Nonconfidential

OyaGen Presents a Novel Treatment Candidate for HIV

- **OyaGen, Inc is an upstate NY biotech company that has developed Irino-L, a highly potent antiviral therapeutic for a novel HIV target with intended use in treatment for patients with an HIV infection as part of a therapeutic and/or cure strategy and for pre-exposure prophylaxis (PrEP).**
- **Irino-L is a prodrug whose active metabolite SN38-L blocks Vif mediated destruction of APOBEC3 (A3) proteins that otherwise would serve in innate immunity against HIV.**
  - A3 proteins prevent the spread of HIV infection by inducing catastrophic mutations in the viral genetic code.
  - In the absence of SN38-L, Vif binds to A3 proteins and induces their destruction.
  - SN38-L has a low nanomolar efficacy and an average selectivity index $\geq$ 185 when tested in PBMCs against multiple viral subtypes.
  - The prodrug strategy enables antiviral levels of SN38-L to be maintained for 24 hours with twice daily dosing.
  - In vitro ADMET and PK analyses for Irino-L, SN38-L and an analog with similar activity, O5-SN, have been completed and show a clear path for formulation of the drug for human clinical trials.
- **Irino-L is the lactam analog of Irinotecan derived from camptothecin. Irinotecan is a chemotherapy that is safely used in humans as a standard of care for multiple cancer types and has been shown to be safe across a range of doses and dose intervals.**
  - Studies conducted by OyaGen and in the literature show that lactam analogs of camptothecin such as Irino-L no longer inhibit the cancer target for Irinotecan, Topoisomerase I and therefore have no cellular off-target effects and lower cytotoxicity by comparison.
- **HIV therapeutic and cure strategies that include Irino-L will be a game changer.**
  - Combined treatments of Irino-L and antiretroviral (ARV) drugs are anticipated to markedly enhance therapeutic efficacy, reduce the total amount of ARV required to suppress viremia and will help to mitigate the emergence of drug resistant HIV. Viral resistance studies showed that HIV did not develop resistance to SN38-L in human white blood cells presumably arising from Vif function in A3 degradation requiring several interactions with A3 and other host cellular proteins.
- **Irino-L treatment in combination with latent virus activation may lead to a functional cure.**
- **OyaGen's APOBEC platform technology holds promise for the discovery of first-in-class drug leads for other antiviral therapeutics and anti-cancer therapeutics.**

The company seeks to partner or license Irino-L or obtain a tranched capital raise enabling OyaGen to complete remaining preclinical studies to determine the optimal formulation in order to complete animal safety studies required by the FDA for approval of an IND and initiation of Phase I/IIA clinical studies.