Evaluate Vantage

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Glaxo needs long-acting HIV gamble to pay off

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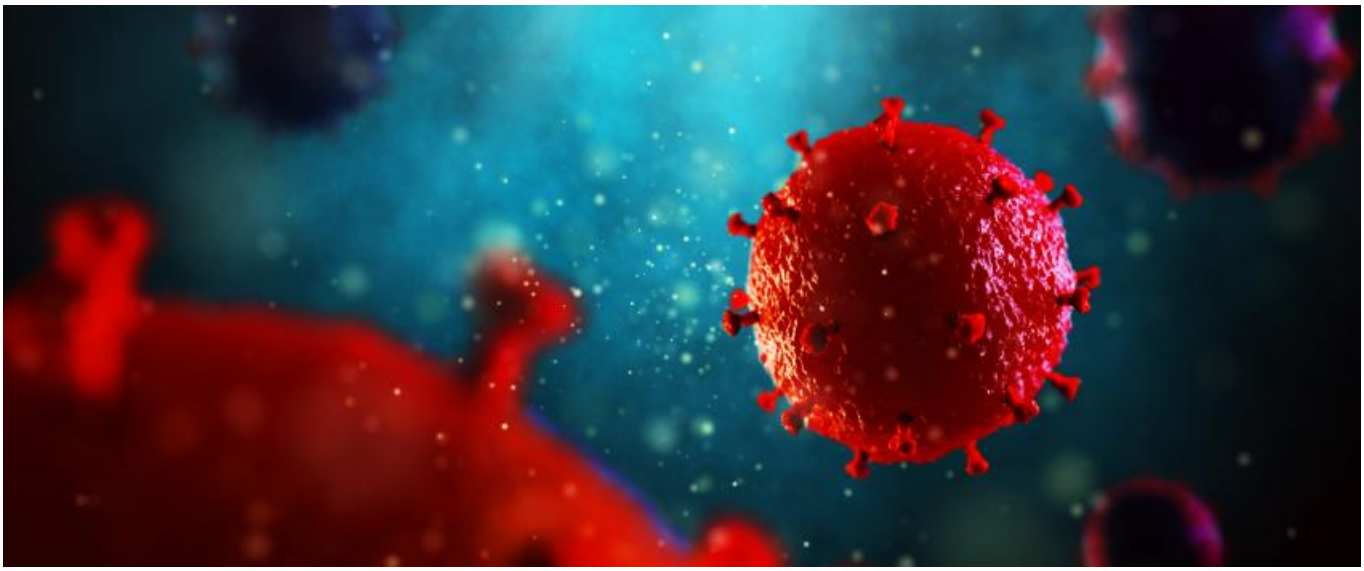


Dolutegravir's patent expiry will pile on the pressure as Gilead and Merck get on the long-acting bandwagon.

Glaxosmithkline's upbeat investor day yesterday appeared to convince shareholders that it is not all doom and gloom at the company, but the group now needs to put its money where its mouth is. A key test will be in HIV, and the next few years should show whether Glaxo's move towards long-acting regimens has paid off.

The company's key oral daily drug, dolutegravir, comes off patent in 2028/29, and before this Glaxo needs to shift patients to long-acting injectables based around cabotegravir. Long-acting competition is on the horizon from Gilead and Merck & Co; although Glaxo execs brushed off concerns yesterday, it seems premature to dismiss such fierce rivals.

It is true that Glaxo, via the Viiv joint venture with Pfizer and Shionogi, has been a trendsetter in long-acting HIV medicines. Several times yesterday execs stressed that Glaxo had a head start of at least a five years in HIV treatment, and three years in prevention.

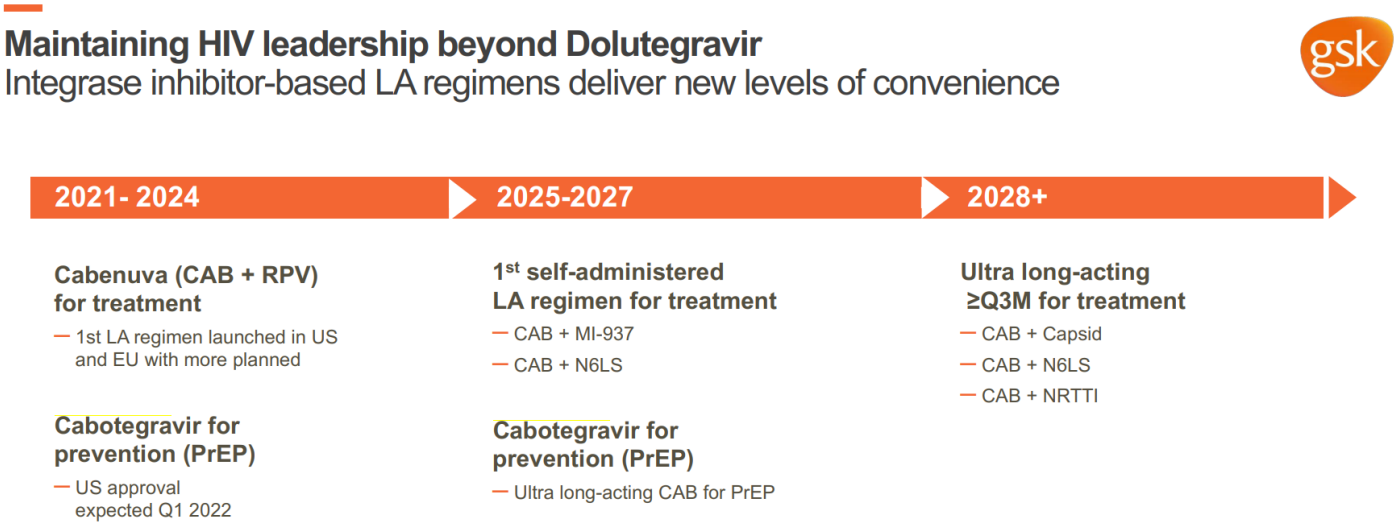
In HIV therapy cabotegravir plus Johnson & Johnson's rilpivirine is already FDA-approved as Cabenuva, a once-monthly injection. A two-monthly injection is under review and could get the go-ahead by the end of the year.

In pre-exposure prophylaxis (Prep) Glaxo recently started a rolling submission of a two-monthly injection of cabotegravir monotherapy, and hopes for approval by the end of this year or early 2022.

Long long acting

Glaxo has ambitions to go even further. First, it is developing a subcutaneous long-acting treatment regimen for once-monthly self-administration. Proof-of-concept data should be reported in the middle of next year, Viiv's head of R&D, Kim Smith, said yesterday. Second, Glaxo wants to push the treatment gap out further – three months or more – and this was the rationale behind its exclusive deal with Halozyme this week.

For the ultra-long-acting projects Glaxo will combine cabo with other novel HIV therapies in development, which it outlined yesterday. If one or more of these combos work this would extend the intellectual property for the long-acting franchise past 2031, when cabo's patent is set to expire.



Source: Company presentation

Glaxo estimates that by 2031 90% of its HIV business will be in long-acting regimens. This hinges on the company being right about patients preferring a less frequent injection over a daily oral – something that Leerink analysts, at least, are sceptical about. Jefferies was more optimistic, putting cabotegravir's non-risk adjusted peak sales at £1.8bn across treatment and Prep, not far off Glaxo's £2bn figure.

Merck and Gilead's recent push into the long-acting space might have left Glaxo feeling vindicated about its long-held stance here.

In March the HIV rivals signed a deal to combine Gilead's capsid inhibitor lenacapavir and Merck's nucleoside reverse transcriptase translocation inhibitor islatravir. The companies plan to develop a once-weekly oral, set to go into the clinic this year, and an injectable given once every three months, slated to start trials in 2023. Assuming all goes well, the projects could reach the market in 2025 and 2027 respectively.

Both companies are separately developing their assets for Prep.

These competitors are not to be sniffed at: Gilead dominates HIV treatment with its daily oral triplet Biktarvy, while its oral drug Truvada was the big force in Prep before its patent expired last year.

Ms Smith dismissed the potential threat from lenacapavir and islatravir. Her argument centred around the importance of including an integrase inhibitor like cabo. She also questioned whether a once-weekly oral would be preferable to a longer-acting injection. Issues with daily pills, such as fears around packets being discovered and a patient's HIV status being exposed, still applied with weekly tablets, she pointed out.

For the "new GSK" to succeed it needs its late-stage pipeline to deliver, and cabotegravir is a big part of that. With the company so far ahead, the long-acting HIV market is Glaxo's to lose.

Notable trials with Gilead's lenacapavir and Merck's islatravir			
Setting	**Dosing**	**Study details**	**Timing**
Lenacapavir + islatravir			
HIV treatment	Once-weekly oral	Ph2, TBC	To start H2 2021
HIV treatment	Once-monthly injectable	TBC	To start 2022
Lenacapavir			
Heavily treatment-experienced pts	Oral lead in then SC every 6 mo	Ph2/3 Capella	Positive data reported, filing due H2 2021
Treatment-naive HIV pts, combo with oral antiretroviral agents	Oral lead in then SC every 6 mo	Ph2 Calibrate	Data due H2 2021
Prep in men/trans/non-binary people who have sex with men	SC every 6 mo	Ph3 Purpose-2	Completes Jan 2024
Prep in young women	SC every 6 mo	Ph3	Due to start H2 2021
Islatravir			
Plus doravirine, switch study	Daily oral	Ph3 Illuminate Switch A	Data due H2 2021
Plus doravirine, switch study	Daily oral	Ph3 Illuminate Switch B	Data due H2 2021
Plus doravirine* in treatment-naive pts	Daily oral	Ph3 Illuminate Naive	Completes Nov 2023
Plus doravirine* in heavily treatment-experienced pts	Daily oral	Ph3 Illuminate HTE	Completes Jul 2024
Plus MK-8507*, switch study	Weekly oral	Ph2 Imagine	Completes Jul 2022
Prep in men/transgender women who have sex with men	Monthly oral	Ph3 3 Impower-024	Completes Jan 2024
Prep in women	Monthly oral	Ph3 Impower-022	Completes Jul 2024
Prep	Yearly implant	"Entering ph2"	Ph1 data presented at CROI in Mar 2021

**Doravirine (Pifeltro) and MK-8507 are non-nucleoside reverse transcriptase inhibitors. Source: Evaluate Pharma, clinicaltrials.gov & company releases.*

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