



## **URGENT PRESIDENTIAL STATEMENT FROM THE JAPAN SARCOMA ASSOCIATION (JSA):**

### **Celebrating the Breakthrough Success of YAP/TAZ-TEAD Inhibitors at ASCO2026 and Welcoming the Era of Cancer Mechanomedicine**

On the historic occasion of the 2026 American Society of Clinical Oncology (ASCO2026) Annual Meeting, opening today, the clinical trial (Phase 2) of revolutionary **YAP/TAZ-TEAD inhibitors** has demonstrated unprecedented, landmark success in halting cancer metastasis. The Japan Sarcoma Association (JSA) officially celebrates this monumental achievement and proudly declares the dawn of a new era: where "mechanobiology" (cellular force) has transitioned from fundamental physics to frontline, life-saving oncology therapeutics for rare soft-tissue sarcomas and advanced malignancies.

It was Japan's foundational biochemical research that first hoisted the flag on this undiscovered continent, proving that physical and mechanical properties dictate cellular destiny. In cell biology, the control of cell movement was historically biased toward chemical signaling on the motor-side myosin. Defying that contemporary mainstream, we isolated, identified, and named "Calponin" for the first time in the world in 1986 as the essential molecular brake on the actin side.

Forty years later, this fundamental biochemical seed has beautifully converged into an unbroken international chain of scientific translation. Prof. Pekka Lappalainen's laboratory (University of Helsinki) structurally defined Calponin as the "mechanical destiny switch" of cell tension. This was further solidified by the landmark publication in January 2025 (Nguyen et al.), which established the definitive molecular link proving that Calponin 3 remodeling directly triggers the nuclear translocation of YAP1. Ultimately, this biophysical force propagates into the **YAP/TAZ-TEAD transcriptional axis**—elucidated by Prof. Kun-Liang Guan (UCSD/Fudan University)—unleashing the genetic programs of metastasis. The newly validated TEAD inhibitors have demonstrated a stunning **86% disease control rate and a 32% objective response rate** in refractory tumors, successfully shutting down metastasis at the root and demonstrating the pinnacle of clinical translation at ASCO2026.



Following these definitive breakthroughs, the criteria for cancer mechanobiology has officially shifted toward real-world translational outcomes. Serving as the presidential body representing sarcoma academia in Japan and backed by the intensive clinical sarcoma bioresource at Kameda Medical Center, the JSA is fully prepared to act as the ultimate translational anchor. We formally invite global pharmaceutical innovators and structural biologists to leverage our resources. Together, we will complete this historic cross-continental relay race, transforming the mechanical physical forces of cancer into the ultimate therapeutic target.

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