Pipeline of 5T4-Targeted Immunotherapies

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Overview of Active 5T4-Targeted Immunotherapy Candidates – 1/2

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
Naptumomab estafenatox; ABR-217620; NTX-352	Oncofetal antigen 5T4 and T-cell recruitment and induction	Rec fusion protein of anti-5T4 Fab + superantigen SEA/E-120	NeoTx Therapeutics (from Active Biotech)	Non-small cell lung cancer + docetaxel solid tumors + durvalumab	IIa Ib/II
VTP-850	5T4; PSA; PAP; and STEAP1 and T-cell induction	Heterologous prime-boost vaccine of ChAdOx1 and MVA	Barinthus Biotherapeutics (formerly Vaccitech)	Men with bio-chemical recurence after definitive local therapy of prostate cancer	I/II
JK06	Two distinct epitopes of 5T4 and tubulin polymerization inhibitor	Rec tetravalent, biparatopic / bispecific mAb site-specifically conjugated via cleavable linker to MMAE (DAR of 2)	Salubris Biotherapeutics	Solid tumors	I/II
TUB-030	5T4 and topoisomerase I inhibitor	Rec humanized, Fc-silenced IgG1 mAb linked via P5 conjugation chemistry to the topoisomerase 1 inhibitor exatecan	Tubulis	Advanced solid tumors (5-STAR 1-01 trial)	I/II
ALG.APV-527	5T4 and CD137 (4-1BB) co-stimulation	Rec bispecific, tetravalent antibody of 4 scFvs fused to modified Fc	Alligator Biosciences & Aptevo Therapeutics	Solid tumors	Ib
CBA-1535; Tb535H	5T4 x CD3 x 5T4	Rec humanized bispecific, trivalent fusion antibody of anti-5T4 Fab + scFv and anti-CD3 scFv	Chiome Bioscience (from Biotecnol)	Solid tumors incl. mesothelioma, SCLC, NSCLC	I
ASN004	5T4 and tubulin polymerization inhibitor	Rec scFv-Fc mAb conjugated via the hydrophilic poly-acetal Fleximer/ Dolaflexin linker to auristatin F (DAR of 10-12)	Asana Biosciences & Kirilys Therapeutics	Advanced solid tumors	I
XB010; 5T4-MMAE-ADC	5T4 and tubulin polymerization inhibitor	Rec monoclonal antibody linked by double-cleavable site-specific aldehyde tag to MMAE (DAR of 2)	Exelixis (technology from Invenra and Catalent)	Advanced solid tumors	I
ACR246	5T4 and topoisomerase I inhibitor	Rec fully human mAb conjugated via cleavable linker to topo I inhibitor D2102 (DAR of 8)	Adcoris Biopharma	Advanced solid tumors	I

Overview of Active 5T4-Targeted Immunotherapy Candidates – 2/2

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
PTRY	5T4 x PD-L1 x CD3	Rec humanized trispecific, trivalent fusion antibody of anti-PD-L1 Fab + anti-5T4 scFv and anti-CD3 scFv	Chiome Bioscience	Solid tumors	0
IM1240; capped-CD3 x 5T4 x NKG2A	5T4 and CD3 and NKG2A (NK cell engagement	Rec trispecific antibody with protease cleavable mask of anti-DC3	Purple Biotech	Solid tumors	0
^{111}In/^{225}Ac-ABD320	5T4 and delivery of radioactive payload	Rec camelid VHH fused to engineered Fc coupled by novel linker-chelator to 111In or 225Ac	Abdera Therapeutics	Imaging and treatment of 5T4-expressing solid tumors	0

Drug Modality: Superantigen Immunotherapy

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
Naptumomab estafenatox; ABR-217620; NTX-352	5T4 targeting and T-cell recruitment and induction	Rec fusion protein of anti-5T4 Fab + superantigen SEA/E-120	NeoTx Therapeutics (from Active Biotech)	Non-small cell lung cancer + docetaxel solid tumors + durvalumab	IIa Ib/II
Naptumomab estafenatox (ABR-217620) is a hybrid (staphylococcal enterotoxin A) SEA/E-120 superantigen sequence with reduced binding to pre-formed anti-superantigen antibodies, lower toxicity, higher affinity for 5T4, and improved tumor cell killing. Tumor-targeted super antigens are recombinant fusion proteins that consist of an anti-tumor Fab moiety genetically fused to a super antigen. Anyara initially has been developed by Active Biotech. The superantigen therapy approach harnesses the ability of bacterial superantigens to activate large numbers of human T cells by binding to the T cells through the TCR vβ chain family and replacing the interaction with MHC class II with the specificity of a TAA-targeting antibody. Therapeutic efficacy comes from direct lysis of tumor cells by the engaged T cells along with secretion of cytokines providing for bystander antitumor activity. After failure of the phase II/III Anyara monotherapy trial in renal cell carcinoma (Press Release Jan 28, 2013), Active Biotech entered into an agreement with NeoTX Therapeutics in October 2016 for the global development and commercialization of ANYARA for the treatment of cancer (Press Release Apr 19, 2023). NeoTx Therapeutics is conducting two clinical trials of naptumomab estafenatox in combination with anti-PD-L1 antibody durvalumab in solid tumors and in combination with docetaxel in non-small cell lung cancer (Active Biotech Homepage Aug 15, 2025).					

Drug Modality: Vaccine

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
VTP-850	5T4; PSA; PAP; and STEAP1 and T-cell induction	Heterologous prime-boost vaccine of ChAdOx1 and MVA	Barinthus Biotherapeutics (formerly Vaccitech)	Men with bio-chemical recurence after definitive local therapy of prostate cancer	I/II
As induction of a monospecific T-cell response against 5T4 by VTP-800 was insufficient, Vaccitech/Barinthus Biotherapeutics initiated clinical development of VTP-850, a multi-antigen immunotherapeutic candidate containing four prostate-associated antigens: PSA, PAP, STEAP1 and 5T4. VTP-850 was designed to induce a targeted polyclonal T cell response to kill remaining tumor cells and prevent advancement to metastatic disease. Barinthus is a spinout company from the Jenner Institute for vaccine research at University of Oxford. The prime-boost platform is licensed from the Jenner Institute at University of Oxford. It comprises Chimpanzee Adenovirus (ChAdOx1: prime) and Modified Vaccinia Ankara (MVA: boost) and is exceptional at inducing, boosting and maintaining CD8+ and CD4+ T cells. The phase 1 trial of VTP-850 in patients with prostate cancer is now complete; VTP-850 was well tolerated in this population of elderly prostate cancer patients. Data shows encouraging signs of immunogenicity and will be used to facilitate partnering discussions (Press Release Aug 07, 2025). The trial was discontinued following completion of the Phase 1 portion. This discontinuation was not based on safety concerns (ClinicalTrials.gov Mar 19, 2025).					

Drug Modality: T Cell Engaging Antibodies

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
CBA-1535; Tb535H	5T4 x CD3 x 5T4	Rec humanized bispecific, trivalent fusion antibody of anti-5T4 Fab + scFv and anti-CD3 scFv	Chiome Bioscience (from Biotecnol)	Solid tumors incl. mesothelioma, SCLC, NSCLC	I
The T-cell engager CBA-1535, previously known as Tb535H, is a humanized trivalent biological construct ("Tribody") with two binding sites to the tumor associated antigen 5T4 and one to the T cell expressed antigen CD3ε. The bispecific tribody CBA-1535 is made up of a Fab and a scFv domain both targeting 5T4 (bivalent binding) and another scFv targeting CD3 (monovalent binding). Chiome Bioscience of Japan purchased the asset from Biotecnol (Press Release Dec 03, 2018). In July 2022, the first patient has been dosed with CBA-1535 in a Phase I clinical trial (Press Release July 4, 2022). As Chiome Bioscience is considering early out-licensing opportunities for CBA-1535, the company decided to extend the clinical study period (ClinicalTrials.gov NCT07016997 June 2025) to confirm its safety and explore signals of efficacy, and, therefore, is advancing the dose-escalation study (Presentation Aug 12, 2025). No significant safety concerns were found at present. Blood marker changes associated with T-cell activation have started to show, which deem the proof of concept for this study drug.					

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
PTRY	5T4 x PD-L1 x CD3	Rec humanized trispecific, trivalent fusion antibody of anti-PD-L1 Fab + anti-5T4 scFv and anti-CD3 scFv	Chiome Bioscience	Solid tumors	0
As a modification of CBA-1535, PTRY is a trispecific antibody construct targeting the tumor-associated antigen 5T4, inhibitis the immune checkpoint PD-L1 and recruits T-cells via CD3. PTRY is the results of joint research of Chiome Bioscience and Ceinge Biotecnologie Avanzate (Presentation Aug 12, 2025). Non-clinical studies are in progress					

Drug Modality: T-Cell and NK Cell Engaging Antibody

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
IM1240; capped-CD3 x 5T4 x NKG2A	5T4 and CD3 and NKG2A (NK cell engagement	Rec trispecific antibody with protease cleavable mask of anti-DC3	Purple Biotech	Solid tumors	0
Purple Biotech (formerly Kitov Pharma) acquired multi-specific T cell and natural killer (NK) cell engagers from Immunorizon (Press Release Feb 02, 2023). IM1240 is a conditionally activated trispecific antibody construct targeting 5T4xCD3xNKG2A for treatment of solid tumors. With an anti-CD3 masking moiety, IM1240 shows a tumor-restricted activation through a cleavable capping system designed to provide a wide therapeutic index (CAPTN-3 platform). T cell engagement is achieved through binding CD3 using a commercially validated antibody fragment. The CD3 binder is activated by protease cleavage in the tumor microenvironment. The NK cell mediated activity is manifested by the NK cell engager arms of NKG2A or NKG2D. The first CAPTN-3 trispecific antibody targeting the tumor associated antigen, 5T4, advances toward first-in-human clinical trials, with IND submission expected in 2026 (Press Release Aug 06, 2025).					

Drug Modality: Bispecific Co-Stimulatory Antibody

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
ALG.APV-527	5T4 and CD137 (4-1BB) co-stimulation	Rec bispecific, tetravalent antibody of 4 scFvs fused to modified Fc	Alligator Biosciences & Aptevo Therapeutics	Solid tumors	Ib
ALG.APV-527 is a bispecific, tetravalent therapeutic containing scFv binding domains targeting the co-stimulatory receptor 4-1BB and the oncofetal antigen 5T4. These are linked to an effector-null Ig Fc domain, providing an antibody-like in vivo half-life. The scFvs originate from the Alligator Gold® human scFv library (Alligator Bioscience) and optimized for use in the bispecific ADAPTIR format. ALG.APV-527 is a bispecific conditional 4-1BB agonist, only active upon simultaneous binding to 4-1BB and 5T4. ALG-APV-527 is being developind in partnership with Aptevo Therapeutics. Positive interim data were reported from the dose escalation phase of the Phase 1 trial evaluating ALG.APV-527 for the treatment of solid tumors likely to express the tumor antigen 5T4 (Marron-Poster-SITC-2024). Nine of 15 efficacy evaluable patients (60%) have a best overall response to date of stable disease (SD). ALG.APV-527 demonstrated positive safety and tolerability across all cohorts. No serious liver toxicity occurred with this conditional 4-1BB bispecific likely due to its TME-specific activating design. A maximum tolerated dose has not been identified (Press Release Sep 16, 2024). Phase 1B dose expansion is considered in combination with CPI, T cell engager/CAR-T or chemo (Presentation July 2025).					

Drug Modality: Antibody-Drug Conjugates – 1/3

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
ASN004	5T4 and tubulin polymerization inhibitor	Rec scFv-Fc mAb conjugated via the hydrophilic poly-acetal Fleximer/ Dolaflexin linker to auristatin F (DAR of 10-12)	Asana Biosciences & Kirilys Therapeutics	Advanced solid tumors	I
ASN004 is a novel 5T4-targeted ADC under development by Asana Biosciencs, but licensed to Kirilys Therapeutics which completed a phase I study, but Kirilys went out of business. ASN004 incorporates an anti-5T4 scFv-Fc antibody and utilizes the hydrophilic polyacetal Fleximer/Dolaflexin ADC linker technology to deliver several cytotoxic Auristatin F hydroxypropylamide (AF-HPA) payload drugs per ADC molecule [drug-to-antibody ratio (DAR) approximately 10 to 12]. In April 2022, the first patient has been dosed in a Phase 1 trial for ASN004 (Press Release Apr 8, 2022). The Phase 1, multicenter, dose-finding study was designed to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and anti-tumor activity of ASN004, in patients with advanced solid tumors in the US (ClinicalTrials.gov NCT04410224). The clinical study is being conducted by Arsana's partner Kirilys Therapeutics. No results from the phase I study have been published.					

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
XB010; 5T4-MMAE-ADC	5T4 and tubulin polymerization inhibitor	Rec monoclonal antibody linked by double-cleavable site-specific aldehyde tag to MMAE (DAR of 2)	Exelixis (technology from Invenra and Catalent)	Advanced solid tumors	I
In August 2024, Exelixis announced the initiation of the dose-escalation stage of the first-in-human phase 1 clinical trial of XB010 (ClinicalTrials.gov NCT06545331) in 396 patients with locally advanced or metastatic solid tumors (Press Release Aug 06, 2024). The dose-escalation stage of this phase 1, global, open-label study is evaluating XB010 as a single agent and in combination with pembrolizumab to inform the cohort-expansion stage. The expansion cohorts are designed to further assess the tolerability and activity of monotherapy and of the combination in specific indications. As of July 2025, the phase I study of XB010 is ongoing (Exelixis Presentation July 28, 2025). XB010 is an antibody-drug conjugate (ADC) consisting of a monomethyl auristatin E (MMAE) payload conjugated to a high affinity monoclonal antibody sourced from Invenra which is targeting the tumor antigen 5T4. XB010 utilizes Catalent's SMARTag® conjugation platform to produce a homogenous ADC with a defined DAR of 2, and incorporate highly stable next-generation proprietary linker technology (requires two cleavage events to release payload). The SMARTag technology utilizes an aldehyde tag for chemo-enzymatic site-specific conjugation.					

Drug Modality: Antibody-Drug Conjugates – 2/3

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
JK06	Two distinct epitopes of 5T4 and tubulin polymerization inhibitor	Rec tetravalent, biparatopic / bispecific mAb site-specifically conjugated via cleavable linker to MMAE (DAR of 2)	Salubris Biotherapeutics	Solid tumors	I

Salubris Biotherapeutics is developing JK06, a humanized, quadrivalent, biparatopic antibody-drug conjugate (ADC) that targets 5T4, and delivers the cytotoxic payload, monomethyl auristatin E (MMAE). JK06 is a humanized biparatopic antibody comprised of a full anti-5T4 IgG1 domain with a C-terminal fusion of a scFv domain binding to *a distinct* 5T4 epitope (Kotecki-abstract-ASCO-2025). JK06 is engineered from 2 monoclonal antibodies (mAbs) that bind to distinct epitopes of 5T4. The first mAb clone was converted to a single-chain fragment variable (ScFv) format and fused to the C-terminal Fc end of a second mAb. The tubulin inhibitor MMAE was conjugated to the Fc backbone of JK06 in a site-specific manner with a cleavable linker at a drug:antibody ratio (DAR) of two (McNally-abstract-AACR-2025). A repeat-dose GLP toxicology study, with a once every 3-week (Q3W) dosing schedule, demonstrated that JK06 was well tolerated, and without any observed adverse effects at the tested doses. Toxicokinetic evaluation showed a half-life which projects sustained exposure in humans with a Q3W dosing regimen.

In August 2024, Salubris Biotherapeutics received approval from the European Medicines Agency (EMA) to initiate a Phase I/II clinical trial (ClinicalTrials.gov NCT06667960) of JK06 in a basket of solid tumors known to express 5T4 (Press Release Aug 05, 2024). The phase I/II study is ongoing.

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
TUB-030	5T4 and topoisomerase I inhibitor	Rec humanized, Fc-silenced IgG1 mAb linked via P5 conjugation chemistry to the topoisomerase 1 inhibitor exatecan	Tubulis	Advanced solid tumors (5-STAR 1-01 trial)	I/II

TUB-030 is a novel ADC targeting the oncofetal 5T4 antigen. TUB-030 consists of a humanized, Fc-silenced IgG1 antibody targeting 5T4 equipped with Tubulis' proprietary Tubutecan technology, which is based on P5 conjugation chemistry and the topoisomerase-1 inhibitor exatecan. The a cleavable linker system provides a homogeneous DAR of 8. P5 conjugation is a novel chemistry for cysteine-selective conjugation that enables ADC generation with unprecedented linker stability and biophysical properties (Press Release Jan 30, 2025). Differently to previous 5T4-targeting ADCs, TUB-030 has efficient bystander activity against co-cultured target-negative cells, which facilitates targeting of tumors with heterogenous 5T4 expression. Preliminary repeat-dose toxicological assessment of TUB-030 in a pharmacologically relevant non-human primate species demonstrated that TUB-030 is well tolerated (Schmitt-abstract-AACR-2024).

In January 2025, TUB-030 has entered clinical evaluation with successful dosing of the first patient in the 5-STAR 1-01 Phase I/IIa trial (ClinicalTrials.gov NCT06657222) (Press Release Jan 30, 2025). The multicenter, first-in-human, dose escalation and optimization Phase I/IIa study 5-STAR 1-01 aims to investigate the safety, tolerability, pharmacokinetics, and efficacy of TUB-030 as a monotherapy to treat a broad range of solid tumors. The trial will enroll a total of 130 patients and will be conducted at sites across the US and Canada.

Drug Modality: Antibody-Drug Conjugate – 3/3

Product Name	Target / Mechanism of Action	Product Description	Csompany	Indication	R&D Stage
ACR246	5T4 and topoisomerase I inhibitor	Rec fully human mAb conjugated via cleavable linker to topo I inhibitor D2102 (DAR of 8)	Adcoris Biopharma	Advanced solid tumors	I

Adcoris Biopharma is developing ACR246, an ADC product candidate targeting 5T4 oncofetal antigen with a proprietary topoisomerase I inhibitor. ACR246 is a 5T4-targeted ADC consisting of a specific fully human mAb site-specifically conjugated with the potent topoisomerase I inhibitor payload D2102 through an innovative stable and cleavable linker. A PK study demonstrated low systemic exposure of payload D2102 after intravenous administration of ACR246 in cynomolgus monkeys, confirming that ACR246 was stable with low off-target toxicity. GLP toxicity studies showed that ACR246 was well tolerated in cynomolgus monkeys, with an estimated therapeutic index of 24 (Jiao-abstract-ASCO-2025). ACR246 has demonstrated substantial anti-tumor activity, safety, pharmacokinetics, and tolerability in preclinical studies involving rodent and non-human primate models (Adcoris Homepage Aug 17, 2025). ACR246 is bearing eight TOP1 inhibitor payloads per ADC and is developed based on Adcoris' MuSC™ ADC technology platform.

In October 2024, ACR246 completed first-in-human dosing in a Phase Ia trial (ClinicalTrials.gov NCT06238401) in China (Press Release Oct 29, 2024). This is an ongoing, phase I/IIa, open-label, multicenter, dose escalation and cohort expansion study of ACR246 to be injected intravenously to adult pts with advanced solid tumors. 5T4 expression is not required for enrollment for phase I, but will be assessed retrospectively. Dose levels of 0.6 mg/kg and 1.2mg/kg has completed enrollment with no DLT (Zhang-abstract-ASCO-2025). Preliminary dose escalation study results in patients with advanced solid tumors indicated that ACR246 was very promising with good tolerance, no DLT incidence, manageable adverse events and significant efficacy in suppressing tumor growth. ACR246 has the potential to be a first and best in class for treating multiple solid tumors (Press Release May 29, 2025).

Drug Modality: RadioImmunoTherapeutic (RIT)

Product Name	Target / Mechanism of Action	Product Description	Company	Indication	R&D Stage
^{111}In/^{225}Ac-ABD320	5T4 and delivery of radioactive payload	Rec camelid VHH fused to engineered Fc coupled by novel linker-chelator to 111In or 225Ac	Abdera Therapeutics	Imaging and treatment of 5T4-expressing solid tumors	0

ABD-320 is a targeted radiopharmaceutical biologic therapy engineered to deliver Actinium-225 (^{225}Ac) to solid tumors expressing 5T4. ABD-320 was developed leveraging Abdera's ROVEr™ platform and is custom-engineered to achieve an ideal balance of tumor uptake and retention while avoiding systemic radiotoxicities (Press Release Apr 2, 2025).

ABD320, a humanized camelid heavy chain only antibody (VHH) fused to an engineered Fc with altered Fc-gamma and neonatal Fc receptor binding, uses a novel linker-chelator to deliver targeted ^{111}In and ^{225}Ac to 5T4 positive cancer cells. The ABD320 VHH-Fc binds human 5T4 with high affinity and specificity and is internalized by 5T4-expressing cancer cells (Melese-abstract-AACR-2025). In preclinical models, ABD320 was well tolerated when used to deliver 12 to 20 kBq of the therapeutic radionuclide ^{225}Ac to 5T4-expressing tumors. ^{225} Ac-ABD320 achieved significant tumor regression, suppression of regrowth and extension of survival. Within-mouse dosimetry estimates a tumor inferred dose of 50 to 80 Gy corresponding to efficacious doses of ^{225} Ac-ABD320.

Thus, preclinical data with ABD-320 demonstrates potent anticancer activity. ABD-320 represents the first radiopharmaceutical therapy in development to address 5T4. ABD-320 is in non-clinical development by Abdera Therapeutics (Homepage Aug 17, 2025). Abdera plans to initiate clinical development with ABD-320 in the first half of 2026.