Macrophages and dendritic cells are among the immune system’s first responders:
- Macrophages are the most abundant immune cells in tumors
- Macrophages either phagocytose or are cytotoxic to cancer cells
- Dendritic cells are key players in the recruitment, activation and presentation of cancer antigens to the adaptive immune system

CD47 is an important checkpoint of innate immunity and its inhibition is key to driving and maximizing innate immune cell activity against tumors

AO-176 is a highly differentiated, humanized anti-CD47 IgG2 antibody with unique characteristics:
- Like other CD47 blocking antibodies, AO-176 blocks the “don't eat me” signal and induces phagocytosis of tumor cells
- Added Highly DifferenCiatiOnal Characteristics of AO-176:
  - Preferentially binds and kills tumor versus normal cells
  - Binds in a context dependent manner to CD47 complexed with β1-integrin
  - Negligibly binds RBCs as they do not express β1-integrin
  - Shows enhanced binding at acidic pH (ex. acidic microenvironment in tumors)

AO-176 exhibits single agent and combination activity in hematologic models:
- **In vitro activity**:
  - AO-176, as a single agent, promotes phagocytosis and/or killing of hematologic tumor cell lines
    - Multiple myeloma
    - Acute myeloid leukemia
    - Non-Hodgkin’s lymphoma
    - T cell leukemia
  - AO-176 in combination with rituximab, daratumumab or bortezomib enhances phagocytosis and/or killing of lymphoma and multiple myeloma cells
- **In vivo activity**:
  - AO-176 mediates potent single agent tumor growth inhibition of hematologic tumors including multiple myeloma and lymphoma
  - AO-176 in combination with bortezomib elicits complete tumor regression
  - Complete responses in 70-100% of animals treated
  - Improves overall survival up to 160 days
  - AO-176 exhibits combination activity with daratumumab

AO-176 is in an ongoing Phase 1 clinical trial (NCT03383498).

**AO-176: A Highly Differentiated Next-generation Humanized Anti-CD47 mAb**

**AO-176 Induces Single Agent Phagocytosis and Killing in Multiple Tumor Types**

**AO-176 Induces Phagocytosis and Killing of Multiple Myeloma Cell Lines in vitro**

**AO-176 CombiNeS with daratumumab to Inhibit Tumor Growth in MM.1S**

AO-176 is an anti-CD47 antibody with direct killing and immune stimulating activity that is highly differentiated from current clinical agents targeting the CD47 axis:
- AO-176 is the first anti-CD47 agent that targets CD47 in a context dependent manner complexed with integrin β1.
- AO-176 is the first anti-CD47 mAb that exhibits complete tumor regression and long-term survival in combination with bortezomib in multiple myeloma xenografts.
- AO-176 shows in vitro and in vivo combination activity with daratumumab in multiple myeloma models.
- AO-176 is currently being evaluated in a Phase 1 clinical trial (NCT033834984) for the treatment of patients with select solid tumors and is a good candidate for clinical development in hematological indications.