.

We used the following age ranges:



2. ACCESS CONSIDERATIONS

2.1. Intellectual property landscape

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
23	Years to patent expiry of API	YEARS TO PATENT EXPIRY OF API	Number of years of blocking patent protection left on the API.
24	Geographical coverage of patents	GEOGRAPHICAL COVERAGE OF PATENTS (INCLUDING SECONDARY PATENTS)	Country scope: how many LMICs are covered.
25	Secondary patents	SECONDARY PATENTS	Specific secondary patents (e.g. formulation, process, method of treatment, platforms) or patent thicket (e.g. biologics).
26	Multiple patent owners	MULTIPLE PATENT OWNERS	If multiple patent owners, might be lengthier to find an agreement with all the involved parties.

2.2. Service delivery enablers

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
27	Diagnostic	REQUIREMENTS FOR DIAGNOSIS	Diagnostic requirements for the diagnosis of the disease.
28	Diagnostic	ACCESS TO DIAGNOSIS	It includes an evaluation on availability/affordability/status awareness of the diagnosis. It also includes and info on whether the diagnosis is generally available in the public sector or only in the private one. A subset of countries is taken as a proxy.
29	Diagnostic	REQUIREMENTS FOR TREATMENT ELIGIBILITY/ TREATMENT MONITORING	Additional diagnostic requirements required to define eligibility to treatment candidate compared to SoC (e.g. sequencing) / requirement for treatment monitoring (e.g. viral testing).
30	Companion drugs	COMPANION DRUG REQUIREMENTS	Need of companion treatments.
31	Companion drugs	ACCESS TO COMPANION DRUGS	Access (availability and affordability) to companion treatment/s.
32	Health system requirements	HEALTH SYSTEM AND INFRASTRUCTURE NEEDS	Additional requirements for the proper and safe use of the candidate e.g. specific treatment efficacy and/or safety requirements/staff training/facilities.

2.3. Manufacturing

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
33	Manufacturing simplicity	MANUFACTURING	This includes the simplicity of the manufacturing process generally for this class of molecules. Small molecules chemically manufactured are classified as "not particularly complex for manufacturing". Synthetic proteins or nucleic acids are considered as "partially complex manufacturing" as it is less standard process than small molecules and requires generally aseptic filling which demands specific competencies. Recombinant proteins are classified as "complex manufacturing" as these involve cell growth steps and precise characterization tools needing specific competencies, and it generally also requires aseptic filling. Any specificity of this product within its category is ranked in the criteria as "standard manufacturing operations".
34	Manufacturing simplicity	MANUFACTURING OPERATIONS	Compared to the general simplicity to manufacture this category of product, any complexity to manufacture this specific product is ranked here (e.g., non-standard manufacturing step requiring specific competency or investment).
35	Manufacturing simplicity	MANUFACTURING FACILITY	Special requirements in terms of manufacturing facilities are captured here. Higher value of MPP intervention is attributed to products with no specific facility requirement other than basic good manufacturing practices (GMP), for example non-sterile products. Medium rating is attributed to products which require some additional control in terms of facility, like requirement of grade C area for sterile products which can be sterilised by terminal sterilisation. Lower value of MPP intervention is attributed to products which would require aseptic processing (Grade A), or special containment like hormones or oncology products with occupational exposure limits (OEL) classification of 4 or 5, thus making likely more challenging the identification of manufacturers and potentially the implementation of the production.
36	Manufacturing simplicity	EXCIPIENTS	If the excipients are well known (pharmacopeia), neither costly nor difficult to supply, the MPP intervention would be considered of high value as the implementation would be facilitated. If the excipient is used only in a few medical products or its cost impacts significantly on the cost of goods or the low availability can hinder the supply of the medical product, it would likely result in more difficulties in supplying the excipients or in affecting the product pricing.
37	Presentation and storage	SHELF-LIFE AND STORAGE CONDITIONS	Higher value of MPP intervention is for products with a shelf-life of at least two years at room temperature. A more moderate value would be for products with a shelf-life between one year (excluded) and two years at non-controlled temperature or storage at controlled temperature (e.g. 2-8°C). Lower value for MPP intervention could be for products with a shelf-life lower than one year (included) or with storage in frozen conditions (e.g. -20°C) as it would likely complexify the product distribution.
38	Presentation and storage	MEDICAL DEVICE	Tablets, pills, and vials presentations are considered as standard and would be in principle facilitated by an MPP intervention. Pre-filled syringes (PFS) are considered a medium standard. Intranasal medical devices, insulin pens, or patches are considered non-standard as they require specific equipment, access to specific and potentially costly devices and could imply specific regulatory requirements. In such situations, the potential impact of an MPP intervention needs to be evaluated on a case-by-case basis. This classification could be revised based on the deeper impact of the different medical devices and other potential variables.

2.4. Regulatory

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
39	Regulatory pathway	**REGULATORY PATHWAY FOR THE LICENSEES**	Probable regulatory pathway for the licensee. Higher rating is attributed to products where the originator product is already approved by SRA/WHO PQ, where the generics have regulatory pathways. Lower rating is attributed to products where the originator is not filed with any regulatory authority, where there is apparently no pathway for the licensee to file their product. Medium rating is attributed to products where the originator has approval in non-SRA countries, but no approval in SRA/WHO PQ. In such cases, potential sub-licensees would need to wait to have the originator product approved with SRA /WHO PQ to file their own product.
40	Regulatory cost and complexities	**COST AND COMPLEXITIES OF REGULATORY FILING**	The costs associated with regulatory filing are to be assessed separately here. This includes the cost of development, including possible studies (bioquivalence (BE), pre-clinical, clinical, etc.), cost of reference listed drug (RLD), etc. Simple generic products could be rated as high (since they have less complexities). Complex generic products like long-acting therapeutics, or complex dosage forms could be treated as with moderate complexity. Sometimes, simple generic products might need population studies which might add complexity to BE studies and could be included in this category. Biotherapeutics, which require a biosimilarity package, wherein a battery of preclinical and clinical studies are required, could be categorised as high level of complexity.
41	Probability of biowaiver / clinical trial waiver	**PROBABILITY OF BIOWAIVER /CLINICAL TRIAL WAIVER**	This aspect gets assessed in regulatory cost but needs to be understood separately if a biowaiver/clinical trial waiver is possible. High probability of biowaiver is there for oral solids of BCS Class I, or solutions. Moderate probability for biowaiver is where a molecule might have a probability of biowaiver/clinical trial waiver but there could be other studies/justifications required. For biotherapeutics, some less complex molecules with a PD marker might be included in this category. Low probability of biowaiver is applicable to BCS Class II /IV molecules. Complex biotherapeutics like mAbs would also fall in this category.

2.5. Market

CRITERIA FOR PRODUCT'S ASSESSMENT			
N	CRITERIA	SUB-CRITERIA	EXPLANATION OF THE CRITERIA
42	Affordability/availability of the candidate	CANDIDATE-PRODUCT'S AVAILABILITY IN LMICS	Availability of target product in LMICs to assess impact of voluntary licensing and business case.
43	Affordability/availability of the candidate	CANDIDATE-PRODUCT'S AFFORDABILITY IN LMICS	Affordability of target product in a sample of countries with reference to SoC, to assess impact of voluntary licensing and business case.
44	Commercial potential for MPP generic manufacturers' network	COMPANY COMMERCIAL FOOTPRINT	Commercial reach of company across the targeted MPP territories to understand if an in-house access program can reach people in need.
45	Commercial potential for MPP generic manufacturers' network	MARKET SIZE	Annual sales of the product globally and in a sample of territories to understand generic business case and impact on originator profit and loss.
46	Commercial potential for MPP generic manufacturers' network	EXISTENCE, AVAILABILITY AND PRICE OF ALTERNATIVE OF MARKETED TREATMENTS	To assess need and business case for originators.
47	Commercial potential for MPP generic manufacturers' network	EXISTENCE AND AVAILABILITY OF ALTERNATIVE TREATMENTS IN PIPELINE	Existence and availability of alternative therapies in development to focus our priorities and generic interest.
48	Commercial potential for MPP generic manufacturers' network	PRODUCT ATTRACTIVENESS FOR THE LICENSEES	Commercial attractiveness in terms of potential sales and volumes (which could be considered as a proxy for generic manufacturers potentially interested in developing the product).
49	Commercial potential for MPP generic manufacturers' network	PROCUREMENT	Whether there are any established procurement mechanisms available for this type of product.
50	Commercial potential for MPP generic manufacturers' network	COMPETITIVE PRODUCTS (INCLUDING ALREADY EXISTING GENERIC VERSIONS OF THE CANDIDATE AND SAME CLASS PRODUCTS)	Market share according to what is in the pipeline.
51	Impact	POTENTIAL SAVING FOR PUBLIC HEALTH	Commercial impact that generic manufacturers would create after MPP intervention. Whether MPP would be improving the *status quo* for patients and governments.

Abbreviations and acronyms

3TC	Lamivudine
ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
ART	Antiretroviral Therapy
ARV	Antiretroviral
AS/AQ	Artesunate/Amodiaquine
ASO	Antisense Oligonucleotide
BCS	Biopharmaceutical Classification System
BE	Bioequivalence
BIC	Bictegravir
BMI	Body Mass Index
bNAbs	Broadly Neutralising Antibodies
BRAF	v-Raf Murine Sarcoma Viral Oncogene Homolog B1
BTKi	Bruton's Tyrosine Kinase Inhibitor
°C	Degree Celsius
CAB	Cabotegravir
CAB-LA	Cabotegravir Long-Acting
CAB-ULA	Cabotegravir Ultra Long-Acting
CADO	Community Advisory Panel
CAP	Community Advisory Panel
CDK 4/6	Cyclin-Dependent Kinase 4 and 6
CF	Cystic Fibrosis
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator
CKD	Chronic Kidney Disease
CLL	Chronic Lymphocytic Leukemia
CNS	Central Nervous System
CONRAD	Contraceptive Research and Development Program
CRL	Complete Response Letter
CROI	Conference on Retroviruses and Opportunistic Infections
CVD	Cardiovascular Disease
DAC	Daclatasvir
DALYs	Disability-Adjusted Life Years
DDI	Drug-Drug Interactions
DOR	Doravirine
DOT	Directly Observed Therapy
DPP4i	Dipeptidyl Peptidase IV Inhibitors
DrpE1	Decaprenylphosphoryl-β-d-ribose-2'-epimerase
DTG	Dolutegravir
DZIF	German Center for Infection Research
EGFR	Epidermal Growth Factor Receptor
EGFR TKI	Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor
EGFRm	Epidermal Growth Factor Receptor mutation
EMA	European Medicines Agency
EML	Essential Medicines List
EML	Essential Medicines List
EPFL	École Polytechnique Fédérale de Lausanne
Eto	Ethionamide
EU MAA	European Marketing Authorisation
EU-M4all	EU-Medicines for all (Scientific opinions by EMA & WHO for markets outside the EU)
EVG	Elvitegravir

FTC	Emtricitabine
FTC	Emtricitabine
GAP-f	Global Accelerator for Paediatric Formulations
GIP	Gastric inhibitory polypeptide
GLP-1	Glucagon-Like Peptide-1
GLP-1 RA	Glucagon-Like Peptide-1 Receptor Agonists
GMP	Good Manufacturing Practices
GSK	GlaxoSmithKline
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HER2	Human Epidermal Growth Factor Receptor 2
HICs	High-Income Countries
HIV	Human Immunodeficiency Virus
HR	Hormone Receptor
HTE	heavily treatment-experienced
HTE	Heavily treatment-experienced
ICI	Immune Checkpoint Inhibitors
IgG1	Immunoglobulin G1
IM	Intramuscular
INSTI	Integrase Strand Transfer Inhibitor
IP	Intellectual Property
ISL	Islatravir
IU	International Unit
IV	Intravenous
KRAS	Kirsten Rat Sarcoma Virus
LA	Long-Acting
LAI	Long-Acting Injectable
LEN	Lenacapavir
LGG	Low-Grade Glioma
LICs	Low-Income Countries
LMICs	Low- and Middle-Income Countries
LRTI	Lower Respiratory Tract Infections
LTBI	Latent Tuberculosis Infection
mAbs	Monoclonal Antibodies
MACE	Major Adverse Cardiovascular Events
MACE	Major Adverse Cardiovascular Events
MAGHP	Marketing Authorisation for Global Health Products
MASH	Metabolic dysfunction-Associated SteatoHepatitis
MATRIX	A USAID Project to Advance the Research and Development of Innovative HIV Prevention
MDR-RRTB	multidrug-resistant or rifampicin resistant tuberculosis
MDR-TB	Multi-Drug-Resistant Tuberculosis
MEK	Mitogen-Activated Protein Kinase Kinase
mg	Milligram
MPP	Medicines Patent Pool
MSD	Merck Sharp & Dohme
NCD	Non-Communicable Diseases
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTTI	Nucleoside reverse transcriptase translocation inhibitor
NSCLC	Non Small Cell Lung Cancer
NSCLC	Non-Small Cell Lung Cancer
OEB	Occupational Exposure Bands
OEL	Occupational Exposure Limits
PADO	Paediatric Antiretroviral Drug Optimization
PAN-TB	Project to Accelerate New Treatments for Tuberculosis
pan-TB	Project aimed to research a pan-TB treatment regimen
Para III	Paragraph III Certification

PCR	Polymerase Chain Reaction
PD	Pharmacodynamics
PD-1	Programmed Cell Death 1
PD-L1	Programmed Cell Death Ligand 1
PD-L2	Programmed Cell Death Ligand 2
PFS	Pre-Filled Syringe
PK	Pharmacokinetics
PK/PD	Pharmacokinetics/Pharmacodynamics
PLHIV	People Living with HIV
PNP	Post-Natal Prophylaxis
PPR	pandemic preparedness and response
PrEP	Pre-Exposure Prophylaxis
PWID	People Who Inject Drugs
Q	Quarter
Q4M	Every 4 Months
QT	a measure of heart's electrical activity
R&D	Research and Development
RA	Receptor Agonist
RNA	Ribonucleic Acid
RPV	Rilpivirine
RR-TB	Rifampicin-Resistant Tuberculosis
RSV	Respiratory Syncytial Virus
SAGE	The WHO Strategic Advisory Group of Experts on Immunization
SAGE	Strategic Advisory Group of Experts on Immunization
SAP	Scientific Advisory Panel
SCLC	Small Cell Lung Cancer
SGLT2i	Sodium-Glucose Transport Protein 2 inhibitors
SNAC	Sodium N-(8-[2-hydroxylbenzoyl] amino) caprylate
SoC	Standard of Care
SOF	Sofosbuvir
SQ	Subcutaneous
SRA	Stringent Regulatory Authorities
STI	Sexually Transmitted Infections
SVR12	Sustained Virologic Response at 12 weeks
Swissmedic	Swissmedic Procedure for Scientific Advice and MAGHP
T1DM	Type 1 Diabetes Mellitus
T2D	Type 2 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TAF	Tenofovir Alafenamide
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
TDF	Tenofovir Disoproxil Fumarate
TKI	Tyrosine Kinase Inhibitor
TLD	Tenofovir/Lamivudine/Dolutegravir
TLD	Tenofovir/Lamivudine/Dolutegravir
TPT	Tuberculosis Preventive Therapy
UMICs	Upper-Middle-Income Countries
USAID	United States Agency for International Development
USFDA	The United States Food and Drug Administration
WHO	World Health Organization
WHO-PQ	WHO Pre-Qualification of Medicines Programme

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