Evaluate Vantage

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# After Immunogen and Sutro, Bristol buys into the folate story

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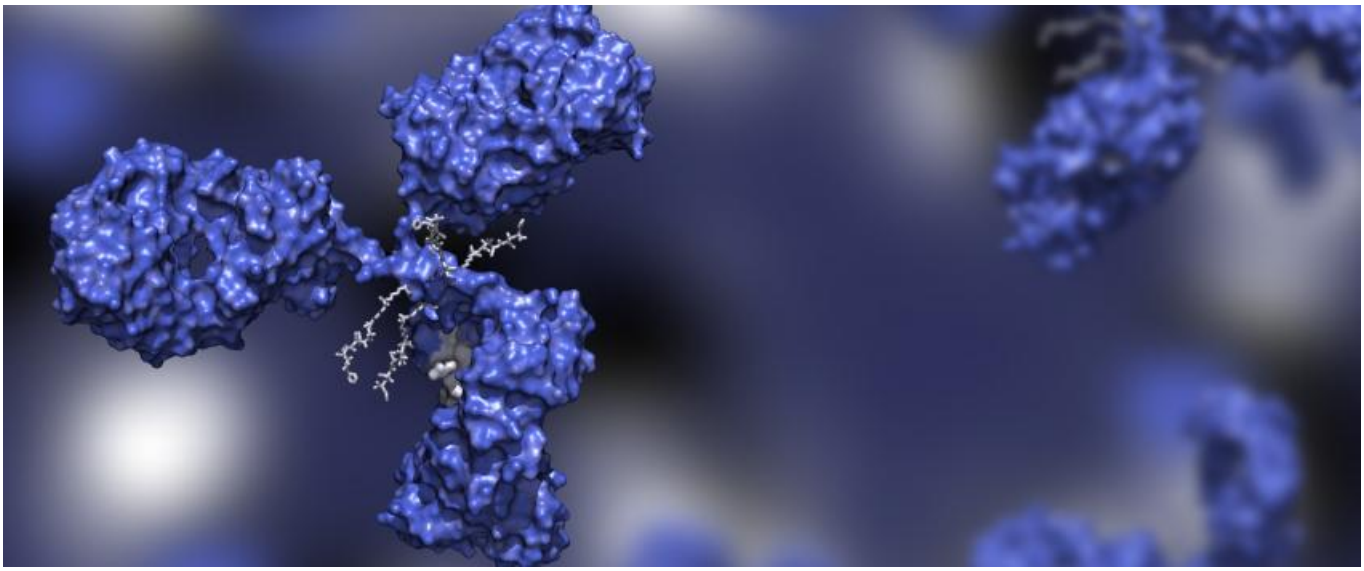

**The deal puts more support behind targeting folate receptor α, a long troubled target, with antibody-drug conjugates.**

Aduhelm's US approval sent Eisai's stock to an all-time high, so yesterday's deal with Bristol Myers Squibb is the icing on the cake for the Japanese group. The tie-up, covering the antibody-drug conjugate MORAb-202, features a $650m up-front fee.

Beyond the impressive-looking economics – MORAb-202 is still in early clinical development – industry watchers will note the asset's pharmacology of targeting folate receptor α. This mechanism had earlier disappointed, but recent successes with the ADC approach from Sutro and Immunogen have given it new life, and Bristol has clearly seen enough to buy in.

If ADCs really are the way to target FRα then the deal shows yet more support for this antibody-based modality. Indeed, a separate *Evaluate Vantage* analysis today ranks the Eisai/Bristol tie-up third among recent phase 1 deals by up-front amount; in first place is another ADC deal, Astrazeneca's licence to Daiichi Sankyo's DS-1062 for $1bn.

MORAb-202 has generated single-agent activity, specifically 10 remissions in 22 patients with refractory, FRα-positive solid tumours. Early trials are ongoing in Japan and the US, but the partners say they plan to speed into registrational studies as early as in 2022.

**New life**

Last year Sutro breathed life into targeting FRα, reporting a clinical success in ovarian cancer with STRO-002, its own ADC (*Sutro bucks the folate trend, December 4, 2020*).

The data were interesting partly because Sutro had not preselected FRα-expressing patients. Imunogen's ADC, mirvetuximab soravtansine, had failed in an all-comers ovarian cancer population in the Forward I trial, but the group pressed on into the Forward II study, in which patients' cancers had to express FRα.

At Asco this year Forward II's Avastin combo cohort yielded a 50% overall remission rate, comprising 33% in medium and 64% in high FRα expressers. Mirvetuximab now awaits a crucial catalyst, with results of its pivotal Soraya study, in FRα-high ovarian cancers, due in the fourth quarter.

Before that, of course, targeting FRα was firing blanks, with the abysmal failure of Endocyte's vintafolide, an

unusual small molecule bearing a toxic payload, perhaps the most notable. The project was filed in the EU as Vynfinit, for FRα-high ovarian cancer, but this was withdrawn.

| Selected folate receptor α (FRα) targeting projects | | | |
|---|---|---|---|
| **Project** | **Company** | **FRα-targeting modality** | **Trial detail** |
| *Phase 3* | | | |
| Mirvetuximab soravtansine | Immunogen | ADC | Soraya, in high FRα expression, reads out Q4 2021 (failed in all-comers) |
| *Phase 2* | | | |
| TPIV200 | Marker Therapeutics | Cancer vaccine | One ongoing trial (one terminated) |
| *Phase 1* | | | |
| STRO-002 | Sutro Biopharma | ADC | 32% ORR in 31 unselected ovarian cancer patients |
| MORAb-202 | Eisai/Bristol | ADC | Studies in Japan & US; registrational trials starting 2022 |
| MOv18 IgE/ IGEM-F | Epsilogen | MAb | Licensed from King's College; ph1 data at AACR 2020 |
| CT900/ BTG945/ ONX-0801 | Carrick Therapeutics | Thymidylate synthase inhibitor | Licensed from BTG; ph1 data at Asco 2020 |
| *Preclinical* | | | |
| EC2629 | Novartis | Small molecule-drug conjugate | NA |
| IMGN151 | Immunogen | Dual-epitope ADC | NA |
| *Discontinued* | | | |
| Farletuzumab/ MORAb-003 | Eisai | MAb | Failed ph3 trials in 2011 and 2013 |
| Vintafolide | Endocyte (now part of Novartis) | Small molecule-drug conjugate | Failed ph2 in 2014; EU filing withdrawn |
| *Source: EvaluatePharma. ADC = antibody-drug conjugate.* | | | |

Eisai too had an early setback, but the Bristol deal shows that the Japanese group learned from its mistakes.

In 2007 Eisai had acquired a private US biotech called Morphotek for $325m, in a move that brought with it assets including farletuzumab, a naked antibody against FRα. This project, also known as MORAb-003, failed a phase 3 trial in ovarian cancer five years later.

But Eisai persisted, jazzing up farletuzumab by conjugating it via a cathepsin-cleavable linker to its in-house anticancer agent eribulin, and thus turning it into the ADC today known as MORAb-202. This entered clinical development in 2017, and four years on, presumably having seen Sutro and Immunogen's ADC successes, Bristol signed on the dotted line.

Though the $650m Bristol has paid Eisai includes $200m earmarked for R&D, in return the Japan group retains some downstream economics. What cannot be denied is the support Bristol is throwing behind ADCs in general, and FRα in particular.

*This is an updated version of an earlier story, adding phase 1 data.*

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