Tobemstomig (PD-1 x LAG3)

Bispecific antibody targeting PD-1 and LAG-3
Tobemstomig – Molecule summary and MoA

Bispecific antibody targeting PD-1 and LAG-3

**Molecule summary**

- **Drug Overview**
  - **Compound**: RG6139
  - **Other names**: Tobemstomig, PD-1xLAG-3, RO7247669
  - **Molecule type**: Bispecific antibody
  - **MOA**: Binds to two co-inhibitory checkpoint receptors, PD-1 and LAG-3, to reinvigorate dysfunctional T-cells enabling them to attack the tumor. Tobemstomig has a 10-20 fold higher affinity for PD-1 than for LAG-3, allowing an avidity driven selectivity gain to PD-1 and LAG-3 double positive T cells

**PD1-LAG3 has the potential to replace current CPI therapies in inflamed tumor types**

- In preclinical models, PD1-LAG3 is superior to aPD-1, and the combination with aLAG-3 in controlling tumor growth and eradicating the tumor
- Ph1a dose finding in solid tumors completed
- Ph1b/2 studies ongoing in melanoma, NSCLC, RCC, HCC, mUC, and TNBC

**References:**
1. Deak L.C. et al., SITC Meeting 2019 [poster P287].
2. Puhr HC et al. ESMO Open 2019;4:e000482. See also Roche’s investor relations event at ASCO 2022.
## Tobemstomig – Clinical development program

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<th>Study ID</th>
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<td>NP41300</td>
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| TALIOS   | II    | a) Tobemstomig  
b) Nivolumab | Advanced or metastatic esophageal squamous cell carcinoma | NCT04785820 | Active, not recruiting | - |
| MORPHEUS-Liver | Ib/II | a) Additional arms  
b) Tobemstomig + bevacizumab | Metastatic or locally advanced and/or unresectable HCC | NCT04524871 | Recruiting | - |
| MORPHEUS-NEO HCC | Ib/II | a) Atezolizumab + bevacizumab  
b) Atezolizumab + bevacizumab + tiragolumab  
c) Tobemstomig + bevacizumab | Surgically resectable hepatocellular carcinoma | NCT05908786 | Not yet recruiting | - |
| MORPHEUS-Melanoma | III | Cohort 1:  
a) Nivolumab + ipilimumab  
b) Tobemstomig  
c) Atezolizumab + tiragolumab  
d) Tobemstomig + tiragolumab  
Cohort 2:  
e) Tobemstomig + tiragolumab | Cohort 1: CIT-naive, resectable Stage III melanoma  
Cohort 2: Stage IV melanoma | NCT05116202 | Recruiting | - |
| BP43963  | II    | Tobemstomig (randomized to high or low dose) | Previously untreated, unresectable or metastatic melanoma | NCT05419388 | Recruiting | - |
| BO44157  | II    | a) Atezolizumab  
b) Tobemstomig  
c) Tobemstomig + tiragolumab | Metastatic or locally advanced UC, ineligible to receive a platinum-containing chemotherapy | NCT05645692 | Recruiting | - |
| BO43936  | II    | a) Tobemstomig + axitinib  
b) Tobemstomig + Tiragolumab + axitinib  
c) Pembrolizumab + axitinib | Untreated locally adv. unresectable or metastatic RCC | NCT05805501 | Recruiting | - |
| CO44194  | II    | a) Tobemstomig + Nab-paclitaxel  
b) Pembrolizumab + Nab-paclitaxel | Previously untreated, PD-L1-positive locally adv. unresectable or metastatic TNBC | NCT05852691 | Recruiting | - |
| BO44178  | II    | a) Tobemstomig + chemotherapy  
b) Pembrolizumab + chemotherapy | Previously untreated, locally adv., unresectable or metastatic NSCLC | NCT05775289 | Recruiting | - |

ClinicalTrials.gov (last verified August 2023).
**Tobemstomig – NP41300**

First-in-human Phase I study multiple ascending-dose study of tobemstomig in advanced and/or metastatic solid tumors

**Anti-tumor activity observed in multiple tumor types in CPI experienced and CPI naive patients**

- **Overall:** 51% DCR (18/35), 17% ORR (6/35)
- **CPI experienced:** 42% DCR (5/12), 17% ORR (2/12)
- **CPI naive:** 57% DCR (13/23), 17% ORR (4/23)

**KEY POINTS:**
- Tobemstomig has a favorable safety profile and has shown encouraging anti-tumor activity in the dose escalation phase.
- Responses have been observed in both CPI naïve and in CPI experienced patients across multiple tumor types.

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**Abbreviations:**
- NSCLC = non small cell lung cancer; ESCC = esophageal squamous cell carcinoma; CPI = checkpoint inhibitor
- Clinicaltrials.gov: NCT04140500 is recruiting (last verified August 2023).

1. Rohrberg et al. ESMO 2022 (745P; POSTER)
Tobemstomig – BP42772 (TALIOS)

A Phase II, randomized study designed to evaluate the safety and efficacy of tobemstomig, compared with nivolumab, in advanced or metastatic ESCC

Primary endpoints:
- OS

Secondary endpoints:
- Safety and tolerability; PK & ADA, investigator-assessed ORR, DCR, DoR, PFS, PROs

- Unresectable advanced or recurrent esophageal cancer
- Squamous histology
- Asian ethnicity
- Refractory to or intolerant of 1 prior fluoropyrimidine-based/taxane based and platinum-based chemotherapy (2L)
- ECOG PS 0/1

(N = 255)

Tobemstomig 2100 mg IV q2w

Nivolumab 240 mg IV q2w

Treat until PD, unacceptable toxicity or loss of clinical benefit

Clinicaltrials.gov: NCT04785820 is active, not recruiting (last verified August 2023)
Tobemstomig – MORPHEUS-Liver

A phase Ib/II study evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations in patients with advanced liver cancers

Primary endpoint
- ORR

Selected secondary endpoints
- PFS, OS, % patients with AEs during each stage, duration of response, disease control

*Participants who experience loss of clinical benefit or unacceptable toxicity during Stage 1 may be eligible to receive treatment with a different treatment combination (Stage 2). Protocol will be amended when a Stage 2 treatment combination is available.
†Participants will receive intervention until unacceptable toxicity or loss of clinical benefit, as determined by the investigator

ClinicalTrials.gov: NCT04524871 is recruiting (last verified August 2023).