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**REFERENCE NUMBER**
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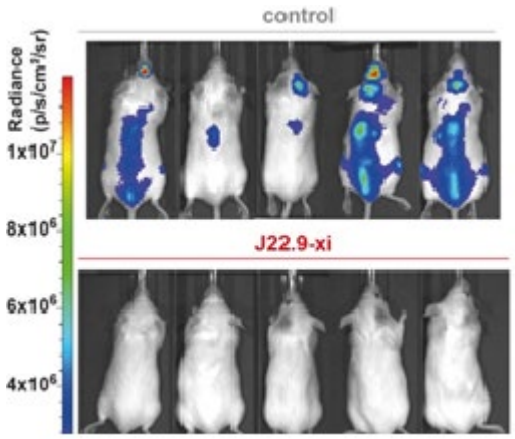
# PLASMA CELL-SPECIFIC ANTIBODIES TARGETING BCMA FOR THE TREATMENT OF MULTIPLE MYELOMA AND AUTOIMMUNE DISEASES

## CHALLENGE

The specific targeting of malignant blood cells or autoreactive plasma cells with minimal effects on other cell types is still a challenge in the therapy of haematological malignancies or autoimmune diseases. Multiple Myeloma (MM), a cancer of plasma cells accumulating in the bone marrow, accounts for approximately 1% of all neoplasms worldwide and for around 2% of all cancer related deaths. The median survival with conventional therapy is 3 to 4 years. Current treatment options are high-dose chemotherapy and autologous hematopoietic stem cell transplantation. MM is still incurable and all available treatment options display serious side effects. Therefore, the need for more effective and safer treatments is considerable. In a variety of autoimmune diseases, the pathogenic role of long-lived autoreactive plasma cells and B cell growth factors such as BAFF is well-known. Strategies to target these pathways may open new ways of treatment in this disease area.




*J22.9-xi significantly decreases tumor burden and prolongs survival.*

## TECHNOLOGY DESCRIPTION

The technology comprises a portfolio of therapeutic antibodies targeting BCMA (B cell maturation antigen, CD269). BCMA is highly expressed in multiple myeloma and on plasma cells but is absent from naïve, germinal center and memory B cells. The B cell growth factors APRIL and BAFF are endogenous ligands and BCMA signaling is important for survival of long-lived plasma cells. A human-mouse chimeric antibody (J22.9-xi) was developed which specifically binds the extracellular domain of human BCMA with a remarkably high affinity. J22.9-xi effectively depletes MM cells in vitro and in vivo. In a xenograft mouse model, tumor burden was decreased significantly and survival was prolonged substantially. Based on the X-ray structure of BCMA in complex with J22.9-xi Fab, several humanized variants were synthesized and characterized. The humanized variants retain high affinity towards BCMA and are optimized regarding removal of potential post-translational modification sites. Through the effective blocking of APRIL and BAFF binding, the antibodies do also have the potential to address autoimmune disorders.

## COMMERCIAL OPPORTUNITY

Available for licensing or collaboration

## PATENT SITUATION

Patent application pending: PCT/EP2015/059562 (priority of 30.4.2014)
Patent applications pending: US, EP, JP, CA, AU (from WO2014068079, priority of 1.11.2012)

## FURTHER READING

Mol Oncol. 2015 Mar 31. "Potent anti-tumor response by targeting B cell maturation antigen (BCMA) in a mouse model of multiple myeloma".

MAX DELBRÜCK CENTER

**Ascenion GmbH**
Herzogstraße 64
D-80803 München
info@ascenion.de
www.ascenion.de

**Licensing Contact**
Céline Christiansen, M.Sc.
Technology Scout
T: +49 30 2576-4931
christiansen@ascenion.de