R. Shrivastava: A. Employment (full or part-time); Significant; Curadev pharma Pvt Ltd. M. Banerjee: A. Employment (full or part-time); Significant; Curadev pharma Pvt Ltd. D. Pryde: A. Employment (full or part-time); Significant; Curadev pharma Pvt Ltd. S. Middya: A. Employment (full or part-time); Significant; Curadev pharma Pvt Ltd. S. Mane: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. M. Mansuri: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. D. Yadav: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. N. Mane: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. R. Ghosh: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. A. Gautam: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. M. Padaliya: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. S. Basu: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. A. Surya: A. Employment (full or part-time); Significant; Curadev Pharma Pvt Ltd. E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; Curadev Pharma Pvt Ltd.

PO1.09  
**CRD3874-SI: A NOVEL ALLOSTERIC STING AGONIST WITH HIGH SYSTEMIC TOLERABILITY**

1SK Middya*, 1M Banerjee, 1R Shrivastava, 1A Middya, 1N Mane, 1N Rawat, 1T Soran, 1D Chakraborty, 1R Ghosh, 1R Mansuri, 1D Yadav, 1A Gautam, 1K Punia, 1D Pryde, 1S Basu, 1F Sónego, 1G Martin, 1K Thiam, 1C Kelly, 1A Surya. 1Curadev Pharma, Noida, India; 2Curadev Pharma, Sandwich, UK; 3genOway, Lyon, France; 4Memorial Sloan Kettering Cancer Center, New York, NY, USA

10.1136/jitc-2024-ITOC10.19

**Background**  
STING activation by natural and targeted competitive ligands leads to the generation of Type 1 interferons as well as pyroptosis and autophagy of the cells expressing STING causing runaway inflammation. This overt inflammation is due to STING’s newly discovered proton channel activity. STING agonists tested in the clinic thus far have shown limited systemic tolerability and also a tendency to kill the very immune cells that they are designed to activate. CRD3874 is a novel allosteric small-molecule human STING agonist with a unique binding mode that activates canonical STING activation by natural and targeted competitors. Transmembrane proteins such as PD-(L)1, CD3 ε, CD28, HER2 represent the most common targets. Their binding kinetics are influenced by neighboring coreceptors as well as by their density and mobility within the membrane. Preserving the high efficacy of a STING agonist while demonstrating systemic safety is unique to CRD3874-SI.

**Conclusions**  
CRD3874-SI is a systemically administered novel allosteric STING agonist with promising single agent activity and an excellent IV safety profile. An investigator sponsored FIH Phase 1 trial with CRD3874-SI has been initiated at Memorial Sloan Kettering, NY, in sarcoma, MCC patients under the supervision of Dr. Ciara Kelly (NCT06021626).

S.K. Middya: A. Employment (full or part-time); Significant; Curadev Pharma. M. Banerjee: A. Employment (full or part-time); Significant; Curadev Pharma. R. Shrivastava: A. Employment (full or part-time); Significant; Curadev Pharma. A. Middya: A. Employment (full or part-time); Significant; Curadev Pharma. N. Mane: A. Employment (full or part-time); Significant; Curadev Pharma. N. Rawat: A. Employment (full or part-time); Significant; Curadev Pharma. T. Soran: A. Employment (full or part-time); Significant; Curadev Pharma. D. Chakraborty: A. Employment (full or part-time); Significant; Curadev Pharma. R. Ghosh: A. Employment (full or part-time); Significant; Curadev Pharma. R. Mansuri: A. Employment (full or part-time); Significant; Curadev Pharma. D. Yadav: A. Employment (full or part-time); Significant; Curadev Pharma. K. Punia: A. Employment (full or part-time); Significant; Curadev Pharma. A. Gautam: A. Employment (full or part-time); Significant; Curadev Pharma.

PO1.10  
**REAL-TIME INTERACTION CYTOMETRY REVEALS DIFFERENT BINDING KINETICS OF ANTIBODIES TARGETING MEMBRANE PROTEINS ON FIXED VERSUS LIVING CELLS**

V Hafner, A Marszal, U Rant, N Matscheko. Dynamic Biosensors GmbH, München, Germany

10.1136/jitc-2024-ITOC10.20

**Background**  
The field of therapeutic antibody development has witnessed significant growth since the introduction of the first-therapeutic monoclonal anti-CD3 antibody, Muronomab, in 1986 [1]. Numerous investigations indicate that the dissociation rate of antibodies plays a predictive role in their clinical effectiveness [2, 3]. Therefore, it is imperative to conduct kinetic rate analyses to enhance the efficacy and safety of these therapeutic agents. Transmembrane proteins such as PD-(L)1, CD3 or HER2 represent the most common targets. Their binding kinetics are influenced by neighboring coreceptors as well as by their density and mobility within the membrane. Preserving these target molecules within their native cell membrane benefit in multiple murine tumor models. Intravenous infusion of the compound was well tolerated at high doses in the primary GLP study and caused exposure dependent increases in cytokines. This profile of retaining the high efficacy of a STING agonist while demonstrating systemic safety is unique to CRD3874-SI.