HIV Business Meeting

March 30, 2023

Shionogi & Co., Ltd.

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Agenda

1. Current Status of HIV Business and Future Prospects

(Isao Teshirogi, Ph.D., Chief Executive Officer (P.4)

2. ViiV/SHIONOGI's HIV Business Strategy

(John Keller, Ph.D., Senior Executive Officer, Senior Vice President, R&D Supervisory Unit (P.6-15)

- Outline of partnership with ViiV
- Current HIV market status
- ViiV/SHIONOGI's medium- to long-term strategy
- Long-acting (LA) formulations performance and market forecast
- Features of ViiV's LA formulations
- Development of self-administration, ultra long-acting (ULA) and cure

1. Current Status of HIV Business and Future Prospects

Current Status of HIV Business and Future Prospects - From Patent Cliff to Patent Hill -

Growth of Current Products

- Strong growth of oral two drug regimens and smooth launch of LA formulations

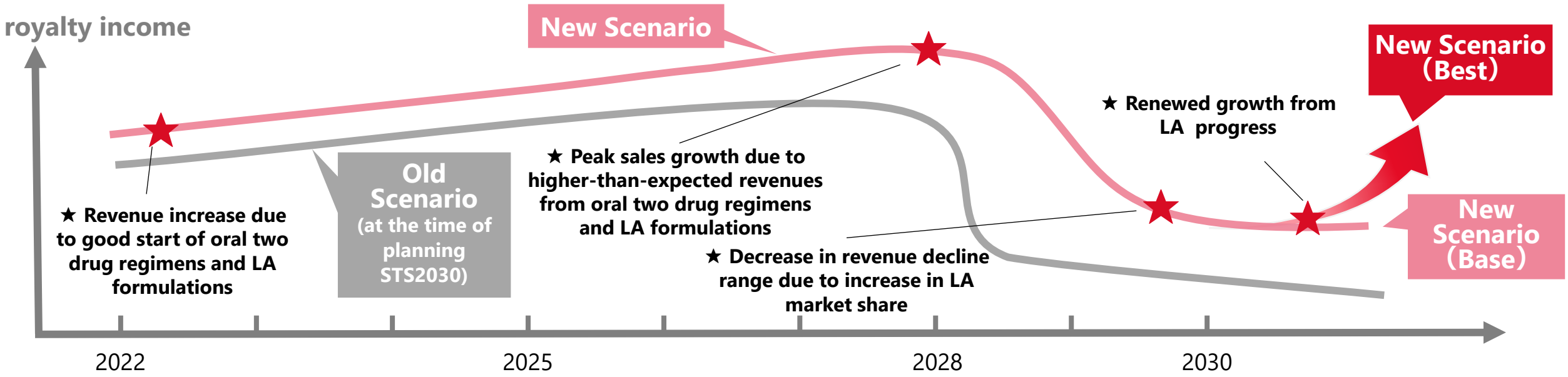
⇒ Counter HIV patent cliff through the growth of LA formulations

Expansion for Future HIV Solution

- Expansion of LA formulations and creation of new solutions to meet future unmet needs in the HIV area

⇒ Focus on HIV business beyond 2030 as a one of profit drivers

＜Image diagram of changes in royalty income＞



＜Currently estimated patent expiration timing* (US and Europe)＞ dolutegravir: Around 2028 (US) Around 2029 (Europe), cabotegravir: Around 2031, S-365598 (VH4524184) : Around 2039 * Working toward patent term extension for all drugs

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2. ViiV/SHIONOGI's HIV Business Strategy

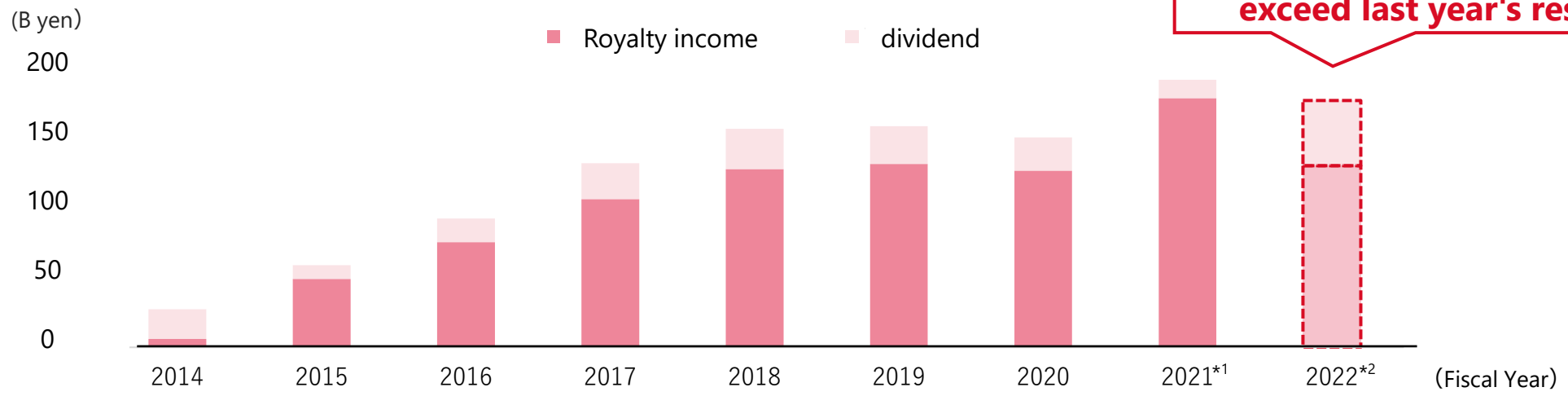
Outline of Partnership with ViiV

Contract with ViiV

- Licensed of dolutegravir, cabotegravir, and S-365598 (VH4524184) to ViiV
  - → **Receive royalty income based on sales of products containing these compounds**
    (Royalty rates are the same for all compounds)
- 10% shareholder of ViiV and retain the right to nominate one director
  - → **Receive 10% ordinary dividend from ViiV quarterly**

Royalty income and received dividends from ViiV

- Results up to the third quarter
- **Full-year forecast expected to exceed last year's results**



* Received lump sum payment from the settlement with Gilead Sciences Inc. as royalty income (GSK press release)
*2 Increase in dividend income due to two temporary factors ①Lump sum payment for the above settlement ②Delay in receipt of dividend income for Q4 FY2021

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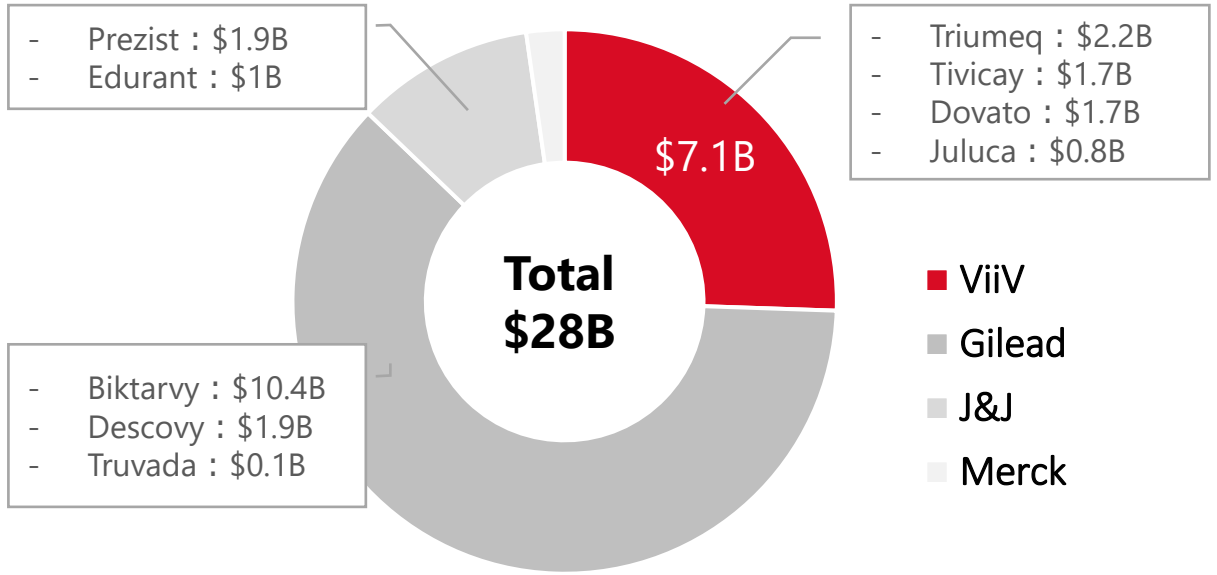
Current HIV Market Status

Anti-HIV drug market（Treatment＋PrEP）

- The top three companies account for about 98% of the market share in this huge market
- US market is about 65% of value share
- ViiV steadily gaining market share (2015: 16.7%⇒2022: 25.5%)



PrEP market

- Currently only three drugs (Descovy, Truvada, Apretude) are indicated for PrEP
- Among the 1.2 million potential candidates in US, only 25% of them actually use PrEP*3
- The market size is expected to more than double by 2030*4
  - US government support to reduce new infection

The current anti-HIV drug market is about $28 billion*1, and the number of infections has been increasing by about 30,000 people / year in US, a major region*2

*1 Calculated based on financial statement, 2022 4Q of major pharmaceutical companies selling anti-HIV drugs
*2 US HIV statistics
*3 N Engl J Med 2023; 388:769-771 DOI: 10.1056/NEJMp2216100 *4 US National HIV/AIDS Strategy

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Integrase Inhibitor “Backbone” Leads HIV Market

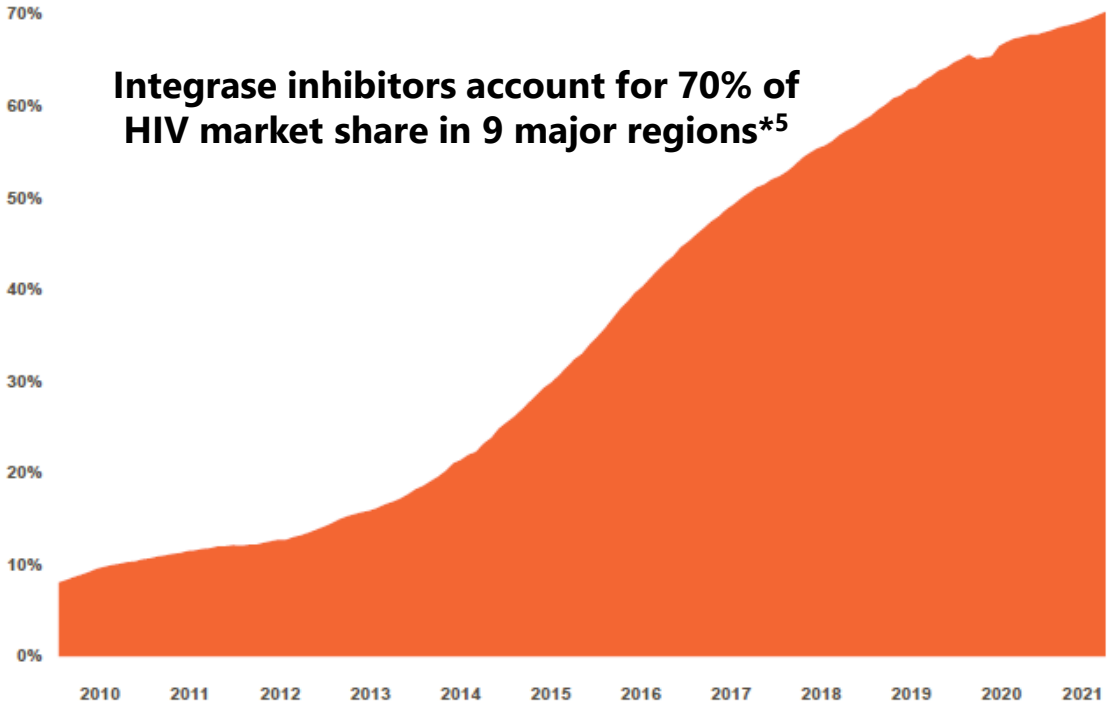
Basic design of highly active anti-HIV therapy*1

- Efficiently suppress HIV replication by combining multiple anti-HIV drugs with different mechanism of action
- Anti-HIV drugs require long-term clinical evidence due to lifelong administration

Characteristics of integrase inhibitor regimens

- Highly ranked global guidelines*2-4
- Extensive clinical and real-world evidence supporting long-term efficacy, safety and high genetic barrier

Integrase inhibitors account for 70% of HIV market share in 9 major regions*5



*1 Anti-HIV care guidelines (Health and Labor Administration Promotion Survey Project Grant: AIDS Countermeasure Policy Research Project) *2 European AIDS Clinical Society
*3 Panel on Antiretroviral Guidelines for Adults and Adolescents（Create by the US Department of Health and Human Services）
*4 Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring（Created by WHO）
*5 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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ViiV/SHIONOGI's HIV Business Strategy - Provide Solutions Based on Unmet Needs -

Current antiretroviral therapy state

- High anti-viral efficacy, safety, and genetic barrier
- HIV cases increase although mortality rates have improved significantly
- Need to improve access to PrEP

Further improvement in QOL is required for a chronic disease

Unmet needs that cannot be fulfilled by oral pills

Relieve burden and anxiety of taking daily oral pills

Live free from thinking of HIV

Privacy and Discretion

Accelerate paradigm shift from oral pills to LA formulations

Medium-to Long-Term Growth Drivers

Innovative products that meet unmet needs

2021-2026

- Average annual growth rate of around 5% for the entire HIV business
- Aim for annual sales of £2 billion for LA formulations

Dovato
Oral two drug regimen

Cabenuva
LA formulation (Treatment)

Apretude
LA formulation (PrEP)

After 2026

- Continuous new product launches that improve upon prior LA formulations

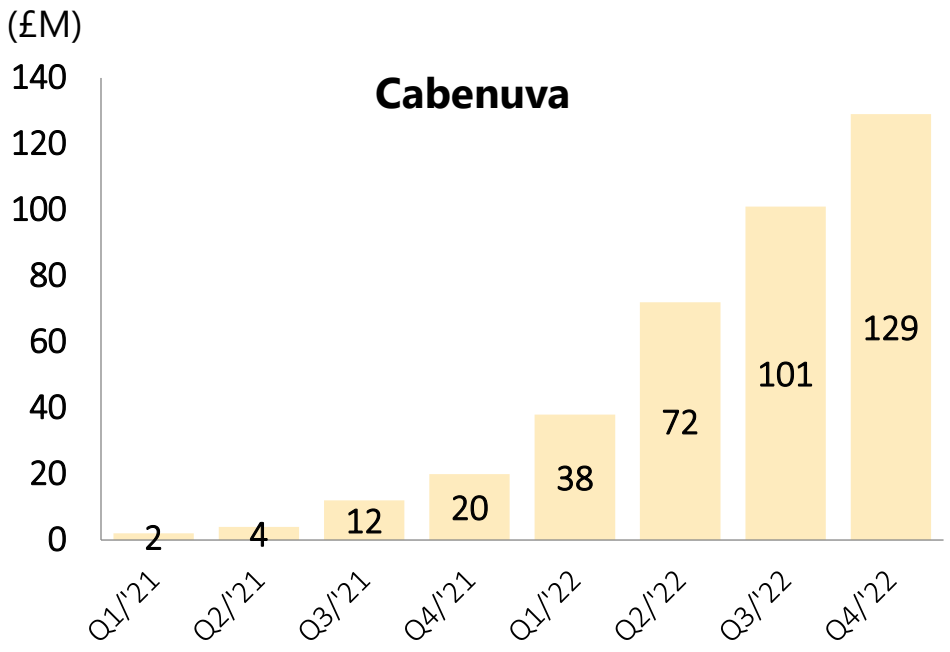
Self-injection

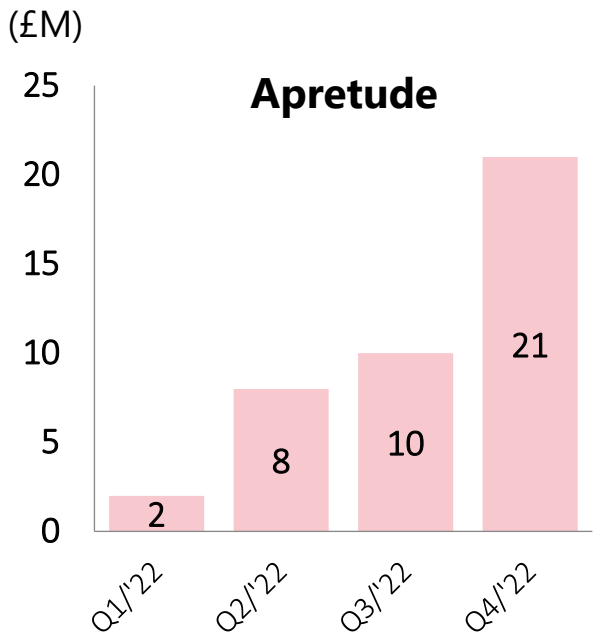
Ultra long-acting (PrEP)

Ultra long-acting (Treatment)

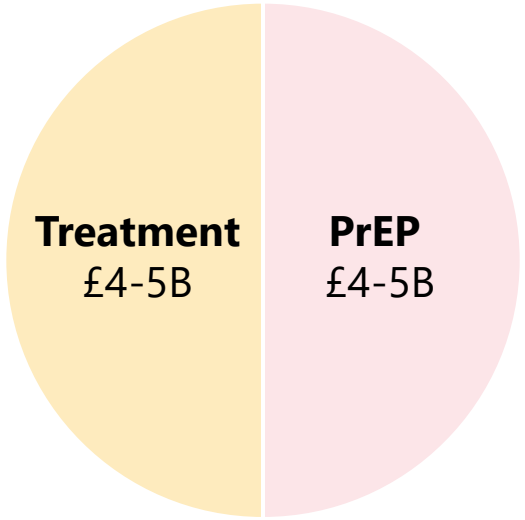
Business Trend of LA Formulations and Market Projections

ViiV sales trend of LA formulations*1





LA market projections*2 (Up to 2030)



Significant lead-time versus competitors in the rapidly growing LA market

*1 Source: GSK financial statement

*2 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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Characteristics of ViiV's LA Formulations

Cabenuva (cabotegravir + rilpivirine)

- Indication: Treatment of HIV-1 infection
- Dosage: intramuscular injection, once every 2 months
- Release Date: Feb 2021 (US)
- Country of Sale: US, Europe, Japan, others

About 90% of clinical trial participants*1 prefer Cabenuva therapy over daily oral pills

Apretude (cabotegravir)

- Indication: PrEP of HIV-1 infection
- Dosage: intramuscular injection, once every 2 months
- Release Date: Jan 2022 (US)
- Country of Sale: US, others

66% of those who have used daily oral prophylaxis or discontinued it are highly interested in LA formulation*2

*1 FLAIR study: NCT02938520, ATLAS study: NCT02951052, ATLAS-2M study: NCT03299049, SOLAR study: NCT04542070

*2 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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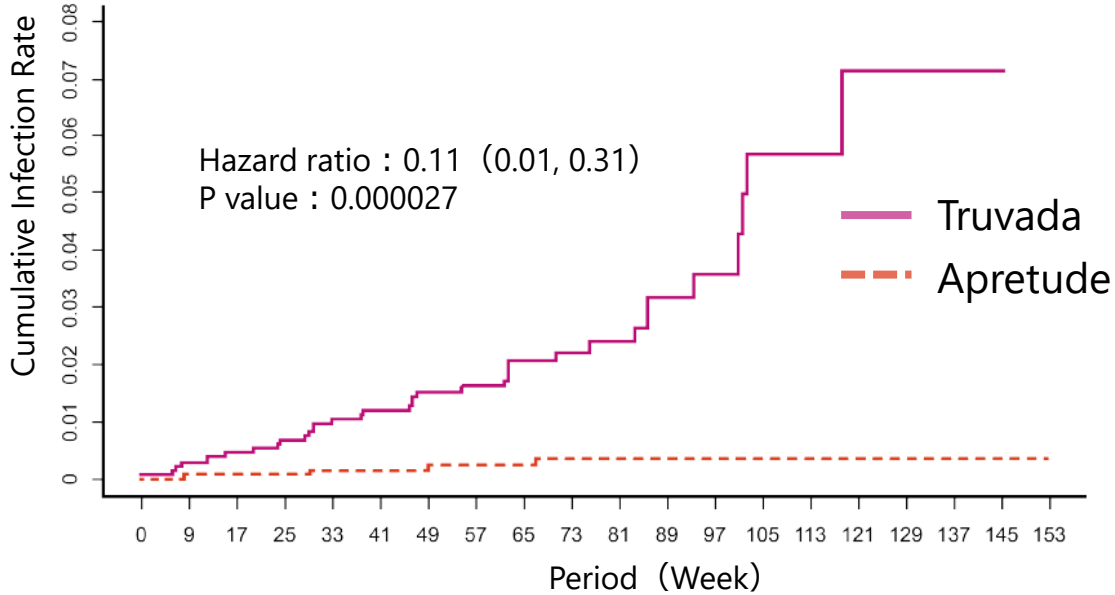
Major Clinical Studies of Cabotegravir Products

Cabenuva (cabotegravir + rilpivirine)

- **FLAIR study*1**
  - Verified non-inferiority of efficacy and safety after 124 weeks in untreated patients
- **ATLAS study, ATLAS-2M study*2**
  - Comparison to daily oral treatment verifying non-inferiority of efficacy at 152 weeks in treatment experienced patients
- **SOLAR study*3**
  - Verified non-inferiority of efficacy and safety in direct comparison with Biktarvy
  - Therapy satisfaction rate statistically superior to Biktarvy

Apretude (cabotegravir)

- **HPTN083 study*4**
  - 66% greater prevention efficacy than Truvada in men or transgender women at high risk of HIV infection
- **HPTN084 study*5**
  - 89% greater prevention efficacy than Truvada in women at high risk of HIV infection



*1 FLAIR study: NCT02938520 *2 ATLAS study: NCT02951052, ATLAS-2M study: NCT03299049 *3 SOLAR study: NCT04542070
*4 HPTN083 study: NCT04692077 *4 HPTN084 study: NCT04824131

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Development of Self-administration, Ultra Long-acting and Cure (1)

Medium-to long-term strategy

- Development of self-injection and ultra long-acting (ULA) formulations with cabotegravir and S-365598 (VH4524184) as key drugs
  - Self-injection and ULA developed as subcutaneous injections
  - Availability of PH20 (Halozyme technology) to assist development of ULA
- Research and development aimed at HIV cure

Timeline*

2025-2027

- **Provide a self-administered LA formulation**
  : cabotegravir＋novel MOAs
- **Provide ULA for PrEP**
  (once every three months or more)
  : cabotegravir

Around 2027

- **ULA for treatment**
  (once every three months or more)
  : cabotegravir＋novel MOAs

2030 and beyond

- **Further ULA for treatment**
  (once every six months or more)
  : S-365598 (VH4524184)＋novel MOAs
- **HIV Cure**

* Meet GSK Management Getting ahead of HIV (Nov. 2021)

Development of Self-administration, Ultra Long-acting and Cure (2)

Actions towards 2030 and beyond

- **Application of PH20*1 （Halozyme Thrapeutics, Inc）**
  - Increase subcutaneous administration volume for longer effect time
  - Phase 1 trial combined with cabotegravir ongoing
- **Development of S-365598 (VH4524184)**
  - Created and licensed by SHIONOGI*2
  - Higher genetic barrier than existing integrase inhibitors
  - May enable ≥ 6m dose interval
  - Phase 1 trial on going
- **Development of combination candidates**
  - Candidates from a wide range of mechanisms of action, including broadly neutralizing antibodies*3, capsid inhibitor, maturation inhibitors
  - Phase 2b trial of cabotegravir in combination with broadly neutralizing antibody N6LS*3 to be initiated in 2023
  - Aiming for combination selection by 2024

HIV Research by SHIONOGI

Research on ULA combination candidates

S-365598 (VH4524184) + **combination candidates**

Multiple approaches are under consideration for the creation of more convenient therapies and the realization of "functional cure"

*1 VIIV press release: license agreement for ENHANZE® drug delivery technology *2 SHIONOGI press release: out-licensing S-365598 (VH4524184), third-generation HIV integrase inhibitor

*3 For details about the development status of concomitant drug, refer to Appendix P.19

Appendix

Major Anti-HIV Drug Development Status including Competitors* (1)

* Source _2022 4Q financial results

	Compounds	Mechanism of action		Phase 1	Phase 2	Phase 3
ViiV	VH3640254	Maturation inhibitor	Self injection			
	VH3810109 (N6LS)	Broadly neutralizing antibody	Every 3 months more / Self-injection			
	VH3739937	Maturation inhibitor	Self injection			
	Cabotegravir 400㎎/ml	Integrase strand transfer inhibitor	Every 3 months or more/ Self injection			
	VH4004280	Capsid inhibitor	Every 3 months or more / Self-injection			
	VH4011499	Capsid inhibitor	Every 3 months or more / Self-injection			
	S-365598 (VH4524184)	Integrase strand transfer inhibitor	Every 6 months or more			
Merck	MK-8591A (Islatravir+doravirine)*1	NRTTI*3/NNRTI	Daily Oral			
	MK-8591B (Islatravir+MK-8507)*2	NRTTI/NNRTI	Weekly Oral			
	MK-8591D (Islatravir+lenacapavir)*1	NRTTI/Capsid inhibitor	Weekly Oral			
	MK-8527	NRTTI	PrEP			

*1 On FDA partial clinical hold for higher doses than those used in current clinical trials *2 On FDA clinical hold *3 Nucleoside reverse transcriptase translocation inhibitor

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Major Anti-HIV Drug Development Status including Competitors* (2)

* Source _2022 4Q financial results

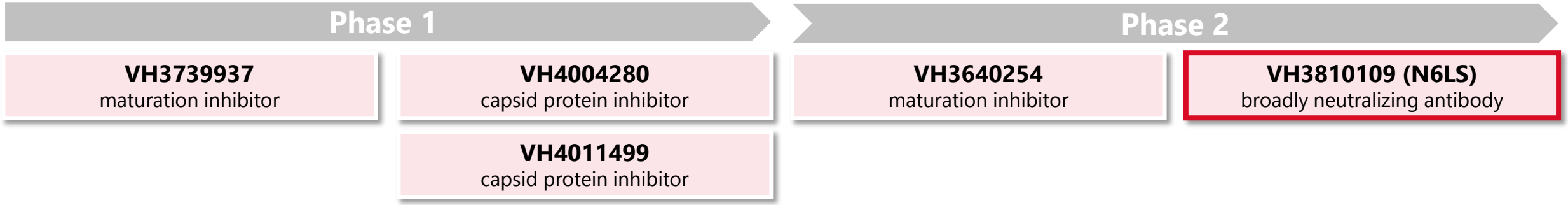
	Compounds	Mechanism of action		Phase 1	Phase 2	Phase 3
Gilead	Lenacapavir	Capsid inhibitor	Every 6 months subcutaneous PrEP			
	Lenacapavir/bictegravir oral combination	Capsid inhibitor/Integrase strand transfer inhibitor	Daily oral Treatment experienced			
	Lenacapavir	Capsid inhibitor	Every 6 months subcutaneous			
	Lenacapavir/islatravir oral combination	Capsid inhibitor/NRTTI*2	Weekly oral			
	bNAb combination (GS-5423, GS-2872) *1	Broadly neutralizing antibody	Every 6 months subcutaneous Cure			
	Lefitolimod*1	Toll like Receptor9 (TLR9) agonist	Cure			
	Vesatolimod	Toll like Receptor7 (TLR7) agonist	Cure			
	HIV bispecific T-cell engager (GS-8588)	Bispecific T-cell engager	Cure			
	Lenacapavir/bNAb combination	Capsid inhibitor/broadly neutralizing antibody	Every 6 months subcutaneous			
	HIV long-acting injectable INSTI (GS-6212)	Integrase strand transfer inhibitor	Every 3 months subcutaneously			
	HIV long-acting oral NNRTI (GS-5894)	NNRTI*3	Weekly oral			
	HIV long-acting oral INSTI (GS-1720)	Integrase strand transfer inhibitor	Weekly oral			

*1 Non-Gilead sponsored trial(s) ongoing *2 Nucleoside reverse transcriptase inhibitor *3 Non-nucleoside reverse transcriptase inhibitor

Development Status of Combination Candidates for ULA

Development status of combination candidates for ULA by ViiV

From GSK financial results in Q3 2022



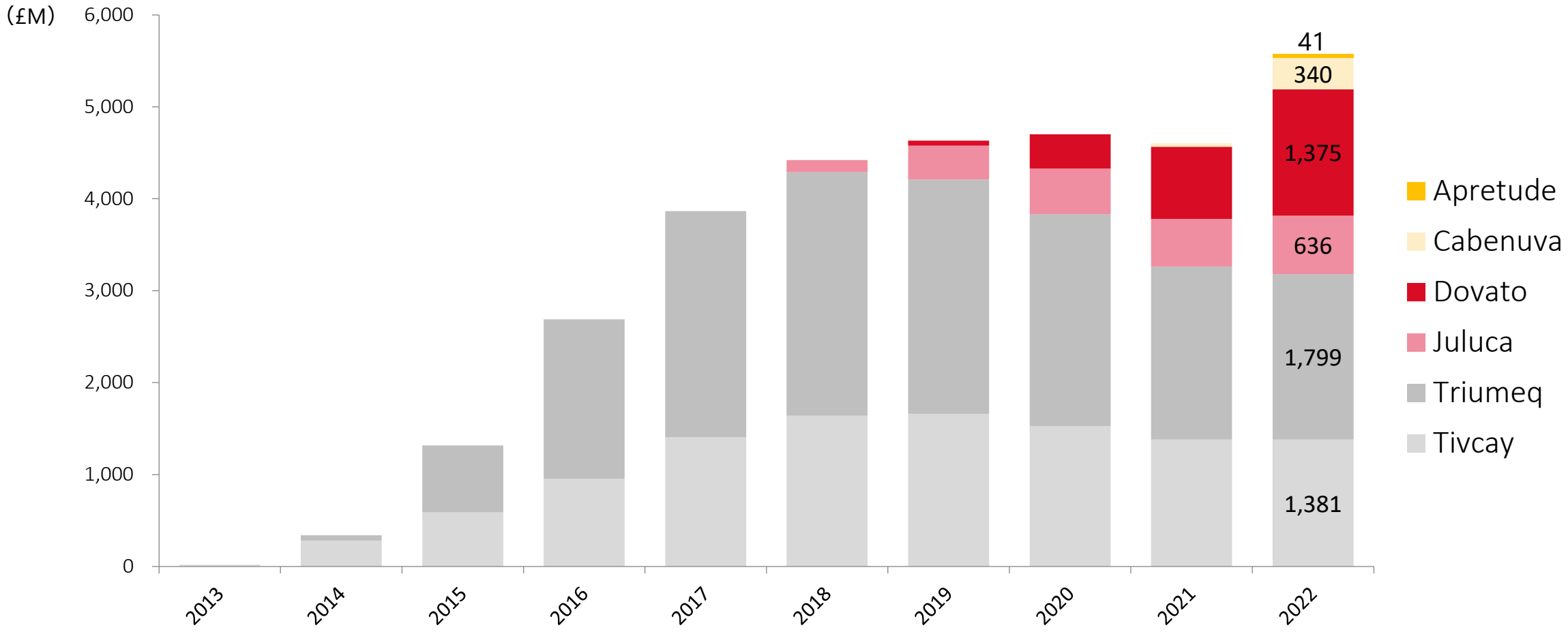
Broadly neutralizing antibody N6LS*

- By blocking HIV's entry into human CD4+ cells, the HIV transmission process may be prevented
- **Positive results of Phase 2a**
  - A single infusion of N6LS demonstrated strong antiviral efficacy while also being well-tolerated by trial participants
  - Expect to begin a phase 2b trial of N6LS in combination with other anti-retrovirals in 2023

* ViiV Healthcare presents positive proof-of-concept findings for N6LS, an investigational, broadly neutralising antibody (bNAb) offering a potential new approach for the treatment of HIV | GSK

ViiV's Growth History

Trends in sales of dolutegravir and cabotegravir products*



* Source: GSK financial statement

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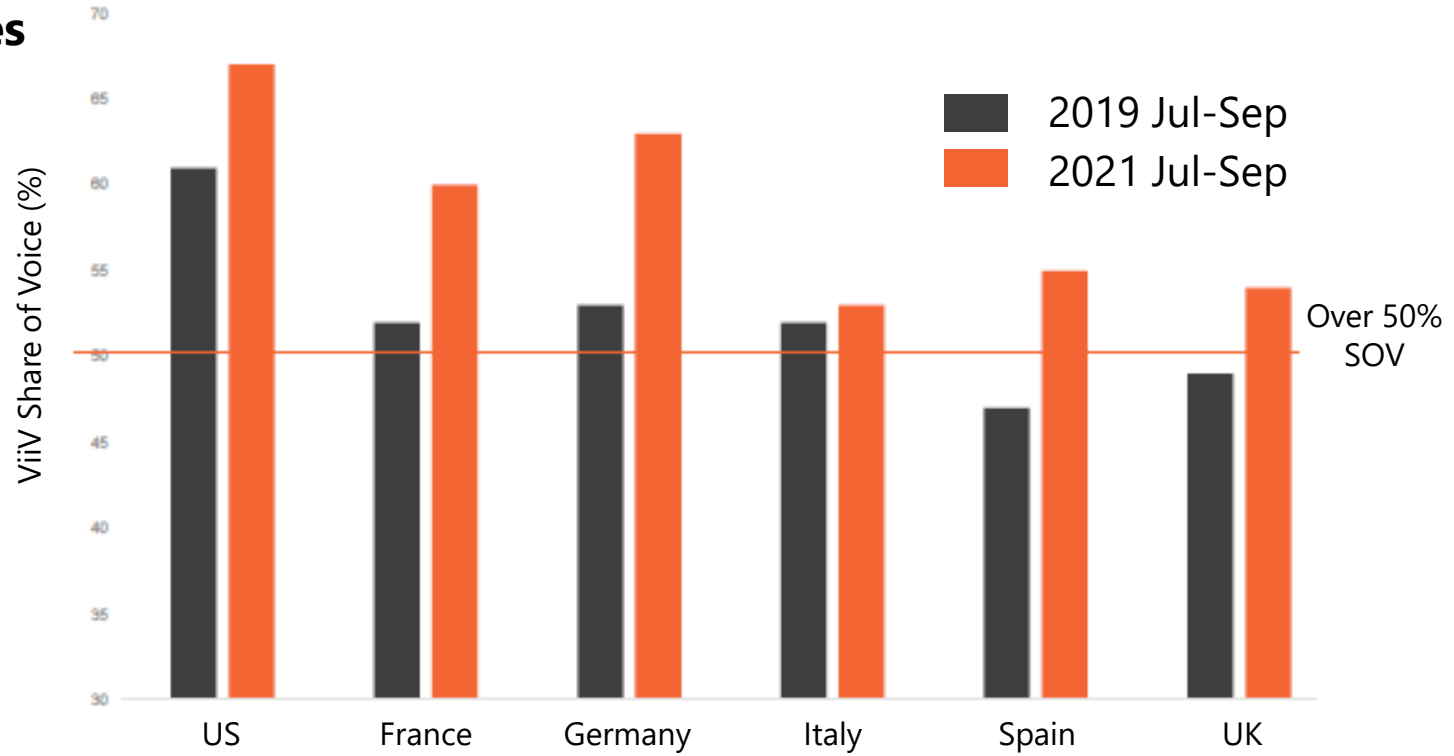
ViiV Presence

Commercial and Medical Competitiveness of ViiV*

- **Highly efficient allocation of sales resources**
  - Focus on top 10 countries in HIV market
- **competitive sales force**
  - Good sales outcomes stably exceeding the industry average
- **Excellence in Digital Data Analysis**
- **Impactful medical affairs**
  - Prompt inclusion in major guidelines
  - Establishment of post-marketing evidence
  - Active submission to major international conferences



Obtained over 50% share of voice in HIV market of major countries

* Meet GSK Management Getting ahead of HIV (Nov. 2021)

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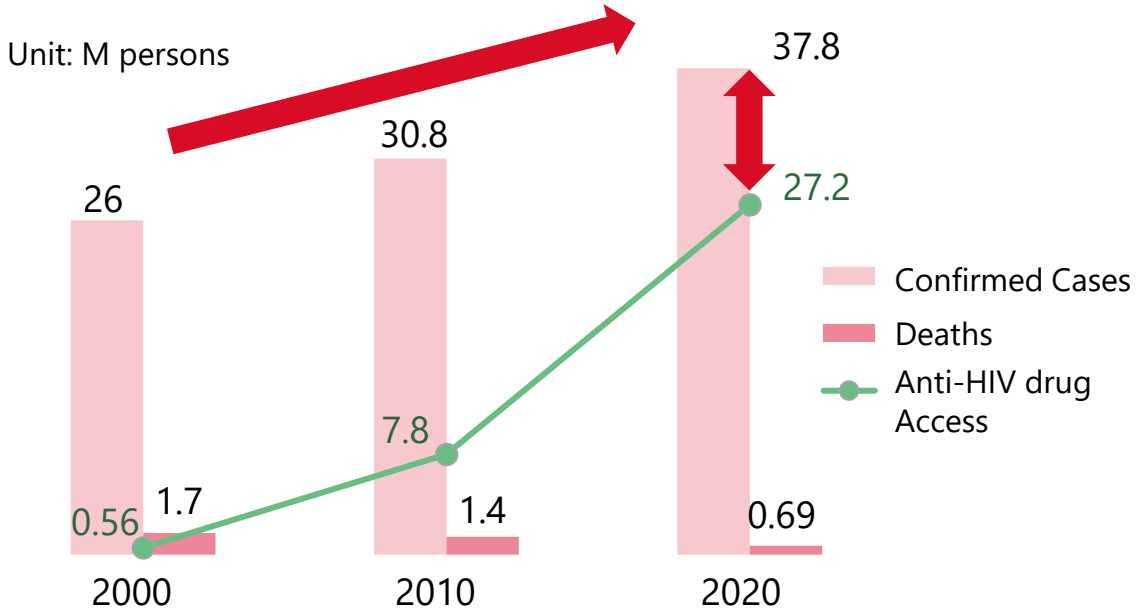
HIV Epidemic Status

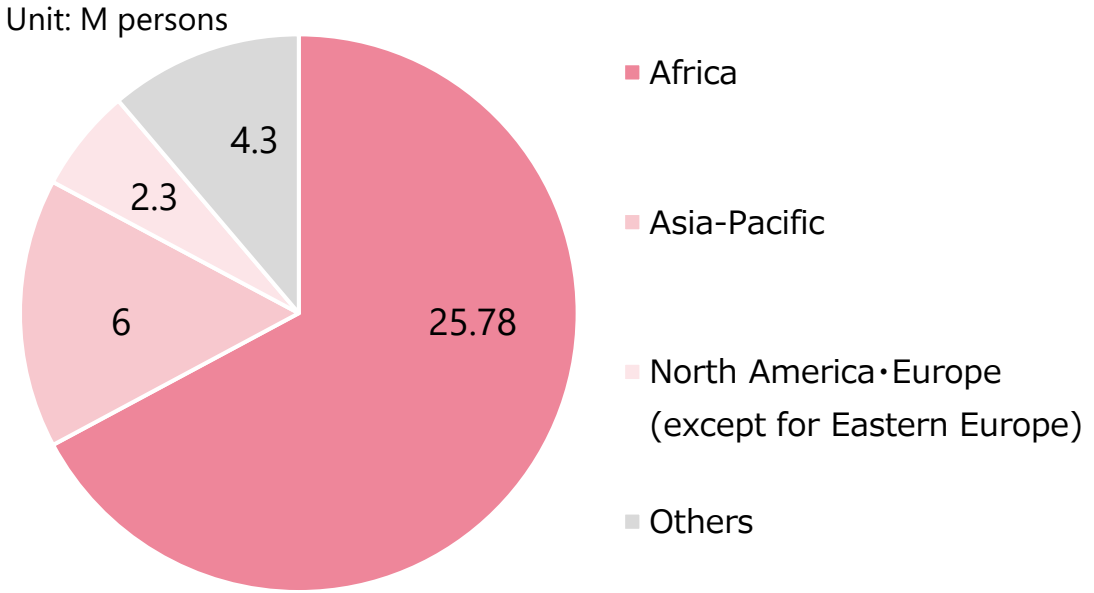
Changes in the number of global HIV cases and deaths*

- The number of death has decreased in the past 20 years while that of infected people has increased
- About one million patients cannot take anti-HIV drug



Number of HIV infections in each region* (2021)

- 38.4 million confirmed cases in total worldwide
  ⇒Major source of anti-HIV drug is US and Europe
  (US：about 1.2 million cases)



HIV presents a global public health threat as a chronic infectious disease

* https://www.unaids.org/en/resources/fact-sheet

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