

OBR Interview with Christian Itin, PhD, CEO, Micromet, Inc.



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Micromet, Inc (Nasdaq: MITI), a Bethesda, Maryland-based biotechnology company, is putting novel concepts in immune therapy to work in oncology. Founded in 1993 as Micromet AG in Munich, Germany and incorporated in the US as Micromet Inc. in 2006, Micromet has developed a treatment approach that empowers the body's own immune system to fight cancer. Its proprietary BiTE[®] antibody technology ("bi-specific T cell engagers") leverages the cytotoxicity

of T cells by mediating contact between the T cells and the cancer cells, thereby inducing an immunological synapse between the two. As a result, the T cells inject a toxic cocktail into the cancer cells and thereby eradicate not only the primary tumor but also micrometastases—the seeds for future metastatic growth.

Several novel BiTE[®] compounds are producing impressive results in preclinical models and early clinical trials. The lead compound, blinatumomab (MT103/MEDI-538), is in Phase 2 trials in heavily pretreated acute lymphoblastic leukemia and non-Hodgkin's lymphoma patients. On June 5, at the International Conference on Malignant Lymphomas (ICML) in Lugano, Switzerland, Micromet reported a 100% response rate (partial and complete) and durable remissions among lymphoma patients in the highest dose cohort (0.06 mg/m²/day).

The MT110 compound is entering Phase 1 trials in solid tumors. Other compounds in the pipeline are aimed at inhibiting angiogenesis, reducing inflammation and treating autoimmune disease. The following interview was conducted at the American Association of Cancer Research's 99th Annual Meeting, where Micromet showcased its data.

OBR: *How and why was Micromet founded?*

CI: Micromet was founded in 1993 as a spinoff of the University of Munich. Gert Riethmüller, MD, the former head of the Institute of Immunology in Munich, was a visionary who wanted to tackle the "elusive state" of cancer, i.e., those tumor cells that current treatments miss. This concept—micrometastasis—led to the name of our company. I came to Micromet in 1999, largely because of Patrick Baeuerle, PhD, its chief scientific officer, and because of an early glimpse at a new class of therapeutic antibodies, which became the BiTE[®] antibodies. Patrick is one of the most published investigators in his field and he was very enthusiastic about Micromet's approach, which was to enable the immune system to recognize and destroy tumor cells. Our R&D efforts are now being realized.

OBR: *What was the rationale behind the development of the BiTE[®] antibody technology platform?*

CI: With conventional antibodies, we are failing to enlist the most potent part of the immune

system, the T cells. The simple idea behind BiTE[®] is to make a patient's T cells capable of seeing the cancer. With the BiTE[®] antibody technology, we developed an adaptor, so to speak, that links the T cell and the tumor cell and activates the T cell.

T cells are on a constant search and patrol mission through the body and with the help of BiTE[®] antibodies they can recognize and attack any tumor cell they encounter. It is absolutely selective for the tumor, and it goes after rapidly growing as well as disseminating tumors (i.e., micrometastases). Remarkably, when T cells meet larger numbers of tumor cells they can get into serial killing mode, start to multiply and form an army of T cells that can take on even large tumor masses.

OBR: *How powerful are the antitumor effects with these novel compounds?*

CI: There are no other cytotoxic or biologic agents that come close to this level of potency, and in contrast to chemotherapy, there are no

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damaging bystander effects. We get very high antitumor activity at incredibly low doses. For example, in lymphoma, compared with standard therapy we need several thousand-times less drug than with a conventional antibody.

OBR: *How is the drug delivered, and what is the treatment regimen?*

CI: The T cells obviously need to scan the entire body, and this ultimately takes several weeks. Typically, we administer the drug for 4 to 8 weeks. We have observed responses in 4 weeks—and with an additional 4 weeks we have managed to convert some partial responses to complete responses. Complete responders are offered another 4 weeks of “consolidation” therapy to give the T cells more time to find the last tumor cell. When the patient progresses, we think we can retreat with the same drug. Currently the treatment is administered with a pump the size of a Blackberry™ that continuously delivers the drug into the blood stream. In the future, we expect to use subcutaneous delivery, much like diabetics receive insulin. We have successfully tested this in primates and we envision going forward with this convenient delivery mode.

OBR: *What are your leading compounds?*

CI: From our BiTE® drug development platform, our most advanced product is MT103/MEDI-538, now known as blinatumomab. The target antigen of this drug is CD19, which is present on all leukemia and non-Hodgkin’s lymphoma cells. Next is MT110, which targets the EpCAM antigen that is expressed in 85% of all solid tumors. Two additional BiTE® antibodies are in preclinical development. We also have other novel agents, including the recombinant humanized IgG1 monoclonal antibody D93, which inhibits angiogenesis, cell growth, and metastasis by targeting cleaved collagen; and adecatumumab, an antibody also targeting EpCAM-expressing tumors.

OBR: *What data did you report at the AACR and ICML?*

CI: Our reports at the AACR showed the depth of what we can do with this platform.

We showed that we can re-engineer trastuzumab, cetuximab, and panitumumab to convert them to highly active BiTE® antibodies. We can essentially teach commercial antibodies new tricks—how to recruit T cells for a very selective and effective lysis of target cells. At ICML in Switzerland, we reported clinical data on MT103/MEDI-538 showing responses in seven out of seven patients at the highest dose level—and these patients had already received a median of three, and up to 12, previous lines of therapy.

OBR: *What clinical trials are underway?*

CI: MT103/MEDI-538 is in Phase 1 and 2 trials in leukemia and non-Hodgkin’s lymphoma and we just announced that MT110, the second BiTE® antibody, is beginning a Phase 1 trial in patients with gastrointestinal cancer and lung cancer.

OBR: *Have you begun partnering with other pharma?*

CI: We have various collaborations with AstraZeneca/MedImmune, Merck Serono, and Nycomed. In addition, we have licensed monoclonal antibodies to Tracoon and Eisai.

OBR: *Would you like to make a final point regarding your business vision and strategy?*

CI: Micromet takes a balanced view with regard to partnering on the one hand and retaining rights on the other. This approach has served us well and this is our strategy going forward. We are at a very exciting point. After a long journey we have demonstrated that our novel approach works clinically and is broadly applicable. We believe we have a great opportunity to have an impact on a broad range of cancer indications.

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