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Interview – Pieris blooms with Astra deal

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Pieris Pharmaceuticals might have only pushed one novel asset into the clinic, but that has not prevented it attracting a lot of big-name partners. Last week Astrazeneca joined Roche, Sanofi, Daiichi Sankyo and Servier in signing on the dotted line, this time for a deal over novel respiratory agents.

The Boston biotech is developing a novel class of recombinant lipocalins, and the $56m that Astra committed up front for a preclinical programme is a substantial bet on the platform's potential. The deal follows two other major transactions this year, and Pieris's chief executive, Stephen Yoder, tells *EP Vantage* that the company is mulling partnering another candidate, this time in immuno-oncology. "But don't expect another deal tomorrow along the lines of Astrazeneca," he says.

He also rules out raising money on the back of the 53% share price jump on the Astra deal, describing Pieris stock as "completely undervalued". The rise in the company's market cap last week almost matches the size of the Astra up-front fee; with a valuation of $158m and around $120m on the balance sheet, investors are showing reluctance to look much further than the company's cash.

"The deals are very de-risking. But ultimately it's about the data. And we believe 2017 will be a year to get two more products in the clinic, and 2018 will allow us to talk about some exciting data," says Mr Yoder, adding that Pieris is "well capitalised to do that without having to raise money".

Take a deep breath

With a bio-buck valuation of $2.1bn and an option to co-develop and co-commercialise in the US, the Astra agreement is the most expansive deal Pieris has closed to date. It includes four undisclosed projects but hinges mostly on PRS-060, an anticalin that targets IL-4r alpha.

Anticalins is the name Pieris has given its projects – the human proteins share features with monoclonal antibodies and can hit the same targets, but they are structurally much smaller. The company hopes that this will translate into important advantages, and in the case of PRS-060 this means inhaled delivery.

The antibody it is following is Sanofi and Regeneron's Dupixent, tipped as a future mega-blockbuster, which helps explain Astra's interest. Dupixent is expected to herald a step-change in the treatment of atopic dermatitis and, if impending trials read out positively, to emerge as the most promising antibody approach to uncontrolled asthma.

Several antibodies have been developed to target the inflammatory cytokines implicated in asthma – IL-4, IL-5 and IL-13 – but these have shown limited efficacy outside very severe forms of the disease. Dupixent, however, has shown potential in much broader populations, thanks seemingly to the specific receptor it targets.

"Following the breadcrumbs, IL-4 receptor alpha seems to be the cornerstone intervention point," Mr Yoder says. "We're going forward on that basis, and will fundamentally test the benefit of going local."

While Dupixent must be injected, as an inhaled therapy PRS-060 should be able to penetrate through to the sub-epithelial space, which is where Pieris believes that it needs to be to have an effect.

Phase I trials will start in the coming months with a nebulised form. The ability to work with an experienced respiratory partner to help push forward quickly with a dry-powder formulation and suitable device were huge motivations for doing a deal, Mr Yoder says.

Doubling down

The Astra agreement follows on the heels of Pierus's other major collaboration, with Servier in immuno-oncology.

That deal was announced in January, included $31m up front and covered undisclosed bispecific programmes, the lead being a dual checkpoint inhibitor called PRS-332. This novel fusion protein comprises an anti-PD-1 antibody and an anticalin against another undisclosed checkpoint target, which should move into the clinic by the end of 2018, Mr Yoder says.

Intriguingly, the company's lead I-O candidate was kept out of the deal. PRS-343 is a bispecific compound comprising a Her2-targeting antibody and a 4-1BB anticalin.

"We are very confident we have a clear line of sight to clinical proof of concept, and the network and the team to get us there without having to partner to improve speed and the probability of success" for PRS-343, Mr Yoder says.

The company intends to take this project all the way to market if the data allow, targeting the fraction of Her2-positive patients who fail on existing therapies.

The rationale is that causing 4-1BB activation – T-cell stimulation – at the tumour bed can provide a potent cancer-killing mode of action while avoiding distant toxicities. This is also the idea behind PRS-342, a bispecific again using a 4-1BB anticalin, but this time fused to a GPC3-targeting antibody. This is the project Mr Yoder says Pieris is considering partnering.

"Do we want to double down on that paradigm in our pipeline – which is taking Her2-positive tumours in one programme and GPC3 on the other – or would we be better thinking about a partnership to mitigate risk and focus our resources for additional proprietary development – so beyond just 4-1BB agonism alone? It's something we're still working through," he says.

With a healthy pile of cash in the bank, Mr Yoder has the luxury of making that decision in no particular hurry.

Pieris's pipeline - the most advanced candidates

Project	Pharma class	Target indications	Licensee (regions)	Up-front milestones
Phase II				
PRS-080	Hepcidin antagonist	Anaemia	ASKA (option for Japan and certain other Asian markets)	$3m
Phase I				
DS-9001	PCSK9 antagonist	Dyslipidaemia	Daiichi Sankyo (WW)	$6m
Preclinical				
PRS-343	Anti-HER2 MAb/4-1BB anticalin bispecific	Immuno-oncology	-	
PRS-342	Anti-GPC3 MAb/4-1BB anticalin bispecific	Immuno-oncology	-	
PRS-332	Anti-PD-1 MAb/checkpoint anticalin bispecifc	Immuno-oncology	Les Laboratoires Servier (WW ex-US)	$31m
PRS-060	IL-4 alpha receptor antagonist	Asthma	Astrazeneca (US)	$56m
PRS-110	c-Met antagonist	Oncology	Zydus Cadila (Emerging markets incl India)	n/d
Sanofi anticalin project	Anti-bacterial	P aeruginosa infections	Sanofi (WW)	$3m
Daiichi Sankyo anticalin project	Undisclosed	Undisclosed	Daiichi Sankyo (WW)	$5m
Roche anticalin project	Undisclosed	Immuno-oncology	Roche (WW)	$6m

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