Tunable Drug Conjugates: A Differentiated Drug Conjugate Platform

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Abstract # 5153

We have innovated a family of novel targeting, linker and payload technologies called Tunable Drug Conjugates (TDCs) that differentiate from other Drug Conjugate approaches via a rapid payload release/rapid systemic clearance design to drive high payload localizations within tumor cells while minimizing toxicities to patients and enabling safer drug development. TDCs use proprietary linker and payload chemistries designed to drive highly-tunable biodistribution and rapid payload release with rapid systemic clearance after internalization and within the necrotic microenvironment of tumors. Payload Cassette cell consistent linker and payload chemistries allow for high degree of differentiation between different cell types that work together synergistically to kill cancer cells.

Another technology - our Novel Domain-Domain (D-D) linking capability provides a proprietary means of specifically targeting a broad array of cell surface receptors while maintaining the rapid clearance characteristics and 1/2 measured in hours (rather than days) for the traditional ADCs. We have validated the TDC technology via imaging, cellular and in vivo xenograft studies.

SiLinkers Demonstrate Rapid Release of Payload after Internalization

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In Vitro Validation of SiLinker and PC Platform

- **Blocking of cellular effects in the presence of several folic acid analogs:**, Folic acid-based linker chemistries endosomal labile SiLinker prototype displays high FR blocking, suggesting that an optimal concentration of Folate-targeted DCs provides high FR blocking and superior tumor/blood ratios enabling clinical management of side effects through dose and schedule adjustments, thereby enhancing safety.

- **Folate payload-release enhancing tumor residence time**, Folate-based payload release protocols allow for tailoring of TDC payload release.

- **Folate-based payload-release enabling broad release of both mixed payloads and high stoichiometric Payload Cassettes ratios**, Folate-based payload release protocols have been validated with strong in vivo efficacy data using Folate targeting SiLinkers.

Acknowledgments: Images used in this poster were generated at The Light Microscopy Facility, The Max Planck Florida Institute.