**Introduction to 4-1BB and ST4**

4-1BB (CD137)

- **Activation-induced co-stimulatory receptor**
- **Membrane receptor expressed on tumor infiltrating T cells**
- **Signaling molecules for immune cell activation and proliferation**
- **Activation involves PTPs**
- **Stimulation of 4-1BB+ T cells and NK cells**
- **Adherence of 4-1BB to the 4-1BB ligand (4-1BB-L) on tumor cells**
- **Enhanced immune cell proliferation and activation**
- **Tumor regression and immune cell infiltration**

**ST4**

- **Tumor-specific immune cell receptor**
- **Identified as a pilot tumor-targeting bispecific antibody by the ADBP® team**
- **Specific for T lymphocytes and NK cells**
- **Overexpressed in various solid tumors**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**About ALG-APV-527**

**ALG-APV-527**

- **Bispecific target-directed**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**ALG-APV-527 Mode of Action**

- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**Summary and conclusions**

**ALG-APV-527**

- **Stimulates immune cells**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**ALG-APV-527**

- **Enhances immune cell infiltration and tumor regression**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**ALG-APV-527**

- **Tumor-specific immune cell receptor**
- **Identified as a pilot tumor-targeting bispecific antibody by the ADBP® team**
- **Specific for T lymphocytes and NK cells**
- **Overexpressed in various solid tumors**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**Dose-range finding pilot toxicity study design**

- **Study was conducted in cynomolgus monkeys to identify a safe dose level for tumor treatment**
- **Dose levels were selected based on a safety margin of 5-10 times the estimated human dose**
- **Monkeys were dosed intravenously (IV) with escalating doses of ALG-APV-527**
- **Safety assessment included monitoring of clinical signs, body weight, food intake, and hematology and serum chemistry measurements**
- **Toxicity was assessed based on the occurrence of any adverse events and changes in the above parameters**

**Cynomolgus is a relevant toxicity specie for ALG-APV-527**

- **Cynomolgus monkeys are used as a model for toxicity studies**
- **Similar anatomical, physiological, and immunological characteristics**
- **Suitable for evaluating the potential toxicity and safety of ALG-APV-527**

**Kinetic profile of ALG-APV-527 in cynomolgus monkeys**

- **Serum concentration of ALG-APV-527 over time in cynomolgus monkeys**
- **Dosing regimen of ALG-APV-527 in cynomolgus monkeys**
- **Serum concentration vs. time in cynomolgus monkeys**
- **Pharmacokinetic parameters of ALG-APV-527 in cynomolgus monkeys**

**Poster #2380**

Aptivus Therapeutics Inc., Seattle, WA, USA

Preclinical safety and efficacy of a tumor-directed T cell activating 4-1BB x ST4 ADAPTIR™ bispecific antibody

Anna Dahlgren, Michelle Nelson, Jeannette Banerjee, Starna Johnson, Doreen Wenzhausen, Anneli Liljas, Li Lijiang, Gabriella Blazhuk-Fujan, Robert Baeber, Peter Elmkamp, Maria Aisikyn, Gabriela Hernandez Hoyos, Cathy McMillan and Sara Stafford

1Alligator Bioscience AB, Malmö, Sweden
2Aptivus Therapeutics Inc., Seattle, WA, USA

**Hepatocellular carcinoma**

- **Significant decrease in tumor burden**
- **Enhanced immune cell infiltration and tumor regression**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**Serum concentration of ALG-APV-527 over time in cynomolgus monkeys**

- **Dosing regimen of ALG-APV-527 in cynomolgus monkeys**
- **Serum concentration vs. time in cynomolgus monkeys**
- **Pharmacokinetic parameters of ALG-APV-527 in cynomolgus monkeys**

**Serum concentration of ALG-APV-527 over time in human recipients**

- **Dosing regimen of ALG-APV-527 in human recipients**
- **Serum concentration vs. time in human recipients**
- **Pharmacokinetic parameters of ALG-APV-527 in human recipients**

**Target specific populations of 4-1BB and ST4 direct T cell activity of ALG-APV-527 in human and cynomolgus (A-B)**

- **Primary NK cells were stimulated with ALG-APV-527 for 24 h and IFN-g production was measured**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**

**Poster #2380**

Aptivus Therapeutics Inc., Seattle, WA, USA

Preclinical safety and efficacy of a tumor-directed T cell activating 4-1BB x ST4 ADAPTIR™ bispecific antibody

Anna Dahlgren, Michelle Nelson, Jeannette Banerjee, Starna Johnson, Doreen Wenzhausen, Anneli Liljas, Li Lijiang, Gabriella Blazhuk-Fujan, Robert Baeber, Peter Elmkamp, Maria Aisikyn, Gabriela Hernandez Hoyos, Cathy McMillan and Sara Stafford

1Alligator Bioscience AB, Malmö, Sweden
2Aptivus Therapeutics Inc., Seattle, WA, USA

**Hepatocellular carcinoma**

- **Significant decrease in tumor burden**
- **Enhanced immune cell infiltration and tumor regression**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**Serum concentration of ALG-APV-527 over time in cynomolgus monkeys**

- **Dosing regimen of ALG-APV-527 in cynomolgus monkeys**
- **Serum concentration vs. time in cynomolgus monkeys**
- **Pharmacokinetic parameters of ALG-APV-527 in cynomolgus monkeys**

**Serum concentration of ALG-APV-527 over time in human recipients**

- **Dosing regimen of ALG-APV-527 in human recipients**
- **Serum concentration vs. time in human recipients**
- **Pharmacokinetic parameters of ALG-APV-527 in human recipients**

**Target specific populations of 4-1BB and ST4 direct T cell activity of ALG-APV-527 in human and cynomolgus (A-B)**

- **Primary NK cells were stimulated with ALG-APV-527 for 24 h and IFN-g production was measured**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**

**Poster #2380**

Aptivus Therapeutics Inc., Seattle, WA, USA

Preclinical safety and efficacy of a tumor-directed T cell activating 4-1BB x ST4 ADAPTIR™ bispecific antibody

Anna Dahlgren, Michelle Nelson, Jeannette Banerjee, Starna Johnson, Doreen Wenzhausen, Anneli Liljas, Li Lijiang, Gabriella Blazhuk-Fujan, Robert Baeber, Peter Elmkamp, Maria Aisikyn, Gabriela Hernandez Hoyos, Cathy McMillan and Sara Stafford

1Alligator Bioscience AB, Malmö, Sweden
2Aptivus Therapeutics Inc., Seattle, WA, USA

**Hepatocellular carcinoma**

- **Significant decrease in tumor burden**
- **Enhanced immune cell infiltration and tumor regression**
- **Induces immune cell activation and proliferation**
- **Enhanced immune cell infiltration and tumor regression**

**Serum concentration of ALG-APV-527 over time in cynomolgus monkeys**

- **Dosing regimen of ALG-APV-527 in cynomolgus monkeys**
- **Serum concentration vs. time in cynomolgus monkeys**
- **Pharmacokinetic parameters of ALG-APV-527 in cynomolgus monkeys**

**Serum concentration of ALG-APV-527 over time in human recipients**

- **Dosing regimen of ALG-APV-527 in human recipients**
- **Serum concentration vs. time in human recipients**
- **Pharmacokinetic parameters of ALG-APV-527 in human recipients**

**Target specific populations of 4-1BB and ST4 direct T cell activity of ALG-APV-527 in human and cynomolgus (A-B)**

- **Primary NK cells were stimulated with ALG-APV-527 for 24 h and IFN-g production was measured**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**
- **IFN-g production was measured in the presence of NK cells and ALG-APV-527 at different concentrations**

**Poster #2380**

Aptivus Therapeutics Inc., Seattle, WA, USA

Preclinical safety and efficacy of a tumor-directed T cell activating 4-1BB x ST4 ADAPTIR™ bispecific antibody

Anna Dahlgren, Michelle Nelson, Jeannette Banerjee, Starna Johnson, Doreen Wenzhausen, Anneli Liljas, Li Lijiang, Gabriella Blazhuk-Fujan, Robert Baeber, Peter Elmkamp, Maria Aisikyn, Gabriela Hernandez Hoyos, Cathy McMillan and Sara Stafford

1Alligator Bioscience AB, Malmö, Sweden
2Aptivus Therapeutics Inc., Seattle, WA, USA