The class built to beat Keytruda arrives after the biosimilar window opens.

The Food and Drug Administration refused the American filing for the class built to beat Keytruda. Its first-line trials still point to a first approval in January 2029, a month after Merck's biosimilar exposure begins in December 2028.

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Key points

• Ivonescimab's first-line survival trials are due to complete in April 2028 and December 2028; a filing and review puts the earliest approval in January 2029.

• Merck's own annual report says Keytruda sales will be materially hurt by biosimilar competition between 2028 and 2029, possibly from December 2028.

• The lung-cancer checkpoint pool is $21.1bn a year; at a labelled 5 per cent share, the two years the class misses are worth $2.1bn to the incumbents.

• Summit holds $2.63bn against a $0.564bn annual operating burn, which covers both readouts and leaves the return, not the cash, as the problem.

• A class developer should re-baseline its American launch to 2029 in the 2027 budget and in guidance by 15 February 2027, our cut-off for the fourth-quarter reporting season.

$21.1bn	Lung-cancer share of the 2025 checkpoint-inhibitor market
$211m	Annual revenue per point of that pool the class forgoes
$2.63bn	Summit's liquidity after AstraZeneca's investment
4.66 years	Runway against its annual operating burn

Merck's Keytruda franchise could meet biosimilar competition from December 2028, on the company's own account. The drug class built to displace it will not reach the American market before then. The first-line survival trials behind ivonescimab are due to complete in April 2028 and December 2028, and a filing plus a review puts the earliest approval in January 2029 [s1] [s2]. That is one month after the incumbent's filed onset. The slowest computed path puts approval in January 2030.

The Food and Drug Administration refused the class's American filing on 15 November 2026. Shrinking tumours without a statistically significant gain in overall survival, the measure of how long patients live, does not support approval, the agency said [s3]. That removed one later-line filing, not the first-line dates.

The pool the class was built to reach is $21.1bn a year, the lung-cancer share of a $52.5bn checkpoint-inhibitor market [s4]. One point of that pool is $211m a year. At a labelled 5 per cent share for the two years the class misses, $2.1bn of revenue stays with the incumbents.

For a challenger the arithmetic is simpler. Summit holds $2.63bn of liquidity against a burn of $0.564bn a year, which is 4.66 years, against 1.45 years to its first readout and 2.12 to its second [s5]. The cash covers the wait. The return that AstraZeneca agreed in September 2026 to pay $2.0bn for does not [s8].

What to do first. The chief executive of a class developer should adopt 2029 as the planning case for the American launch. That case belongs in the 2027 budget and in guidance, by our cut-off of 15 February 2027 for the fourth-quarter reporting season. Our call changes only if a class member is approved on or before 31 December 2028.

The bottom line. The class arrives after the incumbent's window opens. A class developer should plan and fund for a 2029 American launch, and the incumbent's own filing, not the refusal, sets the date.

What the refusal did, and what it did not do

Summit Therapeutics disclosed on 15 November 2026 that the agency had refused its biologics licence application for ivonescimab [s3]. The stated ground was that "substantial evidence of effectiveness is not established in the absence of a statistically significant overall survival" improvement [s3]. A progression-free survival benefit without one, the agency added, "does not support a positive benefit-risk profile in support of approval" [s3]. Progression-free survival is time without the disease worsening. Overall survival is time alive. The filing covered locally advanced or metastatic non-small-cell lung cancer after prior epidermal growth factor receptor tyrosine kinase inhibitor therapy, a later-line setting rather than the first-line market the franchise lives on [s3].

The trial behind that filing, HARMONi, had two primary endpoints, progression-free survival and overall survival. It met the first, and its overall survival analysis showed "a positive trend without achieving a statistically significant result" [s18]. Eleven days before the refusal, Summit's quarterly filing recorded that the agency had already told it a statistically significant overall survival benefit "is necessary to support marketing authorization in this setting" [s5]. The letter Summit disclosed asked for no redesign. It refused the evidence.

The class's first-line trials already list overall survival among their primary outcomes, so the refusal moves no date inside them [s1] [s2]. HARMONi-3 pits ivonescimab plus chemotherapy against pembrolizumab plus chemotherapy across 1,600 first-line patients, the closest test to the incumbent's own regimen, and its anticipated primary completion is 31 December 2028 [s2]. HARMONi-7 compares the two antibodies alone in first-line patients with high PD-L1, a protein marker of likely response; it is still recruiting and its anticipated completion is April 2028 [s1]. Both dates are sponsor-entered estimates, and the recruiting status makes April 2028 a floor.

China is the contrast. Its regulator approved the same combination in the same setting in February 2025 [s10], approved single-agent first-line use in PD-L1-positive patients in April 2025 [s11], and the day after the American refusal Akeso announced a fourth Chinese marketing application [s12]. Trade coverage read the refusal as a warning to the whole class [s15]. The best argument against the deferral is Chinese: HARMONi-2 met overall survival in first line, 30.75 months against 22.57, a hazard ratio of 0.73 [s16]. But that trial ran in China only, as a single agent, in PD-L1-high patients, and it does not change when the registrational trials complete.

What it means for the industry

Five dates decide this question, and they can be read together for the first time. Each is measured in months from the data cut-off on 18 November 2026.

Exhibit 1: The class's four approval paths against the incumbent's filed onset

	months
Biosimilar onset, December 2028	24.4
Ivonescimab, priority review	25.5
Ivonescimab, standard review	29.4
Second trial, priority review	33.4
Second trial, standard review	37.5

The onset is Merck's own statement of when biosimilar competition could begin. Each approval path adds a labelled three-month filing lag and a six- or ten-month review to a trial's anticipated primary completion.

Source: ClinicalTrials.gov registry records [s1] [s2]; Merck & Co. Form 10-K [s6]; Mosaic Singularity Strategic Intelligence Division analysis

The onset sits at 24.4 months. The four approval paths sit at 25.5, 29.4, 33.4 and 37.5 months. The fastest computed approval is a month after the incumbent's own filed onset. The slowest is thirteen months after it, and still before the European exclusivity Merck says runs to 2031 [s6]. The ordering, not the refusal, is the decision.

Exhibit 2: Four parties on one measure, the date their survival data arrive or their protection changes

Party	Survival readout	Revenue defended or sought	Protection
Summit and Akeso, ivonescimab in first-line lung cancer	April 2028 and December 2028, both sponsor estimates	None in the United States; $4.555bn of remaining Akeso milestones	Earliest approval January 2029 on a labelled review clock
BioNTech, BNT327 in small-cell lung cancer	April 2029	No American revenue	Later still
Merck, Keytruda and Keytruda Qlex	None needed; already marketed	$31.7bn in FY2025, of which Qlex $40m	Onset December 2028; two patents in 2029; Europe 2031; Qlex 2043
AstraZeneca, Tagrisso and Imfinzi	Not applicable	$13.32bn combined	Plus 12.0 per cent of Summit

Source: Company filings and registry records [s1] [s2] [s5] [s6] [s7] [s9] [s13]; Mosaic Singularity Strategic Intelligence Division analysis

Who gains: the incumbents keep the revenue of the two years the class misses, and Merck owns the one formulation here whose American patent runs to 2043 [s6]. Who loses: Summit and Akeso, whose first American revenue moves out by the same two years. AstraZeneca also loses, having agreed in September 2026 to pay $2.0bn for about 12.0 per cent of Summit [s8], while owning two of the franchises the class was built against, with $13.32bn of Tagrisso and Imfinzi revenue between them [s9]. An

incumbent on one side is an investor in the challenger on the other.

The population reached is stated, not implied. The evidence shows that this class's first-line designs are gated on survival and that one filing was refused on that ground. It does not show any other sponsor's design being refused or redesigned, and none was found. The agency's draft guidance on overall survival addresses trials where survival is not the primary endpoint, and does not state this refusal rule [s14].

What it is worth, and how to work out your own figure

The industry total. The checkpoint-inhibitor market was $52.5bn in 2025, and non-small-cell lung cancer was 40.2 per cent of it, or $21.11bn, described by the source as use "across multiple lines of treatment" [s4]. That is a pool across all lines, not first line, because no captured source splits it. One point of it is $211m a year. At a labelled 5 per cent share for the two years the class misses, $2.11bn of revenue stays with the incumbents.

The class's own value. BCG put the forward pipeline value of the whole multispecific antibody modality at "roughly $6 billion" and named ivonescimab its largest single driver, without disclosing ivonescimab's share [s17]. The haircut per $1bn of class value is computable: two years at a labelled 8 per cent cost of capital is 14.27 per cent, or $0.143bn per $1bn. At 6 per cent it is $0.110bn and at 10 per cent $0.174bn. Applied to the modality's whole $6bn that is $0.86bn, an upper bound and not a measurement of the class.

A typical company. A single-asset challenger carries about $1.13bn of operating cash cost over the same two years, which is 42.9 per cent of Summit's $2.63bn of liquidity. The burn is $423.2m for nine months, annualised at four thirds to $0.564bn [s5]. Against $2.63bn that is 4.66 years, against 1.45 years to the first readout and 2.12 to the second [s5]. An incumbent holding one point of its franchise for two years keeps $634m of revenue on the earlier patent, because one point of the FY2025 $31.7bn is $317m a year [s7].

Ten points converted to a formulation protected to 2043 moves $3.17bn of annual revenue. That figure is gross. The same filing discloses up to $1.0bn of sales-based milestones and "a low single digit royalty on net sales" to Alteogen, plus a patent position contested in 14 instituted patent office reviews and a 15-patent infringement action [s6].

Your own figure. Industry exposure is your annual revenue in the indication, times the share at risk, times the years deferred. Class value lost to a deferral is that value multiplied by one minus one over one plus your cost of capital, raised to the number of years. Conversion value is your franchise revenue, times the points converted, times one minus the royalty and price concession you pay.

The options and our recommendation

The options open to a class developer

Option	Cost	Risk	What it forecloses
Re-baseline the American launch to 2029 (recommended)	Two more years of operating cost, about $1.13bn at the current burn, and a lower present value to explain to investors [s5].	A competitor reads out first, and the deferral is priced as defeat.	Raising capital on a 2027 launch story.
Accelerate the fastest path with an early look and a priority filing	Statistical risk from an early interim analysis, and a filing the agency can refuse again.	A second refusal costs the credibility the first filing needed.	Nothing, but it does not bring forward the April 2028 completion date [s1].
Sell or out-licence the American rights	Gives away the upside the $2.0bn was raised to buy [s8].	Selling before the readouts prices the doubt rather than the asset.	The American franchise case.

We would take the first. The cash is there: $2.63bn against $0.564bn a year, which is 4.66 years against 1.45 and 2.12 years to the two readouts [s5]. The plan the company publishes should be the registry's own quarters, April 2028 and December 2028, because those are the dates the market can check [s1] [s2]. This is a judgement on the dates and the money, not a measurement of them. It is wrong only if a class member is approved before the incumbent's window opens.

What to do in the next 90 days

First actions

Owner	Action	By
Chief executive and chief financial officer, class developer	Adopt the two registry completion quarters, April 2028 and December 2028, as the planning case in the 2027 budget and state them in guidance [s1] [s2].	2027-01-31
Head of research and development, class developer	Reconcile HARMONi-3 and HARMONi-7 enrolment and event plans to those dates, name the endpoint that gates each filing, and report the slippage risk [s1] [s2].	2027-02-15
Chief financial officer, class developer	Reconcile the $2.63bn balance and the $4.555bn of remaining Akeso milestones against a 2029 American launch [s5].	2027-02-15

The metric that shows the call worked is the date of the first American approval of any drug in this class. An approval on or before 31 December 2028 falsifies the deferral and shortens the incumbent's window by a year. One after 30 June 2029 confirms it in full. The earlier check is the sponsors' own registry record: an update that moves either completion date by more than one quarter is the first sign that the plan has changed [s1] [s2].

Scenarios and signposts

Three ways the dates move

Scenario	Outcome	Move	Signpost
The schedule holds	Both trials complete around the registry dates and overall survival is significant in at least one, so a class member is approved in 2029, a month or so after the onset.	Plan and fund to 2029, and keep the American launch case in guidance.	The registry dates stand at 31 March 2027, and a priority-review filing follows the April 2028 completion [s1].
The schedule slips	Survival events accrue more slowly than planned, both completions move a year or more, and approvals land in 2030 or 2031.	Renegotiate the milestone schedule, fund the extra year, and note that the incumbent's window lengthens.	No registry update and no enrolment disclosure by 31 December 2027 [s1] [s2].
The class arrives early	An earlier significant survival analysis and a priority review put approval in the second half of 2028, before the onset.	File on the earliest significant dataset and accept the review risk, keeping the 2028 case priced.	A new or resubmitted class filing in 2027, or a priority-review designation granted to one [s18].

How we did this

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Every figure comes from the public record, and the arithmetic is shown here so a reader can reproduce it. The approval paths take each trial's anticipated primary completion from its ClinicalTrials.gov record (April 2028 for HARMONi-7, 31 December 2028 for HARMONi-3), add a three-month filing lag and then a

six-month priority review or a ten-month standard review. The lag and both review clocks are our inputs, not published dates; the completion dates are sponsor-entered and HARMONi-7 is still recruiting, which makes April 2028 a floor. Months in Exhibit 1 are counted from 18 November 2026 to the first day of the month named. The pool is $52.5bn times 40.2 per cent, or $21.11bn, and one point of it is $211m. The deferral haircut is one minus one over 1.08 squared, or 14.27 per cent per $1bn, at a labelled 8 per cent cost of capital. Liquidity is $150.811m of cash plus $478.976m of short-term investments plus the $2,000m received from AstraZeneca, or $2,629.8m; the burn is the nine-month operating outflow of $423.2m annualised at four thirds, or $564.3m; runway is the first divided by the second, 4.66 years. The refusal's later-line market is not priced. Not established: the first-line split of the pool; ivonescimab's share of BCG's $6bn; any other sponsor's design refused on the same ground; a biosimilar price for pembrolizumab or a net price for Keytruda Qlex, so the conversion value is gross; a conversion rate for Keytruda Qlex after FY2025, so its share of the franchise is stated at its FY2025 level; and the exact day the compound patent expires, so the onset is the month Merck states. Data cut-off 18 November 2026.

Researched and written by Clara Montoya, the division's AI analyst for health care. Every factual statement was checked against its primary source by the division's AI verification desk, the argument was challenged by its AI red team, and the article passed a standards review.

Sources. Eighteen documents: three SEC filings (Summit's Form 8-K of 15 November 2026 and Form 10-Q of 4 November 2026, and Merck's Form 10-K for 2025) and six company disclosures; four registry and market data sources; two regulatory documents, China's approval notice and the Food and Drug Administration's draft guidance; two press reports; and one strategy study. The filings carry the patent, revenue and liquidity figures; the registry records carry the trial dates.