UVEAL MELANOMA
CLINICAL TRIALS SUMMARY

Section A: Listing of Ongoing Clinical Trials in Uveal Melanoma (*open for accrual*)

Section B: Cumulative Summary of Data from Clinical Trials in Uveal Melanoma

Updated as of: November 28, 2025
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About OM >> Metastatic or Newly-Diagnosed >> ACIS UM Clinical Trials Summary

A. Listing of Ongoing Clinical Trials in Uveal Melanoma (open for accrual)

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Melanoma Research Institute of Excellence

Drug/Sponsor	*Mechanism*	***Updated as of Nov, 28, 2025***
darovasertib, IDE-196 Ideaya	PKC Inhibitor (oral)	**Ph. 1/2** Solid Tumors & Metastatic Uveal Melanoma with mutations in GNAQ, GNA11 or PRCK: monotherapy, and in combinations with crizotinib or binimetib. Enrolling in 8 US sites, Australia, Canada. N=341 NCT03947385 **Ph.2** (ASCO 2024 Trial-in-Progress) Neoadjuvant darovasertib for localized uveal melanoma, treatment prior to definitive management (enucleation, plaque brachytherapy or EBRT) Enrolling in 13 US sites, Australia, Canada, France, Germany, Italy, Netherlands, UK. NCT05907954 **Ph. 3** Neoadjuvant darovasertib in Primary Non-Metastatic Uveal Melanoma (OptimUM-10) N=520 Neoadjuvant darovasertib followed by plaque brachytherapy, compared to immediate plaque brachytherapy or enucleation (control arm). Enrollment ongoing in 27 US sites+AUS+AUT+BEL+CAN+CZ+DEN+EST+FR+GER+GR+IS+IT+NL+PL+ES+CH+UK. NCT07015190 **Ph.2/3** OptimUM-01 (ESMO 2024 Trial-in-Progress poster) 1st Line Metastatic Uveal Melanoma (no prior therapy) which is HLA-A*02:01 negative, combined with crizotinib. Enrolling at 31 sites in US+AUS+BEL+CAN +FRA+ GER+IL+ITA+NDL+POL+ES+CH+UK. N=380. (Ph. 3 randomizes combination vs. Inv. Choice). Endpoints: Ph. 2a RP2D, ORR, PFS, Ph.3 OS). N=442 NCT05987332 (ESMO Oct. 2025): Phase 2 portion of study is now enrolling Metastatic UM patients who are *HLA positive,* in US and Int'l sites.
RP2 Replimune	HSV Type I encoding GM-CSF conjugated to anti-CTLA-4 HuMab	**Ph. 1** Metastatic Solid Tumors. RP2 in combination with nivolumab. Enrolling at 7 sites in UK & Spain. NCT04336241 **Ph.2/Ph.3** 1st Line Metastatic UM (no more than 1 prior line of met. therapy; excludes prior oncolytic virus therapy and prior ICIs since the time of UM dx, involvement of >33.3% of the liver, or a history of prior liver- or lesion-directed therapy). RP2+nivolumab vs. ipilimumab+nivolumab. N=280. Enrolling in 25 US sites. NCT06581406 (SMR 2025 poster)
belzupacap sarotalocan, AU-011, Bel-sar Aura Biosciences	Virus-like Drug Conjugate (VDC), suprachoroidal delivery with laser activation	**Ph. 3** 1st (CoMpass Study) Suprachoroidal injection of bel-sar for Primary Indeterminate Lesions or Small Choroidal Melanoma: Neo-adjuvant 1st Line Treatment-naïve (no prior treatment for) Early Choroidal Uveal Melanoma. Bel-sar vs. sham injection. Enrolling globally at 30 US sites, and Australia, Austria, Belgium, Canada, Czechia, France, Germany, Israel, Netherlands, New Zealand, Spain, UK. N=100 NCT06007690

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
IMA-203 **anzutresgene autoleucel** Immatics	autologous TCR-T cell therapy targeting **PRAME**	**Ph. 1** Recurrent/refractory Solid Tumors (included uveal melanoma): IMA-203 monotherapy, in combination with nivolumab, and separate arm for evaluating IMA203CD8. Enrolling only Gyn. Oncology patients now in 7 US sites and 8 sites in Germany. N=476 **Ph. 2** (Second Portion of IMA-203-101 study above) In Metastatic UM patients (HLA-A*02-01 positive, up to 1 line of prior met. therapy). Now enrolling in Germany, and at MD Anderson-Houston, Univ. Miami, Mass. Gen. Hosp.-Boston, with 5 additional US sites pending initiation. NCT03686124, EudraCT 2019-002370-31. **Ph. 1** (IMA203-102) Recurrent/refractory HLA-A*02-01 positive metastatic *cutaneous* melanoma (Not UM), in combination with mRNA-4203. Accruing at Memorial Sloan Kettering NY, MD Anderson Houston, with 2 US sites pending initiation. NCT06946225 **Ph. 3** (SUPRAME Study, IMA-203-301) in HLA-A*02-01 positive metastatic *cutaneous* melanoma (Not UM). IMA-203 (vs immunotherapy, TIL, chemo). Recruiting in 30 US sites and Germany. NCT06743126
roginolisib, IOA-244 iONCTURA	PI3Kδ modulator (oral)	**Ph. 1** (TRIUMPH study) Metastatic Uveal Melanoma patients who are HLA-A*02:01 positive and currently receiving tebentafusp. This trial combines roginolisib with tebentafusp from cycle 4 onwards, to determine if the combination prolongs T cell homeostasis. N=8 Sydney & Melbourne Australia. NCT07203391 **Ph. 2** (OCULE-1 Study) Metastatic UM with progression after at least 1 prior immunotherapy. For patients who are HLA-A*02:01 positive prior treatment should have included tebentafusp, if available or patients clinically suitable. Patients who have also received prior melphalan hepatic infusion may be included. (2 dose levels of roginolisib 40mg vs. 80 mg vs. investigator's choice). An extension study will be available for patients who have reached the 24-month efficacy evaluation timepoint. Enrolling at 16 sites in Italy, Spain and UK, with several US sites pending initiation. N=85 NCT06717126
225Ac-MTI-201 Modulation Therapeutics	Actinium 225 (alpha) and "carrier" molecule peptide-mimetic targeting Melanocortin-1 receptor (MC1R)	**Ph. 1** (ASCO 2024, Trial In Progress) Metastatic UM with progression after at least 1 prior Tx. Single IV infusion in Single Ascending Dose, Completed 6 of 12 dose levels, study on-going. Update (ESMO 2024): Enrollment continuing, Multiple Ascending Dose levels pending. One site: Moffitt Cancer Center, Tampa NCT05496686

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[225Ac]Ac-A9-3408 (A-3408) Alpha-9 Oncology USA	Mc1R – AC225 conjugate theranostic	**Ph. 1** Unresectable or metastatic melanoma (including UM) with disease progression on prior standard of care therapy. Study will evaluate safety/tolerability and normal organ and tumor dosimetry**.** N=50 (including Ph 1b at RP2D) NCT07076550. Melbourne and Murdoch Australia.
VMT01 Perspective Therapeutics	MC1R-targeted Alpha-particle [203Pb]VMT01	**Ph. 1/2** Monotherapy and Combination Therapy Trial with Nivolumab in Adults with melanocortin subtype 1 receptor (MC1R)-expressing melanomas. Advanced Melanoma. Recruiting in 11 US sites, including Mayo Clinic Rochester MN and Univ WI Madison. NCT05655312
CHEMOSAT® Hepatic Delivery System delivering High-dose Melphalan in sequence with Ipilimumab + Nivolumab	Liver-directed therapy with high-dose cytotoxic chemotherapy	**Ph. 3** (SCANDIUM-III Study) Percutaneous Hepatic Perfusion with Delcath (Chemosat®/Hepzato®) melphalan, followed by 2 cycles of Ipilimumab + Nivolumab, compared to IPI3/NIVO1 Only in Patients with Uveal Melanoma Liver Metastases. Karolinska Inst. Stockholm and 5 sites in Sweden. N=40 NCT06519266
Quisinostat Viriom	Pan-HDAC/HDAC 1 inhibitor (oral)	**Ph. 2** Adjuvant Quisinostat in High-Risk Uveal Melanoma. In patients with >12mm basal diameter tumors, and Castle Class2 GEP (following initial surgery or radiotherapy for primary UM**,** non-metastatic). Accruing at Univ Miami, pending additional US sites. NCT06932757 (ESMO Oct. 2025): Dosing: 12 mg quisinostat orally (P.O.) 3 times a week, taken on a Mon, Wed, Fri regimen for total period of 51 weeks. Imaging studies performed at baseline, then every 12 weeks (± 7 days) for first 24 months, then once every 24 weeks (± 7 days) thereafter.
NBM-BMX NovelWise Pharmaceuticals	Selective HDAC 8 inhibitor (oral)	**Ph. 1/2** Advanced, refractory Solid Tumors. Ph 2 combined with radiotherapy/temozolomide in patients with glioblastoma (Not UM). Accruing in 5 sites in Taiwan. NCT06012695 **Ph. 1b/2** Metastatic Uveal Melanoma, including patients with BAP-1 loss. Prior treatment with tebentafusp is required for HLA-A*02:01-positive patients (*unless unavailable or clinically inappropriate*). No prior HDAC therapy allowed. Activated sites: HonorHealth-Scottsdale, Sarah Cannon Res. Inst.-Nashville, HealthOne SCRI DDU-Denver; with additional US sites pending. Study # NBM-BMX-004. NCT07136181
DCSZ11 DynamiCure Biotechnology	CD93 antagonist (downstream of VEGF)	**Ph. 1** DCSZ11 as Monotherapy and in Combination in Patients With Advanced or Metastatic Solid Tumors. Includes patients with HLA A02:01 positive UM. N=320. Accruing in 14 US centers (including Honor Health, Univ CO Aurora, 8 sites in Australia, 4 sites in South Korea and 4 sites in Taiwan. NCT05785754
IMC-F106C (brenetafusp) Immunocore	ImmTAC targeting HLA-A*02:01 antigen and **PRAME**	**Ph. 1/2** IMC-F106C-101 in Relapsed, Refractory Metastatic Solid Tumors: HLA-A*02-01 and PRAME positive. Multiple combination arms with immunotherapies and targeted cancer therapies. Enrolling in 22 US sites, and Australia, Austria, Belgium, Brazil, Canada, France, Germany, Italy, Ireland, S. Korea, Netherlands, New Zealand, Poland, Spain, Switzerland, UK. N=727 Study IMC-F106C-101. NCT04262466 (Phase I portion enrolled UM patients with data in Section B below; *however combination arms currently not enrolling uveal melanoma pts*). **Ph. 3** (PRISM-MEL-301 Study) IMC-F106C in 1st line metastatic HLA-A2*02-01 positive cutaneous, acral and mucosal melanoma. ASCO 2024 (Trials In Progress poster) IMC-F106C + nivolumab combination regimen, vs. Control (nivolumab or nivolumab+relatlimab) in Previously Untreated Advanced Melanoma. 28 sites in USA, and AUS, AUT, FR, GER, IT, ES, POL, CH, S. America. (*uveal melanoma patients limited to <10% of randomized participants).* PRISM-MEL-301 Study. N=680 NCT06112314

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Kimmtrak® (tebetafusp-tebn) Immunocore	TCR-targeting gp-100 HLA-A*02-01 complex	**Ph. 1b:** (SILVER Study) Adding IL-2 to Tebentafusp to Eradicate Cancer Progression. Met. UM and HLA-A*02:01 positive who have progressed on tebentafusp (and with no other intervening therapies). N=8 Sydney & Melbourne Australia. NCT07063875 **Ph. 1** (TRIUMPH study) Metastatic Uveal Melanoma patients who are HLA-A*02:01 positive and currently receiving tebentafusp. This trial combines roginolisib from cycle 4 of tebentafusp onwards, to determine if the combination prolongs T cell homeostasis. N=8 Sydney & Melbourne Australia. NCT07203391 **Ph. 1** Metastatic UM with 1 or 2 prior therapies, bulky hepatic disease, and HLA-A*0201-positive, with several metastatic UM liver lesion criteria. Combination therapy (tebentafusp-tebn and hepatic Immuno-Embolization, with GM-CSF. Phase II will compare tebentafusp with hepatic IE GM-CSF and combination of TACE with BCNU. Jefferson Univ., Philadelphia. N=109 NCT06626516 **Ph. 2** Tebentafusp +TACE/BCNU chemoembolization in patients with treatment-naiive Metastatic UM, Jefferson Univ. N=109 NCT06626516 **Ph. 2** (TebeMRD Study) Tebentafusp in Molecular Relapsed Disease (MRD) Melanoma. Evaluating Relapse-Free Survival in non-metastatic Uveal Melanoma patients with ctDNA presence in blood but no radiographic-detectable mets. Univ Oxford and 9 additional UK sites. N=850 Active, but Not currently enrolling patients. NCT05315258 **Ph. 2** Neo-Adjuvant UM (no prior treatment for UM or enucleation, large primary eye tumor stage T3/T4 unresectable, HLA-A*02-01 positive, non-metastatic). Primary Endpoint is degree of tumor shrinkage. Also evaluating ctDNA. Pending initiation of enrollment, only at Thos. Jefferson Univ. Philadelphia. N=19 NCT06414590 **Ph. 2** (NEO-TB Study) Neo-adjuvant Tebentafusp in Patients With Metastatic Uveal Melanoma. HLA-A*02-01 positive and no prior metastatic therapy. Enrolling in Berlin and 3 sites in Spain. N=19. NCT07057596 **Ph. 2** Tebentafusp in HLA-A*02-01 Positive Previously Untreated Metastatic Uveal Melanoma. Enrolling only Univ. Pittsburgh. NCT06070012 **Ph. 2** Tebentafusp and Yytrium-90 Radioembolization in the Treatment of Metastatic Uveal Melanoma (part 1 of study in patients with no prior Met. therapy, Part 2 allows multiple prior Met. therapies). Univ. Miami, N=30 NCT06627244 **Ph. 2** Tebeltafusp +Hepzato in Metastatic UM patients with HLA-A*02:01 positive hepatic dominant disease. Moffitt Ca. Ctr. Tampa. Pending **Ph. 3** (ATOM Study) Adjuvant Tebentafusp vs Observation in HLA-A*02:01 Positive Patients Following Definitive (initial) Treatment of High-risk Uveal Melanoma. An EORTC study enrolling only in: France, Germany, Netherlands, Poland, Spain. N=290 NCT06246149
Tumor infiltrating lymphocytes	(TIL) harvest, IL-2 and ex vivo expansion	**Ph. 2** Lymphodepletion Plus Adoptive Cell Transfer With or Without Dendritic Cell Immunization in Patients With Metastatic Melanoma. One site at MD Anderson, Houston. Active, but not currently recruiting patients. NCT00338377.
Tumor infiltrating lymphocytes	Non-myeloablative lymphodepleting prep regimen, then infusion of auto. TIL and high-dose IL-2	**Ph. 2** Adoptive Transfer of Tumor Infiltrating Lymphocytes for Metastatic Uveal Melanoma (including patients with ≤3 brain mets less than 1 cm). Patients will be enrolled in Companion Protocol Cell Harvest and Preparation to Support Adoptive Cell Therapy Clinical Protocol. Univ. Pittsburgh. N=47 NCT03467516

aCUREINSIGHT.org ocular melanoma	**A. *Listing of Ongoing Clinical Trials* in Uveal Melanoma (open for accrual)** ***A Cure In Sight does not offer treatment recommendations, and information provided here is not an endorsement of specific clinical trials, investigational drugs or investigators/cancer centers.*** ***To view available clinical trials and active sites, visit www.clinicaltrials.gov and search "uveal melanoma" in Condition-Disease, or simply search for NCTxxxxxxxx.***	Thomas Jefferson University 200 *Melanoma Research Institute of Excellence*

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
Tumor infiltrating lymphocytes	CD40L-augmented Tumor Infiltrating Lymphocytes (TIL)	**Ph. 1/2** Advanced, metastatic 'second-line' melanomas (including uveal melanoma in Ph. 2 portion). Allows treated, stable brain mets. TIL with short-course IL-2. Enrolling at Moffitt Cancer Center, Tampa. N=36 NCT06961357
Amtagvi®, LN-144 (lifileucel) Iovance **lifeleucil combined with IOV-3001**	Tumor Infiltrating Lymphocytes (TIL) IOV-3001: Antibody-interleukin-2 (IL-2) fusion protein, with modified form of IL-2 incorporated into palivizumab.	**Ph. 1** Study of LN-144 or LN-145 in People With Advanced Metastatic Uveal Melanoma. (Preliminary data in Section B below) Study enrolling at Memorial Sloan Kettering. Supported by grants from MRA and A Cure In Sight. NCT05607095 **Ph. 1/2** A Study to Investigate the Safety and Efficacy of IOV-3001 in Adults With Advanced Melanoma (and metastatic UM patients who have had tebentafusp) who will also receive lifileucel. Enrolling at Sarah Cannon Res. Inst. Sites in Nashville and Denver (HealthOne DDU). N=42 NCT06940739
MAGE-C2 engineered T-cells with selected TCR	MAGE T Cells with MC2 (highly expressed in melanoma_	**Ph. 1/2** MAGE-C2 TCR T Cell in HLA-A2*0201 positive patients with progressing metastatic Uveal Melanoma (after standard of Care therapy), and mucosal melanoma and Head and Neck Cancer (MC2TCR). Erasmus Univ., Rotterdam NL. N=20. NCT04729543
BI-1607 BioInvent	FcγRIIB-blocking antibody	**Ph. 1b/2a** in metastatic melanomas (including uveal melanoma) which has progressed on pembrolizumab or nivolumab. Excludes patients previously-treated with ipilimumab or anti-Lag-3 antibodies. Combined with low-dose ipilimumab, and pembrolizumab in the 3rd and 4th combination doses. Accruing at Univ. Hospital Essen and 3 other German sites, Spain and UK. N=45 NCT06784648
Opdualag® (relatlimab and nivolumab) BMS	Radiotherapy, Anti-Lag3 Antibody + Anti-PD1 Antibody	**Ph. 2** Concurrent Stereotactic Body Radiotherapy With Opdualag in Metastatic Uveal Melanoma. Prior PD1 or tenebtafusp allowed. Excludes patients with prior liver embolization and >50% liver involvement. Pacific Med Ctr Res Inst, San Francisco N=40 NCT05077280
CarT (IL13Ralpha2)	IL13Ralpha2 CART gene inserted via lentivirus	**Ph.1** In 16 solid tumors, including recurrent Uveal Melanoma. Eligibility based on IL13Ralpha2 expression confirmed by IHC Hscore ≥50 in 10% of tumor specimen. Given by intralesional injection after chemo conditioning. N=18 Accruing at UCLA and Stanford. NCT04119024

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GIM-531 Georgiaimmune	T-Reg Inhibitor (oral)	**Ph. 1 /2** Safety and Tolerability Study of GIM-531 in Advanced Solid Tumors (including UM patients in Dose-escalation phase). Will add a PD-L1 inhibitor N=117. Accruing in 11 US centers, incl. HonorHealth Scottsdale, Angeles Clinic LA, Mass Gen Hosp Boston. NCT06425926
Intratumoral ONM-501 OncoNano **+/- Cemiplimab** Regeneron	cGAM/P-PC7A micelles + Anti-PD-1 Mab	**Ph. 1** In advanced, recurrent solid tumors and Met UM. Combination with cemiplimab in Part 2. Accruing in 9 US sites, and 6 Australia sites. NCT06022029
Cemiplimab Regeneron **+ zev-Aflibercept** Sanofi	Anti-PD-1 Mab + anti-VEGF Fusion Protein	**Ph. 2** Met UM (1st line or previously-treated) combination study. No prior bevacizumab, aflibercept or cemiplimab, no symptomatic autoimmune disease, neurodegenerative disease, GBS, SLE, organ or SC transplant. Open at Moffitt Ca. Ctr. Tampa +3 US sites. N=32 NCT06121180
Olaparib AZ **+ Pembrolizumab** Merck	PARP Inhibitor (oral) + PDL-1 Mab	**Ph. 2** in Met. UM, prior hepatic-directed treatment allowed. N=37, Accruing at Moffitt Ca. Ctr., Tampa. NCT05524935
IOV-3001 Iovance	Modified interleukin-2 fusion protein	**Ph. 1/2** Metastatic UM patients who have received tebentafusp. in Ph. 1 IOV-3001 is given prior to lifileucel (TIL therapy); in Ph. 2 IOV-3001 given after lifileucel. N=42 Accruing at Sarah Cannon Res. Inst. centers in Nashville and Denver (HealthOne DDU). NCT06940739
LNS8801 Linneaus	agonist of G-protein coupled estrogen receptor GPER (oral)	**Ph. 2** In Advanced Metastatic refractory solid tumors. Only Cohort 5 will enroll 10 uveal melanoma patients, who have 2 or fewer lines of prior metastatic therapy. Accruing in 10 US sites. N=280 NCT04130516
NN3201 Novelty Nobility Inc.	c-Kit targeting antibody-drug conjugate with MMAE	**Ph. 1** Advanced, metastatic progressive/refractory solid tumors including uveal melanoma UM patients will be in Cohort B3: Progressive/refractory, ineligible, or intolerant to available standard therapy). Accruing at 5 US sites. N=67 NCT06805825

Compiled and Updated by: Kevin@acureinsight.org (Future Updates planned in July and December each year)

<End of Section A>

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
darovasertib, IDE-196 Ideaya	PKC Inhibitor	**Ph.2** (ASCO 2024) Neoadjuvant treatment prior to definitive management (enucleation, plaque brachytherapy or EBRT): n=15 at datalock, **Median tumor shrinkage (maximum height/base/ volume change) was 11.2%/ 7.6%/ 22.7% after 1 month of treatment and 31.7%/ 11.9% /45.3% after 6 months.** At datalock, 6/9 (66%) currently completed neoadjuvant patients were converted to plaque brachytherapy (n=5) or EBRT (n=1) with 3 ongoing. Investigators discussed implications of darovasertib neo/adjuvant Tx for primary UM patients as possibly offering 2-3 fold lower risk of loss of sight from substantially lower radiation doses reaching and damaging the optic nerve and fovea. Ph 2 TRAEs: postural hypotension (Gr1/2 – 5/33%), syncope (Gr3 – 2/13%), rash (Gr1/2/3 – 10/67%), pruritis (Gr1 – 13%), dizziness (Gr1 – 6/40%), fatigue (Gr1/2 – 60%), nausea (Gr1/2 – 13/87%), vomiting (Gr1/2 – 7/47%), and diarrhea (Gr1 – 11/73%). (Company Update Sept. 2024): **Enrolled 31 Plaque-eligible and 18-enucleation eligible patients. 49% (24/49) patients had greater than 30% tumor shrinkage, with 61% of eyes (19/31) preserved.** Serious adverse events in 5% of patients (overall AEs as listed above), with 3% discontinuation rate. (Update ESMO Oct 2025): Efficacy population, **59%** (19/32) of patients in Co1 (require enucleation) **became eligible for Enucleation Prevention**; for patients with available paired simulations in Co2 (require plaque RT) **Dose Reduction** was seen in 14/17 (**82%**) patients, with 59% (10/17) showing both ≥ 20% DR and a lower 3-year predicted risk of 20/200 vision. **Tumor shrinkage** ≥ approx. 20% in the PoD **was noted in 62% (Co1) & 63% (Co2) of pts**. NCT05907954 **Ph.2** (ASCO 2023) Initial data in in metastatic UM: darovasertib + crizotinib (ALK/ROS1 inhibitor): 35 patients were enrolled; **11 (31%) confirmed PR, 2 (6%) unconfirmed PR, 16 (46%) SD.** (Ideaya website further revealed Progression-Free Survival PFS ~ 7 months). **Ph.2/3 OptimUM-01 Study** (ESMO 2024 Trial-in-Progress poster) N=422. 1st Line Metastatic Uveal Melanoma which is HLA-A*02:01 negative, combined with crizotinib (Ph. 3 randomizes combination vs. Inv. Choice). 31 sites in US+AUS+BEL+CAN +FRA+ GER+IL+ITA+NL+POL+ES+CH+UK. Endpoints: Ph. 2a RP2D, ORR, PFS, Ph.3 OS. NCT05987332 (SMR Oct 2025): OptimUM-01 Initial 41 efficacy-evaluable patients: **Median overall survival (OS) 21.1 months**, **Median progression-free survival (PFS) 7.0 months. Confirmed overall response rate (ORR) 34%, disease control rate (DCR) 90%.** Median duration of response (mDOR) 9 months. TRAEs (>30%) of diarrhea, nausea, edema, vomiting, dermatitis, hypoalbuminemia, and fatigue. No Grade 3 TRAEs >5% were observed. Study continues enrollment in US and Int'l.

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
RP2 Replimune	HSV Type I encoding GM-CSF conjugated to anti-CTLA-4 HuMab	**Ph. 1** (ASCO 2024) Metastatic UM (n=17): RP2 monotherapy, n = 3; RP2 + nivo, n = 14. **Most pts had received both anti–PD-1 and anti–CTLA-4 therapy (12/17 [70.6%]), and 3/17 (17.6%) had received ≥3 prior lines of therapy.** The **Overall Response Rate was 29.4%** (5/17; all PRs; RP2 monotherapy, 1/3; RP2 + nivo, 4/14). The **Disease Control Rate (CR + PR + SD) was 58.8% (10/17)**. Median (range) duration of response was 11.5 (2.8–21.2) months, Three patients with PR still responding 500+ days. Patient responses by HLA -A02:01 status: positive (1 PR and 2 SD) and negative 4 PR and 3 SD). One Patient with liver mets who had failure of their prior nivo+ipi had durable SD/PR at 9 months. Adverse Events (Gr. 1-2 TRAEs; ≥20% overall) were pyrexia, chills, fatigue, hypotension, and pruritus. The only gr.3 TRAE in > 1 pt was hypotension (2 pts receiving RP2 + nivo). IHC Subset (AACR 2024): In 9 PR/SD patients with paired biopsies, Increased intra-tumoral PD-L1 expression & increased CD8+ T-cell infiltration in tumor, not found in PD patients.
belzupacap sarotalocan, AU-011, bel-sar Aura Biosciences	Virus-like Drug Conjugate (VDC), suprochoroidal delivery with laser activation	**Ph. 2** dose-escalation (Sept 2024 Retina Society.): Early-stage choroidal melanoma, before plaque. Final Data- Statistically Significant Growth Rate Reduction in 3-Cycle Regimen (n=22). Tumor Control Rate of 80% (with up to 12 mos follow-up). High Rate of Visual Acuity Preservation in 90% of 20 patients. No Tx-related SAEs or DLTs. Gr.1 anterior chamber inflammation (18%) or anterior chamber cell events (9%) eye pain (9%). Low/no posterior inflammation; no vitritis, choroiditis, retinitis, retinal pigment epithelium changes, or vasculitis. Completed: NCT04417530
roginolisib, IOA-244 iONCTURA	PI3Kδ modulator (oral)	**Ph. 1** DIONE-1 Study (ASCO 2024) Met UM pts n=29 pts (Part A: 9 pts; Part B.1: 7 pts, Part B.2: 13 pts), of which 23 were treated at 80 mg QD (RP2D). Mean time on treatment: 10.7 mo (range: 1.5-39.6 mo). **Objective Response Rate (RECIST 1.1): PR: 1/29 (3%); SD: 21/29 (72%). Median Overall Survival for Part A: 20.8 months (5/9 with 4 pts alive); Part B.1 20.1 months (4/7 with 3 pts alive)**; Part B.2 not determined; 1-year OS rate: Part A 66.7%; Part B.1 71%; Part B.2 immature. **Median OS at 16 wks with Stable Disease 28.5 mos (13/29).** **Ph. 1 Final Data** (ESMO and ESMO-IO 2024): **Among the 29 met. UM patients, 85% had prior therapy with a median of 2 prior lines (range 0-8, and 86% hepatic+extrahepatic mets) median Overall Survival was 16 mos.** compared to historic median OS of 7.2 mo (published meta-analysis control study, Rantala et al 2019). Decrease Tregs, Incr. CD8T and NK cells. At Week 16 (=3.8 mo): pts with SD (median OS: 28.5 mo; 13/29; 45%) and pts with PD (median OS: 10.9 mo; 16/29; 55%). Only two grade 3 toxicities among previously-treated uveal melanoma patients: 5% diarrhea and 2% abdominal pain. Completed NCT04328844 (AACR 2025 Patients with Stable Disease at 16 wks had stat. sig, longer median overall survival (28.5 months) compared to those progressive disease (10.9 months). SD patients had enhanced $CD8^+$ T cell/Treg ratios and downregulation of PI3K/mTOR-associated proteins in plasma.)
IHP and Immunotherapy: **Chemosat® with melphalan, plus ipilimumab + nivolumab** (**Hepzato®**) Delcath, BMS	Delcath IHP (melphalan) Anti- CTLA-4 and PD-1 blockade	**Ph. 2** Rand. CHOPIN Trial (ESMO Oct. 2025): Metastatic UM. 2 cycles Chemosat alternating with 4 cycles of ipi+nivo (n=38) vs PHP x2 (n=38). **Best Overall Response Rate: Combination group: 76.3% (13% CR + 63% PR; 13% SD) vs. PHP group: 39% (3% CR + 37% PR; 45% SD).** **Progression-Free Survival Median months: Combination group 12.8 vs. PHP group: 8.3 (1-year PFS: 54.7% vs 15.8% respectively)** **Overall Survival Median months: Combination group: 23.1 vs. PHP group: 19.6 (2-year OS: 49.6% vs 22.1% respectively)**

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
IHP Chemosat® with melphalan	Delcath IHP	**Ph. 2** SCANDIUM I Trial (ASCO 2024): Long-term follow-up N=87. Delcath Chemostat with melphalan versus Std of Care (immunotherapy, chemo, local control). **The overall response rate was 40% in the IHP group, with a median duration of response of 13.7 months** (95% CI, 11.6-18.3, n=17). At a minimum follow-up of 36 months, the **3-year Overall Survival rate was 18.6%** (95% CI, 10.0-34.8%) in the IHP group compared to 9.1% (95% CI, 3.6-23.1%) in the control group (p=0.23, fisher exact test), and the **5-year OS rate was 16.3%** (95% CI, 8.3-32.1%) compared to 6.8% (95% CI, 2.3-20.3%). The **median OS in the IHP group was 21.4 months** (95% CI, 19.0-30.4 months) compared to 17.3 months (95% CI, 13.8-22.3 months) in the control group (p=0.11, log-rank test). Study conducted at Sahlgrenska Univ. and other sites in Sweden. Completed.
IHP Chemosat® with melphalan combined with ipilimumab + nivolumab Delcath, BMS	Delcath IHP Anti- CTLA-4 and PD-1 blockade	**Ph. 2** SCANDIUM II Study (ASCO 2024): isolated hepatic perfusion (melphalan) in combination with ipilimumab and nivolumab in met UM. IHP followed by combination immunotherapy (four cycles IPI3/NIVO1) (Arm A), or one cycle of IPI3/NIVO1 before IHP followed by three cycles IPI3/NIVO1 (Arm B). N=18, 78% were treatment naïve; 28% had both hepatic and extra-hepatic metastases. Patients received a mean of 2.4 cycles of IPI/NIVO in Arm A and 3.0 cycles in Arm B. There were more IPI/NIVO related adverse events (grade I-IV) in arm B (48 vs. 86). The overall response rate was 38%, 57% in arm A and 22% in arm B, and the median duration of response was 11.9 months (95% CI, 8.2-NE, n = 6). At a minimum follow-up of 18 months, the overall survival rate was 50% (95% CI, 31.5-79.4%) in the whole study population, 56% (95% CI, 31-99%) in arm A and 44% (95% CI, 21-92%) in arm B. **The median OS in arm A was 18.2 months (95% CI, 13.2-NA months) and 17.2 months (95% CI, 14.0-NA months) in arm B.** Sahlgrenska Univ. Sweden. Completed. NCT04463368
ipilimumab + nivolumab with liver Immunoembolization BMS	Lobar Immunoembolization (Lipiodol + GM-CSF) Anti- CTLA-4 and PD-1 blockade	Retrospective Study (ASCO 2023; Univ Iowa) 11 Met UM patients received a total of 58 lobar IE treatments (Lipiodol + GM-CSF q4wks) concurrently with IV Pembrolizumab (200mg q3wks). **4 patients achieved stable disease, and 2 patients achieved partial response**. 6 patients received additional lines of therapy; of these, 4 were enrolled into clinical trials. 5 patients were alive at the time of analysis, and 2 patients were actively receiving IE plus Pembrolizumab therapy. The **median overall survival (OS) from diagnosis was 25.6 months**, and the **median OS from the first IE treatment was 21.3 months**. Complications related to IE treatments: bleeding (1), severe post-procedural pain (2), infection (1), and anaphylactic reaction (1). No unexpected immune-related side effects occurred with Pembrolizumab. Specifically, no immune-related hepatic toxicity was reported in any patient.
IMA-203 Immatics	autologous TCR-T targeting PRAME	**Ph. 1** (ESMO Oct. 2025): Clinical update of IMA203, Ph1 subset of patients with HLA-A*02-01 pos. PRAME Pos. met. Uveal Melanoma (**n=16**): 13 UM patients (81%) having liver and/or extrahepatic metastases, with a median of 2 prior lines of therapy (62.5% had prior tebentafusp). **Confirmed Objective Response was achieved by 67% of the UM efficacy-evaluable patients (10/15) (with 1 patient having an ongoing unconfirmed Partial Response); all patients (16/16) experienced tumor shrinkage. Median Duration of Response 11.0 months, Median Progression-Free Survival 8.5 months** (range 1.4 to 32.9). **Median Overall Survival 16.2 months** (range 3.2+ to 34.2+). Rapid engraftment (median Tmax: 3 days) and sustained persistence of IMA203 T cells (up to 903 days). Safety: LD-related cytopenias in 99% (G3/4). Cytokine release syndrome occurred in 95%, and was mostly low grade (G1: 37%; G2: 47%; G3: 11%; no ≥G4) and mostly resolved by day 14. The Phase 2 portion of the study is now beginning to enroll patients (Study numbers: NCT03686124, EudraCT 2019-002370-31).

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
Ipilimumab + nivolumab BMS	Anti- CTLA-4 and PD-1 blockade	**Ph. 2** (J Clin Onc, Feb 2021) Progressive Metastatic UM GEM1402 Study. 52 patients enrolled. Liver mets in 79%, extrahepatic mets in 56%, elevated LDH in 32%. Stable disease was the most common outcome (51.9%). The primary end point was 12-month OS, which was 51.9% (95% CI, 38.3 to 65.5). The median OS and PFS were 12.7 months and 3.0 months, respectively. PFS was influenced by higher LDH values. Study conducted at L'Hospitalet de Llobreget, Barcelona and 9 other sites in Spain. Completed. NCT02626962 **Ph.2** Met UM with no prior Liver-Directed Tx or Checkpoint inhibitors, with ipilimumab + nivolumab. Jefferson Univ., Philadelphia. Completed NCT03472586 **Ph. 2** (ASCO 2024) **High-risk UM Adjuvant treatment:** nivolumab and ipilimumab, in patients with Primary Uveal Melanoma and Castle Decision Dx UM GEP results of Class 2, and larger primary tumor size (or other 'high-risk' size or chromosomal features). **(HCRN MEL17-309)**. N=50, with median follow-up of 36 months, **3-year median distant metastatic-free survival (DMFS) rate vs. COOG control, was 69.1% vs 45.1%** (two-sided p = 0.012) without any adjustment; and 70.4% vs 43.4% (two-sided p = 0.018) with the propensity score method. The median DMFS was not reached (NR) in the tx cohort vs 33.8 months. **There was a reduction in the risk of distant recurrence with Nivo/Ipi vs control cohort (RR 0.52, 95%CI, 0.309-0.888)**. Median OS has not been reached with only 7 deaths from UM in the Tx cohort so far. Grade ≥3 any-cause AE occurred in 27 pts (54%) . Grade ≥3 treatment-related (TR) AE occurred in 48% (colitis, diarrhea, ALT increase, adrenal insufficiency) . 22 pts (44%) discontinued the treatment due to toxicity (myocarditis, pneumonitis, colitis, hepatitis). One patient died due to immune-related myocarditis. Georgetown Univ. plus 5 US Sites. Completed. NCT03528408 (SMR Nov 2025): Long-term Survival follow-up - Distant Metastasis-Free Survival (alive, without mets) at the 3-year mark was 75% of the 50 patients receiving ipi+nivo, versus 30% of the COOG 1 study's 119 matched patients. **Overall Survival at the 3-year mark among the 50 patients receiving ipi+nivo was almost 83%**, versus 54% of the COOG 1 matched patients. Major side effects from ipi+nivo were as anticipated: most frequently colitis, diarrhea, myocarditis, pneumonitis and hepatitis; each occurring in 10% or less of the patients. Discontinuation due to side effects of ipi+nivo occurred in 22 (44%) of study patients.
BCNU via Transarterial Chemoembolization (TACE) (aka: CE)	High-dose cytotoxic chemotherapy	**Ph. 2** (ASCO 2025) Metastatic UM previously-untreated, with limited liver mets. High-dose BCNU chemoembolization (TACE). 8 patents treated, Overall Survival 14.1 mos, Progression-free survival 9.9 mos. Adverse events gr.3: pain (n=5), hypertension (n=4), incidental pulmonary emboli (n=3), thrombocytopenia (n=1) and an infected biloma. Sixteen (57.1%) patients developed new/nontarget hepatic tumor progression (n=13) or progression of target and nontarget lesions (n=3). Study completed at Jefferson Univ. NCT04728633
relatlimab + nivolumab BMS	LAG3 inhibitor in combination with nivolumab PD-1 inhibitor	**Ph. 2** (ESMO 2024): 27 Met UM patients were enrolled and treated. No prior PD-1, CTLA-4 and/or LAG-3 blocking antibody treatment was allowed. Overall Response Rate in 26 evaluable patients was 7.7% (Partial Response in 2/26). SD and PD were 42.3% (6/18) and 50% (10/18) respectively. 92.6% of patients experienced treatment related adverse events (TRAE): fatigue (55.6%), ALT elevation (40.7%), AST elevation (29.6%) arthralgias (25.9%) and hypothyroidism (25.9%). Note: The Phase 3 Relativity-127 study in metastatic cutaneous melanoma …excludes uveal melanoma patients. **Ph.2** Met UM no prior ICI. Univ Miami & UTSW (Completed enrollment Jan 2025). NCT04552223

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
Sitravatinib Mirati -Plus- **Tislelizumab-jsgr (TEVIMBRA)** BeiGene and Novartis	Multi-TKI VEGFR family, c-MET, and the TAM (TYRO3, AXL, and MER) PD-1 Inhibitor	**Ph. 2** SITISVEAL Study (GEM-2101) Metastatic UM (ESMO 2024): Treatment-naïve patients Met Liver UM (or after failure of 1st line tebentafusp if HLA-A02:01 positive). 16 patients enrolled. 37.5% of the patients had prior tebentafusp, and two-thirds had no prior therapy for metastatic UM. Extrahepatic disease was present in 43.8%, high LDH in 56.2% and high ALP in 31.2%. Median duration of treatment was 6.6 months (95% CI: 3.5-12.2). Overall Response Rate was 18.8%, with 3 confirmed partial responses. Stable disease was the most common outcome (81.2%), achieving a disease control rate of 100% with a median follow-up of 6.9 months (range: 2.8-13.4).Median Progression-Free Survival was 8.3 months (95% CI: 7.2-NR). The projected 1-year OS rate was 79.6% (95% CI: 61.1-100). Grade 3-4 treatment-related adverse events were reported in 8 (50%) patients, the most common being hypertension (25%) and diarrhea (18.5%). Treatment was discontinued due to toxicity in 3 (18.8%) patients. Stuyd conducted at Hospitalet de Llobregat, Barcelona & 3 other Spanish sites. Completed. NCT05542342
225Ac-MTI-201 Modulation Therapeutics	Actinium 225 (alpha) and "carrier" molecule peptide-mimetic targeting Melanocortin-1 receptor (MC1R)	**Ph. 1** (ASCO 2024) MetUM with progression after at least 1 prior Tx. Single IV infusion in SAD, Completed 6 of 12 dose levels, study on-going with no dose-limiting toxicity to-date. **Ph. 1** Update (ESMO 2024) Enrolled eight patients (3 female), median age 65 years (46-83), with median 2 (0-3) prior lines of systemic therapy, four with prior liver directed therapy. Best response has been stable disease n=3, at DL 4 and 5; one response is ongoing at 32 weeks post-dose. There has been no DLTs. Toxicities include leucopenia (1 G3; 1 G2, 2 G4), lymphopenia (1 G3, 1G2, 1G4), neutropenia (1 G3, 2 G4), ↓ platelets (1 G2, 1 G4), anemia (2G1) & high AST (1 G1). Enrollment continuing, MAD pending. Study still opne at one site: Moffitt Ca Ctr, Tampa NCT05496686
IMC-F106C (brenetafusp) Immunocore	ImmTAC targeting HLA-A*02:01 antigen and **PRAME**	**Ph. 1** (ESMO 2022) In multiple tumor types. Among 26 Metastatic Uveal Melanoma patients 11 were evaluable for efficacy: 2PR and 2 SD in six tebentafusp-naïve pts (2 at 11+ mos), no responses in 5 pts with prior tebentafusp.
AMTAGVI (lifileucel, LN-144) Iovance	Tumor Infiltrating Lymphocytes (TIL)	**Ph. 1** (MRA Sci. Summit 2025) Metastatic UM: 10 patients had successful T-cell harvest with 9 patients treated with lifileucel (7 had intra-and extra-hepatic mets) no objective responses seen, median Progression-free Survival 4 mos, Med. Overall Survival 8 mos. Most treated patients had severe depletion of white cells and platelets. Total TIL cell infusions ranged from 100mil - 31.5 Bil. This Pilot study demonstrated lifileucel can be successfully made for Met UM patients. Study now completed at Memorial Sloan Kettering. Supported by grants from MRA and A Cure In Sight. NCT05607095

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
Tumor infiltrating lymphocytes	(TIL) harvest, IL-2 and ex vivo expansion	**Ph. 2** (ASCO 2023) Lymphodepletion Plus Adoptive Cell Transfer With or Without Dendritic Cell Immunization in Patients With Metastatic Melanoma and Metastatic UM. n=96, only 9 patients underwent TIL harvest successful ex vivo TIL expansion. All had active liver mets with a median of 3 lines of prior treatment for advanced disease. 8 of the TIL products were from UM mets (4 soft tissue, 3 liver, 1 combination of soft tissue and liver tumors), and 1 was from primary UM tumor. Best overall response rate per immune-related response criteria was 22% partial response (PR, duration of response was 22.1 months and 16.5 months), 44% stable disease (SD), and 33% progression of disease (PD) for a disease control rate of 66% (PR + SD). Study at MD Anderson, status unknown. **Ph. 2** (SITC Nov 2025) Univ. Pittsburgh-own TIL therapy in 33 patients with metastatic uveal melanoma, regardless of HLA status or number and type of prior metastatic therapies. Median 2 prior therapies, 64% were HLA negative, 70% had both liver and extrahepatic mets (27% had liver mets only), 64% had prior immune checkpoint blockade therapy. Genomic mutations: GNAQ 46%, GNA11 49%, SF3B1 42%, and BAP-1 loss 58%. Patients pre-treated with non-myeloablative lymphodepletion chemo (NMALD: flu+cyclo), then IL-2, and them TIL therapy for up to 6 treatments. Patients' cells were "manufactured" in a specialty immunology lab for an average time of 33 days to compose the TIL therapy with average potency of 52 billion cells. TIL infusion cell product was 69% CD4 positive and 29% CD8 positive (all key factors that may support the following clinical results). Safety: 100% of patients had experienced neutropenia, lymphopenia and leukopenia, 91% thrombocytopenia, 70% anemia, 52% serious hypophosphatemia and 21% hyponatremia, one patient died from myocarditis. Among 31 evaluable patients: Objective Response Rate (ORR) was 23%, with 7 patients having Partial Responses, and median duration of response was 10.8 months. **Among 19 patients who had "reactive TILs" following infusion, the ORR was 36.8% and with 7 PRs observed**, supporting the observation that potency of the TIL infusion product may impact more favorably on efficacy outcomes.
Endogenous T cell therapy	(ECT) targeting SLC45A2-specific CD8 T cells	**Ph.1b** (ASCO 2023) MD Anderson dose escalation study in met. UM pts who express HLA-A*02:01 or A*24:02. Median age 58 years (30-77): 34 pts were enrolled, 33 (97%) pts underwent apheresis and 11 (32%) received infusion of ETC. One dose limiting toxicity (DLT) thought to be unrelated to treatment or underlying cancer (cardiac disorder Grade 5) occurred at the starting dose level with no additional DLTs. The maximum tolerated dose was established as 1 x 1010 cells/m2. The most common treatment-related grade 3 and 4 toxicities were lymphocyte count decrease 9 (82%), hyponatremia 1 (9%), and hypophosphatemia 1 (9%). Per immune-related response criteria (irRC), 4 (36%) pts had stable disease (SD), 6 (55%) had progression of disease (PD), and 1 (9%) was not evaluable for best response. Median overall survival (OS) was 8.9 weeks (wks). OS was 91% at 4 wks, 55% at 8 wks and 46% at 13 wks. **Median progression-free survival was 5.9 wks.** In the 4 patients with stable disease, the median duration of SD was 5.7 months. Study not currently recruiting. NCT03068624 Case Study (AACR 2024): Met UM patient HLA-A2*02-01 Negative. After 12 weeks of stable disease post-first infusion of ETC, a duodenum lesion progressed during treatment, and RNA sequencing demonstrated reduced expression of genes associated with HLA presentation and SLC45A2. Reduced TIL infiltration suggesting tissue-specific immune editing of the tumor cell population.

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
TBio-4101 (TIL) (Turnstone) + **Pembrolizumab** (Merck)	Autologous TIL/IL-2 and Anti-PD-1 Blockade	**Ph. 1** TBio-4101, Lymphodepleting Chemo, IL-2 for Relapsed/Refractory Melanoma, including Met UM patients. Active, not recruiting at Moffit Ca. Ctr. Tampa. N=17 NCT05628883 **Ph. 1** In advanced solid tumors and met UM - US and CA. *Study Terminated Feb 2025*. NCT05576077
lenvatinib Eisai	VEGF, FGF, PDGF, KIT, RET Inhibitor	**Ph. 1b** Study of lenvatinib + pembrolizumab had excluded UM patients (completed). Japan NCT03006887 **Ph.2** (PLUME Study) (ESMO Oct 2025) **lenvatinib + pembrolizumab** in Metastatic UM, no prior Tx with Checkpoint inhibitors: Cohort 1 (n-22) HLA neg. No prior tebe vs. Cohort 2 (n-9) HLA pos. tebe-treated. Pts. Per Protocol at 27 weeks: 15 progressions were observed in Cohort 1, corresponding to a 27-week **PFS of 31.8%** (95% CI 13.9 – 54.9), while Cohort 2 had 11 progressions with a 27-week **PFS of 60.7%** [40.6 - 78.5]. Lenvatinib was held in 39 patients (76%), dose reduced in 13 (26%) and permanently discontinued in 2 (4%) for toxicity. Pembrolizumab was held in 11 patients (22%), and permanently discontinued in 2 (4%) for toxicity. Pembro+lenva met the predefined 27-week PFS success criteria in both Tebe-naïve and Tebe-pretreated cohorts, with particularly encouraging activity in Tebe-pretreated patients. N=51 at Institut Curie, Paris. N=6 Providence, Portland OR. Not currently accruing. NCT05282901
Defactinib (VS-6063) + **Avutometinib (VS-6766)** Verastem	PTK inhibitor (FAK, PyK2 and MELK) Ras-Raf-MEK-ERK inhib.	**Ph. 2** Combination study in Metastatic Uveal Melanoma. N=13 at Jefferson Univ., Philadelphia. Not currently accruing. NCT04720417
SD-101 (nelitolimod) in PEDD LDT system Trisalus	TLR-9 agonist delivered via pressure-delivery to liver	**Ph. 1/1b** Final report: PERIO-01 study (SITC 2024) N=67 Met UM, 45% prior ICI, 18% prior tebe. Among 23 pts receiving SD-101 with nivo or ipi+nivo: 1-year OS rate 74.7% (median, 20.6 mos), 1-year PFS rate 47.6% (median, 8.7 mos), disease control rate 65%. Similar OS in ICI-refractory or ICI-naïve, and not dependent on HLA-A*02:01 status. ctDNA reduction in 77% of 29 pts at all dose levels. Reduction of reduced tumor MDSCs, arginase and increased circulating IL-15 and IL-18. 13% Serious TRAEs observed only in +ICI arms. NCT04935229 Trisalus will announce results for SD-101 in pancreatic cancer in mid-2025, and ACIS will watch for any news from Trisalus if they partner the product with another pharma for further development.
DYP-688 Novartis	PMEL17 targeting antibody-drug conjugate: melanocyte lineage protein highly expressed in UM & cutaneous melanoma	**Ph. 1/2** DYP=688 in Patients With Metastatic Uveal Melanoma and Other GNAQ/11 Mutant Melanomas. (ASC0 2025): Enrolled 60 metastatic UM patients across 7 dose/schedule levels. 60% of patients had 2 prior lines of metastatic treatment (including 33% with prior tebentafusp). Adverse Events in 10-25% of pts: increased calcium levels, dry mouth, fatigue, edema, anemia and constipation. No DLTs, MTD not determined. One patient with metastatic uveal melanoma achieved complete response, with an additional 10 UM patients achieving Partial Response and 26 achieving stable disease. ACIS will watch for any news from Novartis if they will partner DYP688 with another pharma for further development. Sites were in Boston and NYC, AUS, FR, GER, NL, ES, CH. Completed. NCT05415072

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
APG-115 (Ascentage) **+ + pembrolizumab** (Merck)	MDM2/p53 inhibitor + Anti-PD-L1 Blockade	**Ph. 1** (ASCO 2022) in solid tumors: In the cutaneous and uveal melanoma sub-cohorts, confirmed ORR was 24% (2 CRs + 2 PRs/17 Efficacy Eval. pts) and 9% (1 PR/11 EE pts**)**, respectively. **Ph. 2** In metastatic melanoma including UM patients. Enrolling or opening in 13 US sites and 4 sites in Australia. N=230 Keynote B66 Active but no longer recruiting patients as of Aug 2025. NCT03611868
Intratumoral ONM-501 (OncoNano) **+/- Cemiplimab** (Regeneron)	cGAM/P-PC7A micelles + Anti-PD-1 BMab	**Ph. 1** In advanced, recurrent solid tumors and Met UM. Accruing in 9 US sites, and 6 Australia sites. NCT06022029
AloCelyvir	allogenic mesenchymal stem cells infected w/ oncolytic adenovirus: ICOVIR-5	**Ph. 1/2** In Metastatic UM liver mets, prior immune checkpoint blockade allowed. N=16. Hospitalet de Llobregat, Barcelona. Study has concluded enrollment. NCT05047276. EUclinicaltrials.com: 2024-515032-76-00.
SEA-CD40 (cifurtilimab) Pfizer	CD40 agonist antibody, promotes APC and T-cell activation	**Ph. 2:** SEA-CD40 given 10 mcg/kg as an IV infusion on Day 1 and Day 22 of 42-day cycles, along with Pembrolizumab 400 mg as an IV infusion on Day 8 of 42-day cycles. 39 patients enrolled (relapsed/refractory met. UM), 25 evaluated. Confirmed Overall Response 5 of 39 (13%), Progression-free survival 4 mos, Overall Survival available (8 deaths on study). *Study discontinued* (reported on clinicaltrials.gov -Nov 2024).
IKKb-matured, RNA-loaded Dendritic Cells Vaccine	Vaccine Loaded With Autologous Tumor-RNA + RNA Coding for Defined Antigens and Driver Mutations	**Ph. 1** in Met UM N=12 Protocol indicates both SAD and MAD dose levels and schedules, 4pts x 3 cohorts. Universitätsklinikum Erlangen, Hasumi Intl Research Fdn. (CCC ER-EMN), Erlanger Germany. Study status Unknown. N=19 NCT04335890.
LNS8801 Linneaus	agonist of G-protein coupled estrogen receptor GPER	**Ph. 1** (ASCO 2023) 15 patients with metUM, previously treated with a median of 2 prior lines of systemic therapy, were treated with LNS8801 alone/monotherapy (n = 8) or a combination of LNS8801 and pembrolizumab (n = 7). 6 of 7 combination patients had AEs potentially related to study drugs (grades 1-2), with fatigue occurring in more than one patient. Of the 14 patients evaluable for efficacy (7 mono, 7 combo), 7 had disease control (4 mono, 3 combo) resulting in a disease control rate of 50%. 1 patient on combination achieved confirmed PR.
NBM-BMX NovelWise Pharmaceuticals	Selective HDAC 8 inhibitor (oral)	**Ph. 1** Advanced, refractory Solid Tumors. Conducted at Next Oncology, San Antonio. Completed. NCT03726294 **Ph. 1** Advanced, refractory Solid Tumors, in Asian Patients. 2 sites in Taiwan. Completed. NCT03808870
Optune Gio Novocure	Alternating electrical fields (wearable device)	**Ph. 1** Tumor-Treating Fields in Combination With Nivolumab and Ipilimumab in Metastatic Uveal Melanoma HonorHealth Res. Inst., Scottsdale and Angels Clinic, Los Angeles. N=10. Study Completed Aug 2025. NCT05004025

Drug/Sponsor	*Mechanism*	***Updates as of Nov. 28, 2025***
Belinostat (+ Binimetinib) Acrotech	HDAC Inhibitor (oral) (+ MEK Inhibitor)	**Ph. 2** Belinostat plus Binimetinib for patients with Metastatic Uveal Melanoma. Active but no longer recruiting patients at Moffitt Ca Ctr, Tampa. N=32 NCT05170334
[225Ac] FPI-1434 Fusion Pharm/AstraZeneca	IGF-1R radioligand with Actinium 225	**Ph. 1/2** Advanced, refractory solid tumors including metastatic UM. Excludes prior organ or stem cell transplantation. As of Oct 2026, study is no longer recruiting patients at 7 US sites, and in Australia and Canada. N=253 NCT03746431
T-Plex TScan Therapeutics	Autologous Customized T Cell Receptor-Engineered T Cells Targeting Multiple Peptide/HLA Antigens	**Ph. 1** Basket Study Evaluating Safety and Feasibility of T-Plex, in Participants With Antigen-positive Locally Advanced (Unresectable) or Metastatic Solid Tumors (Including patients with HLA A02:01 positive UM in dose-escalation phase). N=840. As of Nov. 2025, active, but NOT recruiting, as TScan decided to pause further enrollment of patients with solid tumors. NCT05973487
Prognostic Lab Tests in Uveal Melanoma:		
Decision Dx-UM® (Approved in US) Castle Biosciences	15-Gene Expression Panel + PRAME in UM	(JCO October 2024) Prospective study (COOG2.1), 1577 primary UM patients, integrated analysis of 15-GEP and PRAME, with 5yrs. follow-up. Med. Time to metastases 22.6 mos (among 17% of pts), local recurrence at 23.0 mos (among 4.3% pts). **At the 5-year study endpoint, Metastasis-Free Survival: Class 1-PRAME neg 95.6%, Class 1-PRAME pos 80.6%, Class 2-PRAME neg 58.3% and Class 2-PRAME pos 44.8%.**
16-Protein prognostic test (Investigational) Castle Biosciences	16-protein panel	(ASCO 2025) Prospective study of 71 patients/samples of aqueous humor with 16-protein panel + PRAME + 7gene NGS to assess malignant potential of small uveal melanocytic tumors. Significant difference in tumor diameter (P=0.003) and tumor thickness (P=0.001) between Class 1 and Class 2 patients. The proteins primarily belonged to Signal Transduction, Disease, and Cytokine Signaling pathways. **The 16-protein test had a sensitivity of 92%, specificity 52%, NPV 92%, and PPV 51%.** *This test remains under development.*
Oncobit® (Approved in EU/CH, pending in US) Oncobit AG	Digital PCR ctNDA test: UM: GNAQ, GNA11, SF3B1 Cut.Mel: BRAF, NRAS	(SMR Oct Nov 2025) Univ. Zurich and MGH evaluated 75 patients with metastatic uveal melanoma. Key findings: metastatic UM patients with a baseline high mutant allele fraction (MAF >5%); before first met. treatment) had a worse prognosis, with median Overall Survival of 4 months (compared with patients with low MAF (med. OS 21 months). Median Progression-Free Survival was 2.5 vs. 3.6 months, respectively.

Compiled and Updated by: Kevin@acureinsight.org (Future Updates planned in July and December each year) <End of Section B>