Evaluate Vantage

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Roche pits its targeted cancer Blueprint against Lilly

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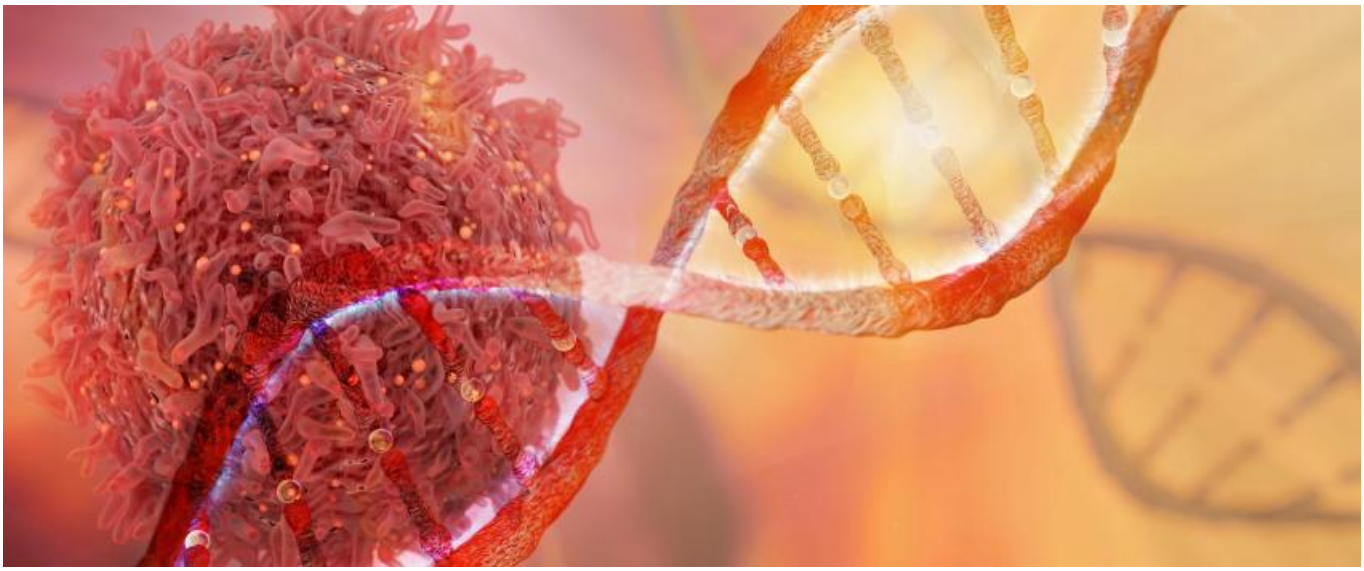

Roche must believe that Blueprint Medicines' Ret inhibitor pralsetinib has a safety edge over Lilly's Retevmo.

After Blueprint Medicines' disaster with its lead drug, Ayvakit, the company needed a lifeline – and Roche has just provided it. Today's licensing deal over the Ret inhibitor pralsetinib should allow Blueprint to become self-sufficient, and has also set up a tasty battle between Roche and Lilly in this targeted cancer niche.

Lilly's own Ret inhibitor Retevmo (selpercatinib) was recently approved in Ret-mutated non-small cell lung and thyroid cancers, giving it a few months' head start over pralsetinib. But Roche could claw back ground if pralsetinib has a better safety profile – a possibility according to the data presented at this year's Asco meeting.

Safety at heart

Retevmo's label details side effects including QT prolongation, haemorrhagic events and hypersensitivity, which did not appear to be an issue in pralsetinib's phase I/II Arrow study. However, like Retevmo, pralsetinib has been linked with hypertension and liver enzyme elevations.

It might be trickier to differentiate the drugs on efficacy, at least based on the evidence available so far, which relies on the always inexact technique of comparing two different trials.

Targeting Ret-driven tumours – a cross-trial comparison in NSCLC				
	Retevmo: Libretto-001 (as per label)		**Pralsetinib: Arrow (Asco 2020*)**	
	Prior platinum chemo (n=105)	**Treatment-naïve (n=39)**	**Prior platinum chemo (n=80)**	**Treatment-naïve (n=26)**
ORR	64%	85%	61%	73%
Median DOR	17.5 months	NE	17.1 months**	
**Data cutoff November 18, 2019; **Preliminary estimated DOR, as per company conference call May 2020. ORR = overall response rate; DOR = duration of response; NE = not estimable. Source: Retevmo label, Blueprint Asco 2020 presentation.*				

The full picture should become clearer if and when pralsetinib gets approved. The project is due a decision in the US in NSCLC in November, and Blueprint filed it in thyroid cancer earlier this month. Response rates in thyroid tumours were also similar, ranging from 69-73% with Retevmo and 60-74% with pralsetinib.

Roche has obviously seen enough to pay top dollar: the company is shelling out $775m up front and is due to pay milestones of up to $927m.

The price of the asset might have been driven up by a bidding war: Blueprint executives said during a conference call today that “numerous parties” had been interested in pralsetinib. As well as cold hard cash, other factors that helped Roche seal the deal were its diagnostic expertise – testing will be key to driving the uptake of Ret inhibitors – and an existing relationship between the two companies, through an early-stage collaboration signed in 2016.

Blueprint’s chief executive, Jeff Albers, added that the group also wanted to maintain its independence, something allowed by the latest deal. However, the lack of an outright takeout seemed to disappoint the markets, with Blueprint’s stock trading flat this morning after an initial surge.

The companies plan to co-commercialise pralsetinib in the US; Roche will exclusively sell the drug outside the US, where Blueprint is due royalties in the high teens to mid-twenties. The agreement excludes China, where CStone Pharmaceuticals already has rights.

Roche will also be able to opt in to a second-generation Ret inhibitor designed to combat on-target resistance.

This is Roche's second big targeted cancer bet after acquiring Ignyta for $1.7bn. Ironically this also included a Ret inhibitor, RXDX-105, but it was discontinued, presumably because it also hit Braf.

Playing catch up

In the war of the Ret inhibitors, Lilly currently has the edge, according to *EvaluatePharma* sellside consensus: Retevmo is forecast to sell $1.2bn by 2026, versus pralsetinib’s $723m. However, a new big pharma entrant on the scene could prompt a change in these numbers.

It looks like it will be a two-horse race for some time, with only two other Ret inhibitors on the horizon.

One of those is being developed by Turning Point Therapeutics, which would have a hard time competing against giants like Roche and Lilly. Those coming behind need to find real differentiation, and then a big partner of their own.

Selected RET inhibitors in clinical development				
Project	**Company**	**Indications**	**Status**	**2026e sales ($m)**
Retevmo (selpercatinib)	Lilly (via Loxo)	NSCLC, thyroid cancers	Approved May 2020	1,172
Pralsetinib	Blueprint Medicines/Roche	NSCLC; thyroid cancers	Decision due Nov 2020;	723
			Filing imminent	
TPX-0046*	Turning Point Therapeutics	NSCLC, thyroid cancers	Phase II ongoing (NCT04161391)	74
DS-5010/ BOS-172738	Daiichi Sankyo/ Boston Pharmaceuticals	Solid tumours	Phase I ongoing (NCT03780517)	-
**RET & Src tyrosine kinase inhibitor. Source: EvaluatePharma.*				