Evaluate Vantage

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# The Sting is dead; long live the Sting

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## Yesterday's deal between GSK and Mersana threw the spotlight back on a forgotten oncology mechanism.

Given the previous failures of Sting agonists, yesterday's move by GSK for Mersana's XMT-2056 came as a surprise. But a look at the pipeline shows that Mersana is not alone in continuing to pursue this once-hot mechanism.

These contenders will have to hope that they can improve on the lacklustre efficacy that hit Merck & Co, and partners Novartis and Aduro; and some groups are taking interesting approaches to try and do just that.

**As easy as ADC?**

GSK already had a conventional small-molecule Sting agonist in the shape of GSK3745417. Yesterday's deal gave it an option over an antibody-drug conjugate targeting Her2 that has a Sting agonist payload. XMT-2056 is still preclinical, making GSK's $100m up-front payment all the more remarkable.

Of projects that have already reached the clinic, only Takeda appears to be trying something similar. The Japanese group's TAK-500 is an ADC hitting CCR2, a chemokine linked with various cancers, and delivering TAK-676, a Sting agonist that is also being trialled separately.

Codiak Biosciences is another company taking a novel tack: its exoSTING comprises exosomes loaded with a small-molecule Sting agonist, designed to allow delivery directly to antigen-presenting cells. The company reckons exoSTING is a hundredfold more potent than free Sting agonists while avoiding systemic exposure.

Codiak reported phase 1/2 single-agent data in June, and plans to take the agent into phase 2 in bladder cancer next year.

**Free Sting**

There are also plenty of groups continuing to look at free Sting. Of these, F-Star, which recently agreed to be bought by China's Sino Bio, claims that its candidate, SB 11285, is differentiated from the first generation as it is intravenously delivered, rather than being injected directly into a patient's tumour. This, the group says, will allow treatment of hard-to-reach cancers.

F-Star is due to report further data from a dose-escalation trial this year; whether SB 11285 will be a priority for the group's new owner is anybody's guess. The project originally came from Spring Bank, with which F-Star merged in 2020.

Aside from GSK and Takeda, some other big players still have an interest in Sting, including Bristol Myers Squibb, via its 2017 purchase of IFM Therapeutics. However, Abbvie has gone quiet on MAVU-104, the preclinical asset its picked up with Mavupharma in 2019.

GSK's latest foray into this mechanism shows that there could be life here, but this story could still have a sting in its tail.

| Sting pipeline | | | |
|---|---|---|---|
| **Project** | **Company** | **Description** | **Trial details** |
| ***Phase 1/2*** | | | |
| exoSTING | Codiak Biosciences | Exosomes loaded with small molecule Sting agonist | Ph1/2 monotherapy data in solid tumours reported, ph2 to start Q1 2023 |
| IMSA101 | Immunesensor Therapeutics | Intratumoral Sting agonist | NCT04020185 +/- checkpoint inhibitor in refractory cancers |
| ***Phase 1*** | | | |
| BI 1387446 | Boehringer Ingelheim | Intratumoral Sting agonist | NCT04147234 +/- BI 754091 (PD-1 inhibitor) in solid tumours |
| BMS-986301 | Bristol Myers Squibb | Intratumoral/IV Sting agonist | NCT03956680 +/- Opdivo + Yervoy in solid tumours |
| E7766 | Eisai | Macrocycle-bridged Sting agonist | Input-102 in bladder cancer withdrawn, Instal-101 monotherapy in solid tumours/lymphomas ongoing |
| GSK3745417 | GSK | IV Sting agonist | NCT03843359 +/- Jemperli in solid tumours; NCT05424380 monotherapy in AML/HR-MDS |
| ONO-7914 | Ono Pharmaceutical | Sting agonist | JRCT ID: jRCT2031210530 +/- Opdivo in solid tumours |
| SB 11285 | F-star Therapeutics | "Next-gen" IV Sting agonist | NCT04096638 +/- Tecentriq in solid tumours |
| TAK-676 | Takeda | Sting agonist | NCT04879849 & NCT04420884 +/- Keytruda in solid tumours |
| TAK-500 | Takeda | ADC comprising anti-CCR2 antibody & TAK-676 payload | NCT05070247 +/- Keytruda in solid tumours |
| ***Fallen by the wayside*** | | | |
| ADU-S100 | Novartis/Aduro | Intratumoral Sting agonist | Discontinued, Aduro became shell for Chinook Therapeutics |
| MK-1454 | Merck & Co | Intratumoral Sting agonist | Disappointed at Esmo 2018, presumed deprioritised |
| SYNB1891 | Synlogic | Synthetic biotic strain of *E coli Nissle* that produces cyclic di-AMP, stimulator of Sting pathway | Ph1 data presented 2021, no further studies planned |
| *Source: Evaluate Pharma & clinicaltrials.gov.* | | | |

*This table has been updated to include IMSA101.*

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