Evaluate Vantage

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Lilly joins the cytokine gold rush with Armo deal

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Eli Lilly confirmed today that cytokines are the hottest area in immuno-oncology with a $1.6bn buyout of Armo Biosciences. Pegilodecakin's successful passage through an interim analysis in a phase III pancreatic cancer trial was enough for the Indiana-based company to pull the trigger, joining Bristol-Myers Squibb as a big pharma offering a billion-dollar payday for developers of cytokine cancer drugs.

Pegilodecakin is one of only two phase III oncology projects aimed at stimulating interleukins, and its intended use in hard-to-treat pancreatic disease means it has a low threshold for success. Lilly, meanwhile, has an oncology business but has missed out on the immuno-oncology wave – with this IL-10 it gains a near-market asset that could help it chase the likes of Merck & Co or Bristol.

The price? An Armo and a leggo

The $50-a-share takeout represents a big windfall for Armo's venture capital backers, whose average pre-IPO share value stood at $8.18; the group floated in January at $17 a share. Among those who may be kicking themselves for missing out on Armo is Celgene, which took part in a $67m series C crossover round last August, and Merck & Co, which licensed certain patents to Armo around pegylated human IL-10 polypeptide back in 2012.

Pegilodecakin, a pegylated recombinant human IL-10, is said to expand cytotoxic CD8-positive T cells (*Cytokine therapy focus – riding on Nektar's coattails, March 6, 2018*). Also known as AM0010, the compound is currently in the Sequoia trial in combination with the chemotherapy regimen Folfox against Folfox alone in pancreatic cancer patients who have progressed following treatment with a gemcitabine-based treatment.

A small phase I trial achieved an overall response rate of 16%, and median progression-free survival of 3.5 months and overall survival of 10.2 months. That compares very favourably to Folfox alone, with PFS of 1.7 months and OS of 4.3 months, or Ipsen's pancreatic cancer drug Onivyde, which has figures of 3.1 months for PFS and 6.1 month for OS.

The final phase III analysis in pancreatic cancer is not expected until 2020, and it is likely that the safety profile at the interim analysis gave Lilly enough comfort to sign a billion-dollar cheque. The bigger immediate catalyst with pegilodecakin is work in non-small cell lung cancer in combination with Merck's Keytruda (Cypress 1) and Bristol's Opdivo (Cypress 2), which began recruiting earlier this year.

These phase II trials are expected to generate early response data late this year. With Keytruda, it is a first-line test in patients with at least 50% PD-L1 expression, and with Opdivo, it is second-line in PD-1-naïve patients with less than 50% PD-L1 expression.

Lilly in I-O

Leerink analyst Michael Schmidt wrote in February that Armo will probably want to expand the Cypress programme to add its own PD-1 agent, AM0001. Now this is in Lilly's hands, however, a likelier outcome would be using Cypress to kickstart development of Lilly's own phase I PD-1/L1 assets.

Lilly's massive payout should lend some hope that other small drug developers working in the cytokine space will receive the same reward. Shares in Intrexon, Ziopharm and Celsion, listed small biotechs active in IL-10 & 12 signalling, were up 2%, 1% and 3%, respectively, in early trading today (see table below).

Selected oncology projects based on IL-10 & IL-12 signalling				
Project	**Company**	**Status**	**Mechanism**	**Detail**
AM0010 (pegilodecakin)	Armo Biosciences	Phase III	Pegylated rhIL-10	Armo claims that this stimulates expansion of CD8+ T cells
Ad-RTS-hIL-12	Ziopharm/Intrexon	Phase II	Intratumoural IL-12 gene therapy	Adenoviral vector controlled with Rheoswitch system by veledimex
GEN-1	Celsion	Phase II	IL-12 gene therapy	IL-12 DNA plasmid vector formed nanoparticles with a lipopolymeri delivery system
HemaMax	Neumedicines	Phase II	rhIL-12	Studies in acute radiation syndro well as CTCL
LipoVIL12	Regulon	Phase II	IL-12 gene therapy	Uses liposome encapsulation; no listed in pipeline
Tavokinogene telsaplasmid	Oncosec Medical	Phase II	IL-12 gene therapy	Delivered by electroporation via Immunopulse Keytruda combo
EMD 521873/M9241	Merck KGaA	Phase I	IL-12/Ab fusion protein	Ab portion meant to direct agent regions of tumour necrosis and apoptosis
AVR-ONC-01	Avrobio	Phase I	IL-12 gene therapy	Ex vivo, for AML; no longer listed pipeline
MK-1966	Merck & Co	Phase I	IL-10 downregulator	Aims to counteract suppressive e of IL-10, inhibiting Treg productio
mRNA-2905	Moderna/Astrazeneca	Preclinical	mRNA encoding IL-12	Potential for combo with checkpo inhibitor
AM0012	Armo Biosciences	Preclinical	rhIL-12	Potential for combo with AM0010
Immunalon	Provecs Medical	Preclinical	IL-2, IL-12 & 4-1BBL gene therapy	Intratumourally injected adenoviral vector

Source: EvaluatePharma.

More widely, Alkermes, whose IL-2/CD25 ALKS 4230 is in phase I development, has risen 5% today.

Lilly sat out the first round of immuno-oncology development and as a consequence has tumbled from the sixth-largest cancer company to number nine – and is headed for number 13 by 2024, in spite of having two relatively new cancer drugs on the market. Armo is a $1.6bn signal that it intends to reverse that slide.

An EP Vantage report on the cytokine space can be downloaded for free here: Cytokines emerge as 2018's immuno-oncology stars

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