Ocular distribution and efficacy after suprachoroidal injection of AU-011 for treatment of ocular melanoma

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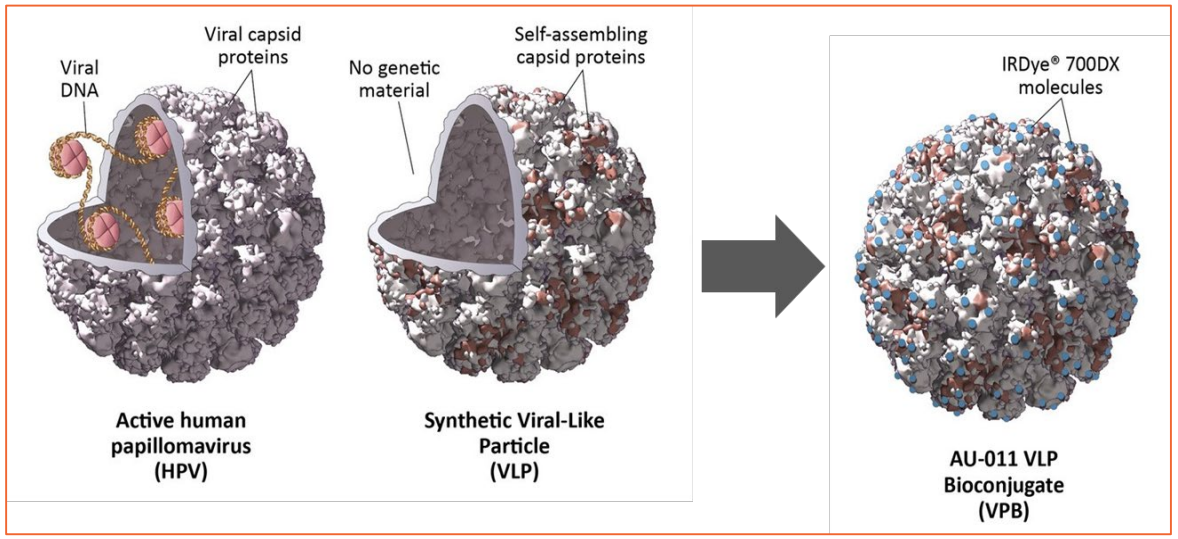
Disclosures

- Anneli Savinainen: Employee at Aura Biosciences
- Cadmus Rich: Employee at Aura Biosciences

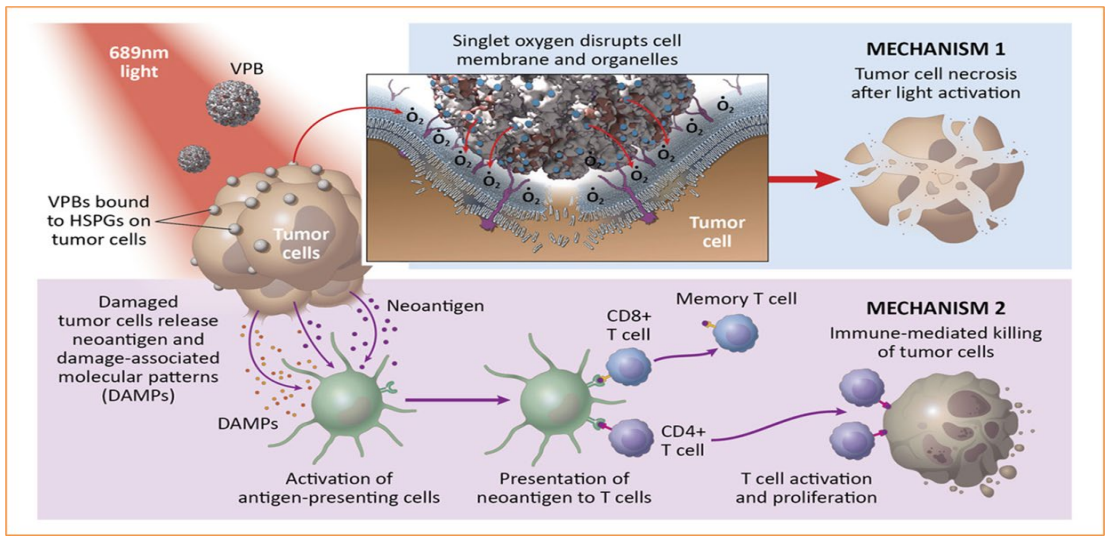
AU-011: A Novel Approach to Target Tumors with Dual Mechanism

- Background:
  - AU-011 is a highly tumor targeted investigational treatment for choroidal melanoma which is designed to selectively bind to specifically modified heparan sulphate proteoglycans (HSPGs) that are upregulated in tumors
  - AU-011 is currently in a Phase 1b/2 open label clinical trial for the first line treatment of primary choroidal melanoma in adults delivered by intravitreal injection followed by photoactivation 6-8 hours later

Structure of AU-011

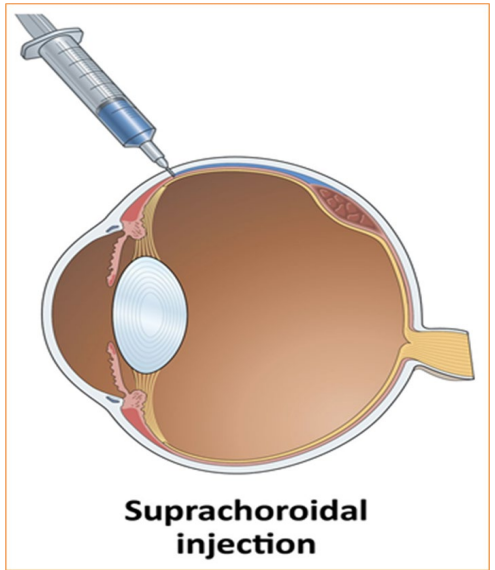


MOA of AU-011

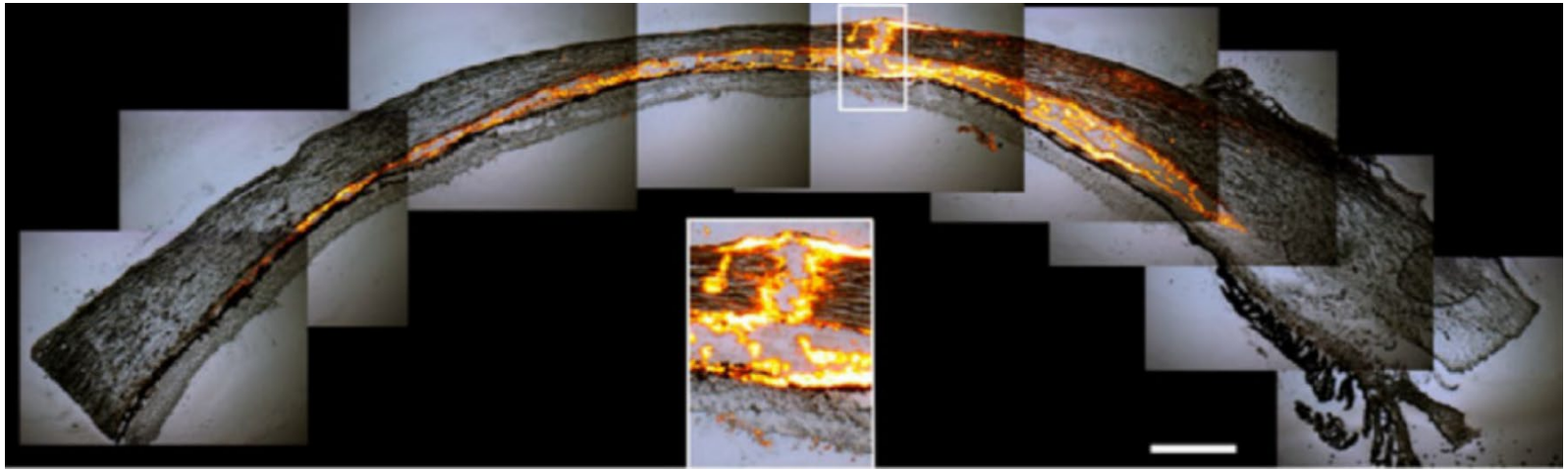


Suprachoroidal (SC) Injection

- The suprachoroidal space (SCS) is a potential space between the sclera and choroid that traverses the circumference of the posterior segment of the eye
- The SCS is an attractive site for drug delivery because it enables targeting of the choroid (the site of the tumor) with high bioavailability, while maintaining low levels elsewhere in the eye
- We believe this route of administration has the potential to improve the therapeutic index of AU-011



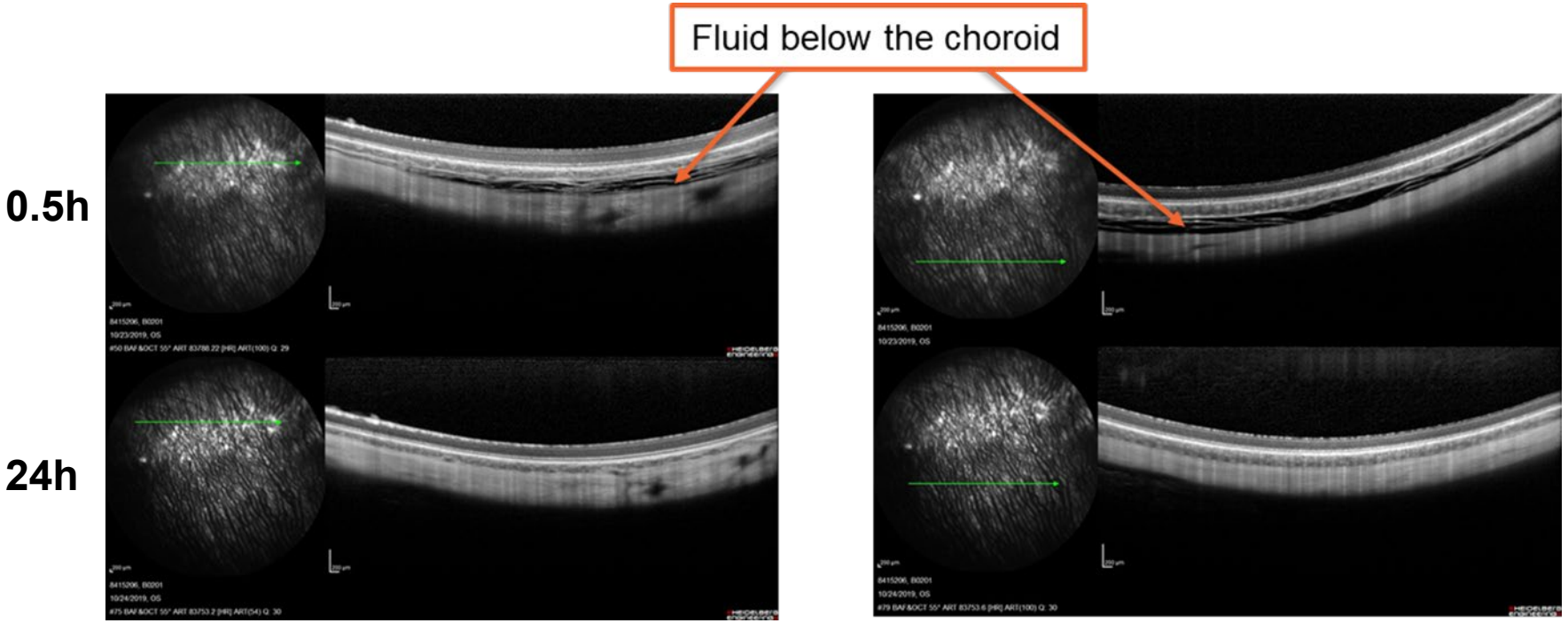
Supra choroidal administration delivers drug (blue) to tumor



Histology of ex vivo porcine eye immediately after microneedle injection of fluorescent particles into the SCS (Chiang et al, Adv Drug Deliv Rev, 2018)

Excellent Distribution in the Suprachoroidal Space after SC Injection in NZW Rabbit

- Immediately after SC injection of VLP-488* (similar physiochemical characteristics as AU-011 with better imaging properties) a bleb is formed in the SCS
- Choroid/retina anatomy returns to normal by 24 hours with flat, potential SCS
- Ocular distribution after SC injection was volume dependent
  - When 100 µl is injected the distribution is approximately 75% of the SCS

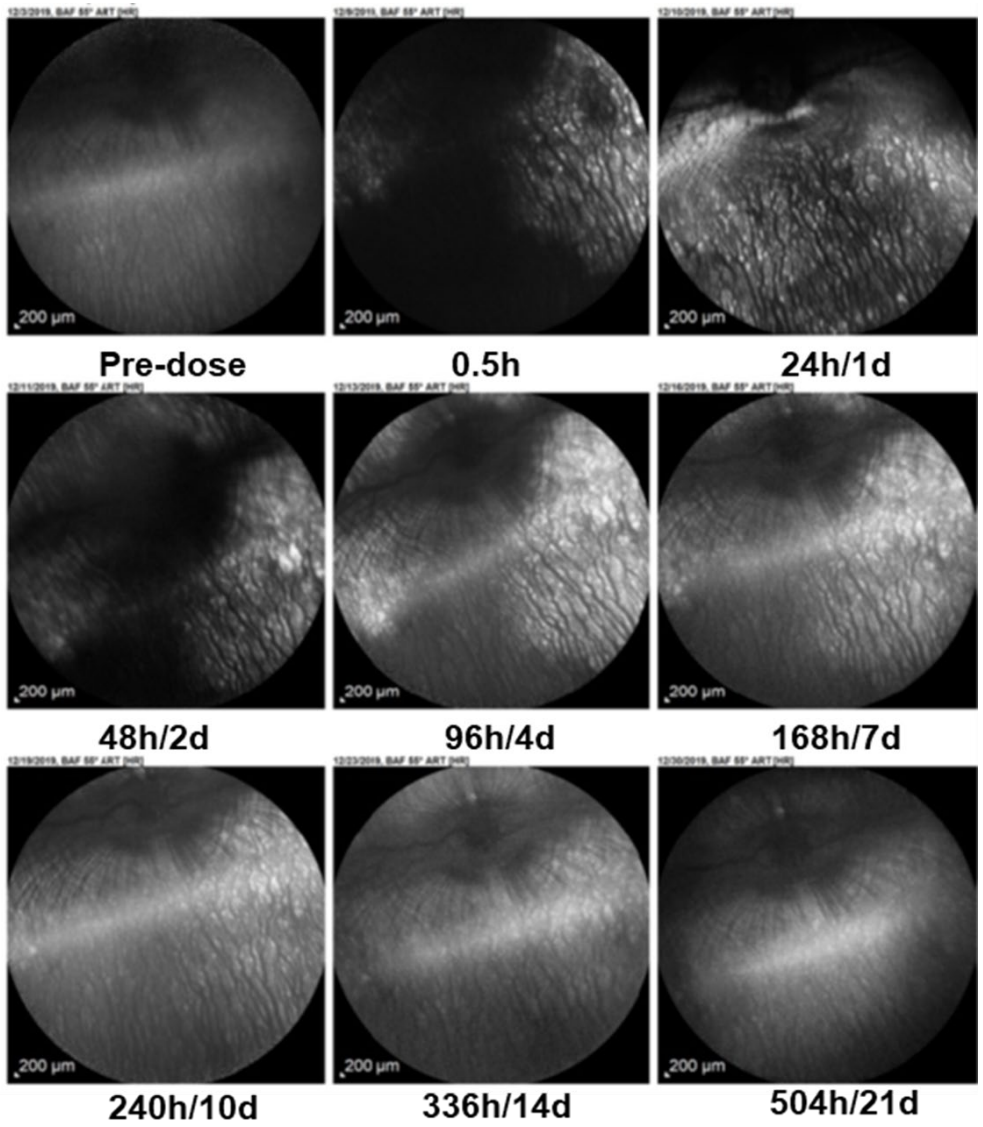


*VLP-488 is the same VLP as in AU-011 conjugated to AlexaFluor488

VLP*Alexa488 was administered in New Zealand White (NZW) rabbits by suprachoroidal injection at different volumes (n=2). Using optical coherence tomography (OCT) and fundus autofluorescence (FAF) ocular distribution was followed over time

Duration through 7-14 days in the Suprachoroidal Space after SC Injection in NZW Rabbit

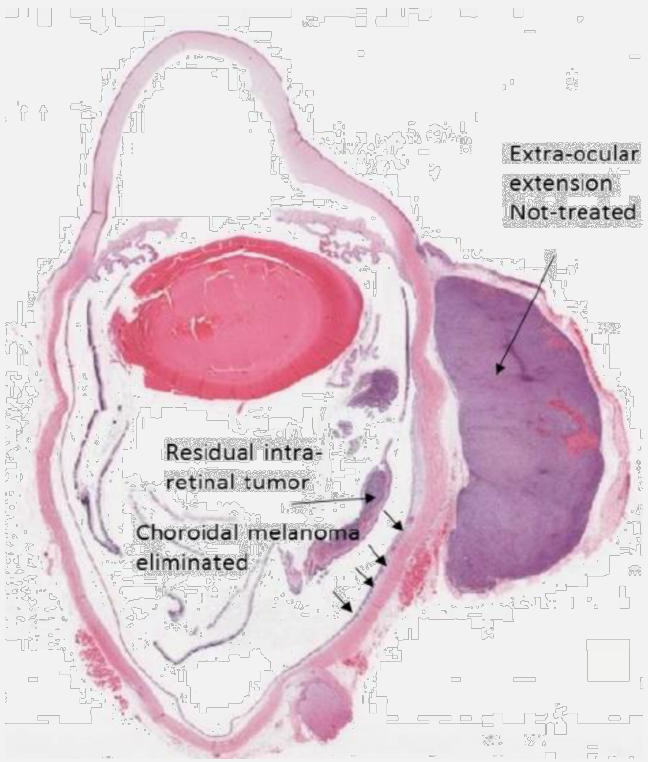
- AlexaFluor488*VLP distributed to the suprachoroidal space after 0.5h with some further distribution at 24h
- Fluorescence was strong through the 168 hour (7 days) post-dose interval
- At the 240 hour (10 days) the fluorescence was starting to fade
- At the 504 hour (21 days) no significant fluorescence above background present



VLP*Alexa488 (100 µl) was administered in New Zealand White (NZW) rabbits by suprachoroidal injection at different volumes
Using optical coherence tomography (OCT) and fundus autofluorescence (FAF) ocular distribution was followed over time
(N=2, Representative images)

Rabbit CM Model: AU-011 Induced Potent Tumor Necrosis

- Orthotopic Rabbit Tumor Model: Choroidal melanoma was induced in New Zealand White rabbits by implanting human uveal melanoma cells (92.1 cell line) into the SCS
- Treatment was initiated when tumors reached ~5mm in tumor diameter
  - AU-011 (100 µg) was administered by suprachoroidal injection followed by laser 16-18h later once/week for 3 consecutive weeks
- Un-treated animals and extra-ocular extensions showed progressive tumor growth
- In AU-011 treated animals there was evidence of acute tumor necrosis by histological evaluation
- Tumor was eradicated in 80% of animals after three treatments with AU-011 followed by laser
- No AU-011 related adverse events were observed

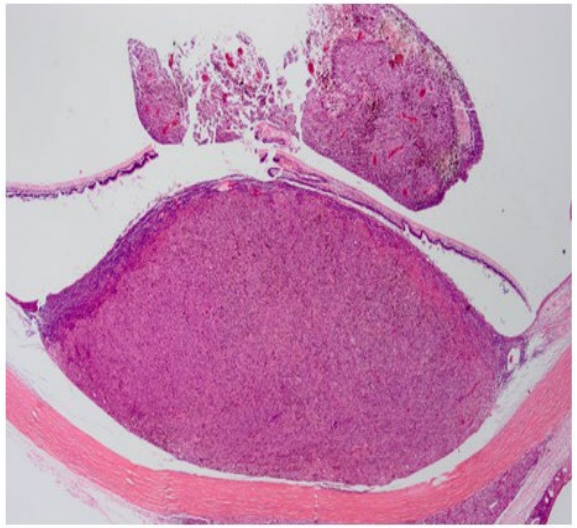


Anti-tumor effect of AU-011 was assessed in a NZW rabbit model of ocular melanoma. Human melanoma 92.1 cells were implanted in the choroidal space. AU-011 was administered by suprachoroidal injection followed by photoactivation once a week for three consecutive weeks. Tumors were evaluated by histopathology. (Model created by and studies performed by Dr. Hans Grossniklaus – Emory University)

AU-011 SC Administration in a Rabbit Tumor Model of CM

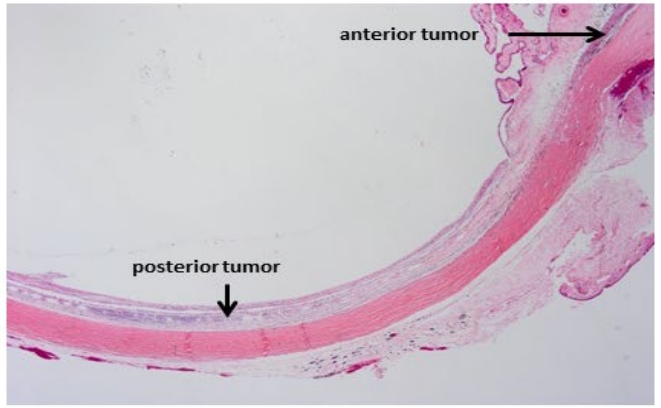
Induced Potent Necrosis in 100% and Complete Responses in 80% of Animals

Control Eye - treated with saline



H&E 5X

Rabbit Eye Treated with AU-011 + laser activation QW3 (day 1, 8 and 15)



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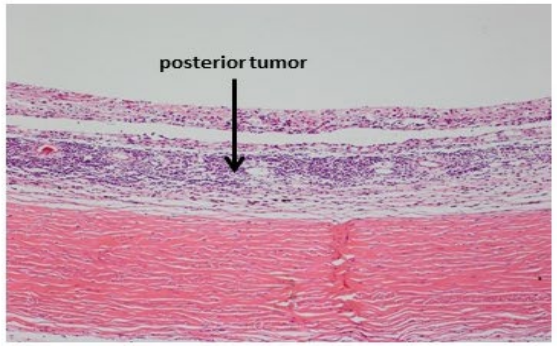
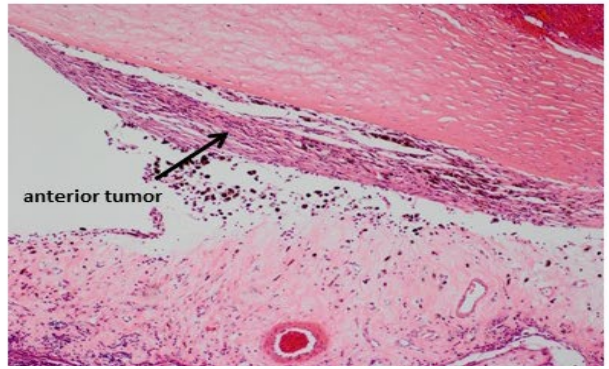


25X



Interior tumor gone, inflammation in choroid, atrophy of overlying retina

Anterior tumor gone, replaced by fibrous tissue and macrophages

Conclusion

- SC injection of AU-011* resulted in excellent distribution and duration at the site of the tumor in the choroid
- Drug exposure in the SC space lasted for at least 10 days
- SC administration of AU-011 followed by photoactivation resulted in a robust tumor response in an orthotopic rabbit ocular tumor model

In summary: Study results support further evaluation of AU-011 administration directly into the suprachoroidal space as a potential first line treatment for primary choroidal melanoma

* VLP-488 has the same physicochemical characteristics as AU-011. VLP-488 is the same VLP as in AU-011 conjugated to AlexaFluor488

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