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: July 25, 2025

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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, visit www.clinicaltrials.gov and search "uveal melanoma" in Condition-Disease, or simply search for NCTxxxxxxxx.

aCUREINSIGHT.org ocular melanoma

Thomas Jefferson University

Melanoma Research Institute of Excellence

Drug/Sponsor	*Mechanism*	***Updated as of July 30, 2025***
darovasertib, IDE-196 Ideaya	PKC Inhibitor (oral)	**Ph. 1/2** Solid Tumors & Metastatic Uveal Melanoma with GNAQ/111 or PRCK: mono, and with crizotinib or binimetib. Enrolling in 8 US sites, Australia, Canada. N=341 NCT03947385 **Ph.2** (ASCO 2024 Trial-in-Progress) Darovasertib for localized uveal melanoma, neoadjuvant 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 beginning Sept 2025, sites not yet listed. NCT07015190 **Ph.2/3** (ESMO 2024 Trial-in-Progress poster) 1st Line Metastatic Uveal Melanoma which is HLA-A*02:01 negative, combined with crizotinib. Enrolling at 31 sites in US+AUS+BEL+CAN +FRA+ GER+ISL+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
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 Met. UM (excludes 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. Enrolling in 20 US sites. NCT06581406
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: 1st Line Tx-naïve (no prior treatment) Uveal Melanoma vs sham injection, Enrolling globally at 30 US sites, Australia, Belgium Canada, Czechia, France, Germany, Israel, Netherlands, UK. N=100 NCT06007690
roginolisib, IOA-244 iONCTURA	PI3Kδ modulator (oral)	**Ph. 2** (OCULE-1 Study) Metastatic UM with progression after at least 1 prior immunotherapy. (2 doses of roginolisib vs. investigator's choice). An extension study will be available for patients who have reached the 24-month efficacy evaluation timepoint. Enrolling at 15 EU sites, with several US sites pending initiation. N=85 NCT06717126

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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) 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. Update (ESMO 2024): Enrollment continuing, MAD pending. One site: Moffitt Ca Ctr, Tampa NCT05496686
[225Ac] FPI-1434 Fusion Pharm/AstraZeneca	IGF-1R radioligand with Actinium 225	**Ph. 1/2** Advanced, refractory solid tumors including UM. Excludes prior organ or stem cell transplantation. Accruing at 7 US sites, and in Australia and Canada. N=253 NCT03746431
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 10 US sites, including Mayo Clinic Rochester MN and Univ WI Madison. NCT05655312
CHEMOSAT® Hepatic Delivery System for Melphalan in sequence with Ipilimumab + Nivolumab Delcath	Liver-directed therapy with high-dose cytotoxic chemotherapy	**Ph. 3** (SCANDIUM-III Study) Percutaneous Hepatic Perfusion with 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, additional COOG sites pending. NCT06932757
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. Accruing in 5 sites in Taiwan. NCT06012695 **Ph. 1b/2** Metastatic Uveal Melanoma, including patients with BAP-1 loss. Pending initiation in US sites late 2025. Study # NBM-BMX-004.
Belinostat (+ Binimetinib) Acrotech	HDAC Inhibitor (oral) (+ MEK Inhibitor)	**Ph. 2** Belinostat plus Binimetinib for patients with Metastatic Uveal Melanoma. Moffitt Ca Ctr, Tampa. N=32 NCT05170334
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

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Melanoma Research Institute of Excellence

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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*02021 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. 14 sites in USA, 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
Kimmtrak® (tebetafusp-tebn) Immunocore	TCR-targeting gp-100 HLA-A*02-01 complex	**Ph. 1/2:** Metastatic UM bulky hepatic disease, and HLA-A*0201-positive. Combination therapy (tebentafusp-tebn and hepatic Immuno-Embolization with GM-CSF. Phase II will compare tebentafusp with hepatic IE GM-CSF and combination of BCNU with TACE. Jefferson Univ., Philadelphia. Enrolling late 2025. N=109 NCT06626516 **Ph. 1b:** (SILVER Study) Adding IL-2 to Tebentafusp to Eradicate Cancer Progression. Met. UM and HLA-A*02:01 positive. N=8 Sydney & Melbourne Australia. NCT07063875 **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 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 enrollment later 2025 only at Thos. Jefferson Univ. Philadelphia. N=19 NCT06414590 **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. Univ. Miami, N=30 NCT06627244 **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
IMA-203 Immatics	autologous TCR-T targeting PRAME	**Ph. 1** Recurrent/refractory Solid Tumors (appears to include uveal melanoma) IMA-203 monotherapy, and in combination with nivolumab. N=476 Enrolling at 5 US sites and in Germany. eNCT03686124 **Ph. 1** Recurrent/refractory HLA-A*02-01 positive metastatic *cutaneous* melanoma, in combination with mRNA-4203. Accruing at Memorial Sloan Kettering NY and MD Anderson Houston. NCT06946225 **Ph. 3** (SUPRAME Study) in HLA-A*02-01 positive metastatic cutaneous melanoma. IMA-203 (vs immunotherapy, TIL, chemo). eNCT06743126

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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. Not actively accruing. 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). Patients will be enrolled in Companion Protocol Cell Harvest and Preparation to Support Adoptive Cell Therapy Clinical Protocol. Univ. Pittsburgh. N=40 NCT03467516
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. Pending initiation July 2025 at Moffitt Ca. Ctr, 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. eNCT05607095 **Ph. 1/2** A Study to Investigate the Safety and Efficacy of IOV-3001 in Adults With Advanced Melanoma (and metastatic UM patients) who will also receive lifileucel. Enrolling at two Sarah Cannon Res. Inst. sites in Nashville and Denver. N=42 NCT06940739
MAGE-C2 engineered T-cells with selected TCR	MC2 highly expressed in melanoma	**Ph. 1/2** MAGE-C2 TCR T Cell in HLA-A2*0201 positive patients with progressing Uveal Melanoma and Head and Neck Cancer (MC2TCR). Erasmus Univ., Rotterdam NL.
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

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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 >ctx conditioning. N=18 Accruing at UCLA and Stanford. NCT04119024
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. Accruing at 20 US centers, including HonorHealth Scottsdale, Sara Cannon Res Inst Nashville. NCT05973487
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). N=117. Accruing in 9 US centers, including HonorHealth Scottsdale, Angeles Clinic LA, Mass Gen Hosp Boston. NCT06425926
Intratumoral ONM-501 OncoNano **+/- Cemiplimab** Regeneron	cGAM/P-PC7A micelles + Anti-PD-1 BMab	**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 + ant-VEGF	**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. Accruing at Moffitt Ca. Ctr., Tampa. 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** in Metastatic UM. **In** Ph. 1 IOV-3001 given prior to lifileucel (TIL therapy), in Ph. 2 IOV-3001 given after lifileucel.
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. NCT05004025
APG-115 (Ascentage) **+ + pembrolizumab** (Merck)	MDM2/p53 inhibitor + Anti-PD-L1 Blockade	**Ph. 2** In metastatic melanoma including UM patients. Enrolling or opening in 13 US sites and 4 sites in Australia. N=230 NCT03611868
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. NCT04130516
NN3201 Novelty Nobility Inc.	c-Kit targeting antibody-drug conjugate with MMAE	**Ph. 1** Advanced, metastatic progressive/refractory solid tumors including uveal melanoma. 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 July 30, 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. **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** (ESMO 2024 Trial-in-Progress poster) N=380. 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+ISL+ITA+NDL+POL+ES+CH+UK. Endpoints: Ph. 2a RP2D, ORR, PFS, Ph.3 OS.
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

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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** Delcath, BMS	Delcath IHP (melphalan) Anti- CTLA-4 and PD-1 blockade	**Ph. 2** CHOPIN Trial (ISOO June 2022): Metastatic UM. Cycles of Delcath alternating with ipi+nivo. N=8 Met UM, Phase Ib update: best overall response rate of 75%, with 1 Complete Response, 5 Partial Responses and 2 Stable Disease. Jan. 2023 Publication Update: **Median progression-free survival 29.1 months, median duration of response was 27.1 months.** So far, no deaths on-study. Leiden Univ Med Ctr, NL Study completed accrual Nov 2024, pending results Fall 2025. NCT04283890
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

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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.
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 nivolumab and ipilimumab, in patients with high-risk Primary Uveal Melanoma (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. Six US Sites. Completed. NCT03528408
BCNU via Transarterial Chemoembolization (TACE)	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

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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
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
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
IMA-203 Immatics	autologous TCR-T targeting PRAME	**Ph. 1** (ASCO 2025): Clinical update of IMA203, in patients with PD1 refractory metastatic melanoma: 70 patients to-date, 16 patients have been enrolled with metastatic uveal melanoma. Ten of the uveal melanoma patients have already achieved a confirmed Objective Response, for an ORR rate of 67% in this small Phase I sub-population. This result appears larger than the 50% of ORRs achieved in 14 patients with cutaneous melanoma in this study.

Drug/Sponsor	*Mechanism*	***Updates as of July 30, 2025***
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. 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. eNCT05607095
Tumor infiltrating lymphocytes	(TIL) harvest, IL-2 and ex vivo expansion	**Ph. 1b** (ASCO 2023) Autologous (patient-specific) CD8+ SLC45A2-Specific T Lymphocytes With Cyclophosphamide, Aldesleukin, and Ipilimumab in Treating Patients With Metastatic Uveal Melanoma. Among 34 patients enrolled, 11 were harvested and treated. Maximally tolerated dose established at 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%). Responses: 4 (36%) pts had stable disease (SD), 6 (55%) had progression of disease (PD), and 1 (9%) was not evaluable for best response. 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. MD Anderson, Houston. Study not enrolling. NCT03068624. **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 status unknown.
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 status unknown. 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 July 30, 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) lenvatinib + pembrolizumab in Metastatic UM, no prior Tx with Checkpoint inhibitors: 2 cohorts in pts with/without prior tebentafusp. N=51 at Institut Curie, Paris. Not currently accruing. NCT05282901 **Ph. 2** Lenvatinib Plus Pembrolizumab In Patients With Immune Checkpoint Inhibitor Naïve Metastatic Uveal Melanoma N=6 at Providence, Portland OR. Not currently accruing. NCT05308901
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 July 30, 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.
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
Decision Dx UM 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 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.*

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