Alpha particles from the decay of Thorium-227 kill the tumor cells by inducing DNA double strand breaks which cannot be easily repaired.2,3

1. Thorium-227 is a powerful radionuclide that releases energy-rich alpha radiation. When bound via a chelator to a tumor-targeting molecule, such as an antibody, Thorium-227 can be carried directly to the tumor.1

2. After injection, the tumor-targeting molecule recognizes and binds to specific proteins on the surface of tumor cells. The TTC accumulates at the tumor.2

3. Alpha particles from the decay of Thorium-227 kill the tumor cells by inducing DNA double strand breaks which cannot be easily repaired.2,3

4. As alpha particles only penetrate two to ten cell layers, limited damage is caused to the surrounding tissue. TTCs therefore allow for highly-targeted tumor damage.4

*The TTC technology has yet to be validated in clinical development. The depicted pathways and research approaches are investigational and have not been approved for market use.
Two potential mechanisms of action
There are two potential mechanisms of action thought to play a role in the anti-tumor effect of TTCs:

- **Direct killing of tumor cells as a result of alpha particles inducing clusters of DNA double strand breaks.**
- **Release of factors from the tumor which could stimulate and activate components of the body’s own immune system.**

Emerging TTC platform:
Using a variety of tumor-targeting molecules such as antibodies, conjugates are in development to specifically target different tumor types including breast, prostate, and hematologic cancers as well as mesothelioma. Bayer has three TTC compounds now in the clinic, with another in preclinical development.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>In development for patients with</th>
<th>Clinical trial status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PSMA-TTC</strong> (BAY 2315497)</td>
<td>Metastatic castration-resistant prostate cancer (mCRPC)</td>
<td>Phase 1 clinical trial in progress in patients with mCRPC (NCT03724747)⁶</td>
</tr>
<tr>
<td><strong>MSLN-TTC</strong> (BAY 2287411)</td>
<td>A number of solid tumors expressing mesothelin (MSLN), including mesothelioma and some pancreatic and ovarian cancers</td>
<td>Phase 1 clinical trial in progress in patients with solid tumors known to express mesothelin (NCT03507452)⁷</td>
</tr>
<tr>
<td><strong>CD22-TTC</strong> (BAY 1862864)</td>
<td>Hematologic cancers</td>
<td>Phase 1 clinical trial in progress in patients with relapsed or refractory CD22-positive non-Hodgkin’s lymphoma (NCT02581878)⁸</td>
</tr>
<tr>
<td><strong>HER2-TTC</strong></td>
<td>A number of solid tumors expressing HER2 including breast, gastric and gastric-esophageal cancers</td>
<td>Preclinical development</td>
</tr>
</tbody>
</table>

*The TTC technology has yet to be validated in clinical development. The depicted pathways and research approaches are investigational and have not been approved for market use.

References