**Blocking Antibodies Against Human CD47 for Cancer Immunotherapeutics**

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**BACKGROUND**

Rationale for anti-CD47 antibodies as cancer therapeutics:
- CD47 is ubiquitously expressed on normal cells but highly expressed on various cancer cells (e.g., AML, NHL, solid tumors such as WCLC).
- CD47 acts as a “Don’t eat me” signal and cancer cells escape phagocytosis via CD47 binding to SIRPα on macrophages and deliver an inhibitory signal to macrophages.
- Blocking CD47-SIRPα interactions with antibodies can abolish the “Don’t eat me” signal and lead to enhanced phagocytosis of tumor cells.
- The phagocytosed tumor cells are processed and tumor associated antigens are presented by these APCs on their MHC and activate tumor-antigen-specific T cells.

**APPROACHES**

- Generation of mouse anti-human CD47 hybridoma antibodies through our Therapeutic Antibody Discovery Platform.
- Screen for mAbs specifically binding to CD47 expressing cells.
- Screen for mAbs blocking CD47/SIRPα interactions.
- Determine the effect of anti-CD47 blocking antibodies on phagocytosis of tumor cells.
- Evaluate the effect of anti-CD47 mAbs on hemagglutination.
- Antibody humanization.

**RESULTS**

**Anti-human CD47 Antibody Binding to Plate-bound Human CD47**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Binding at 0.25g/ml</th>
<th>Binding at 1g/ml</th>
<th>Binding at 5g/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB6.12</td>
<td>0.12</td>
<td>0.16</td>
<td>0.19</td>
</tr>
</tbody>
</table>

**Blocking SIRPα Binding to Human CD47 on CHO Cells by Anti-CD47 Chimeric Antibodies**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>IC50 (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB6.12</td>
<td>0.59</td>
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</tbody>
</table>

**Chimeric Anti-CD47 Antibodies Enhance Macrophage Phagocytosis of B Lymphoma Cell**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>IC50 (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB6.12</td>
<td>1.69</td>
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**SUMMARY**

- We have identified a panel of high affinity anti-human CD47 monoclonal antibodies via mouse hybridoma approach.
- These anti-CD47 antibodies bind to human CD47 with a range of affinities and block CD47/SIRPα interaction.
- The lead anti-CD47 mAbs showed robust activities in stimulating macrophage-mediated phagocytosis of cancer cells.
- The lead anti-CD47 mAbs did not induce significant hemagglutination of red blood cells and may have better safety profiles.
- Lead antibodies have been humanized and are moving into preclinical evaluations.
- Anti-CD47 mAb bispecific antibodies have been generated to target tumor microenvironment.
- Anti-CD47 “Pro-drug” has been generated to reduce nonspecific binding.

*This program is available for licensing and collaboration. For further information, please contact us at hlin@accurusbio.com or richard@accurusbio.com