PHOTOSOFT™ SHOWS ACTIVITY AGAINST DENGUE IN PRELIMINARY ASSAYS

Highlights:

- **Eight out of ten Photosoft™ compounds showed antiviral activity against the Dengue virus after exposure to light**
- **The eight compounds have superior Therapeutic Index (TI) values to Monensin**
- **The most effective compound had an EC50 (half maximal effective concentration) value that is >90 times lower than Monensin (control drug)**
- **No compound displayed antiviral activity when protected from light**
- **The global Dengue treatment market is estimated to hit US$1.3bn by 2030 (11.2% CAGR)[1]**

MELBOURNE (AUSTRALIA) 24 October 2022: Invion Limited (ASX: IVX) ("**Invion**" or the "**Company**") is pleased to announce the positive screening results from *in vitro* studies of Photosoft™ on the inhibition of the Dengue virus.

The tests, which were done on ten Photosoft™ photodynamic compounds at eight concentrations, found that eight of the 10 compounds displayed antiviral activity against the Dengue virus after exposure to a specific light wavelength (660nm).

The EC50 (half maximal effective concentration) values of the eight Photosoft™ compounds that showed antiviral activity ranged between 11.1nM and 539nM. These values were significantly below that of Monensin (1031nM), an antibiotic with known activity against Dengue virus was used as a control. None of the compounds were antiviral in the absence of this light source.

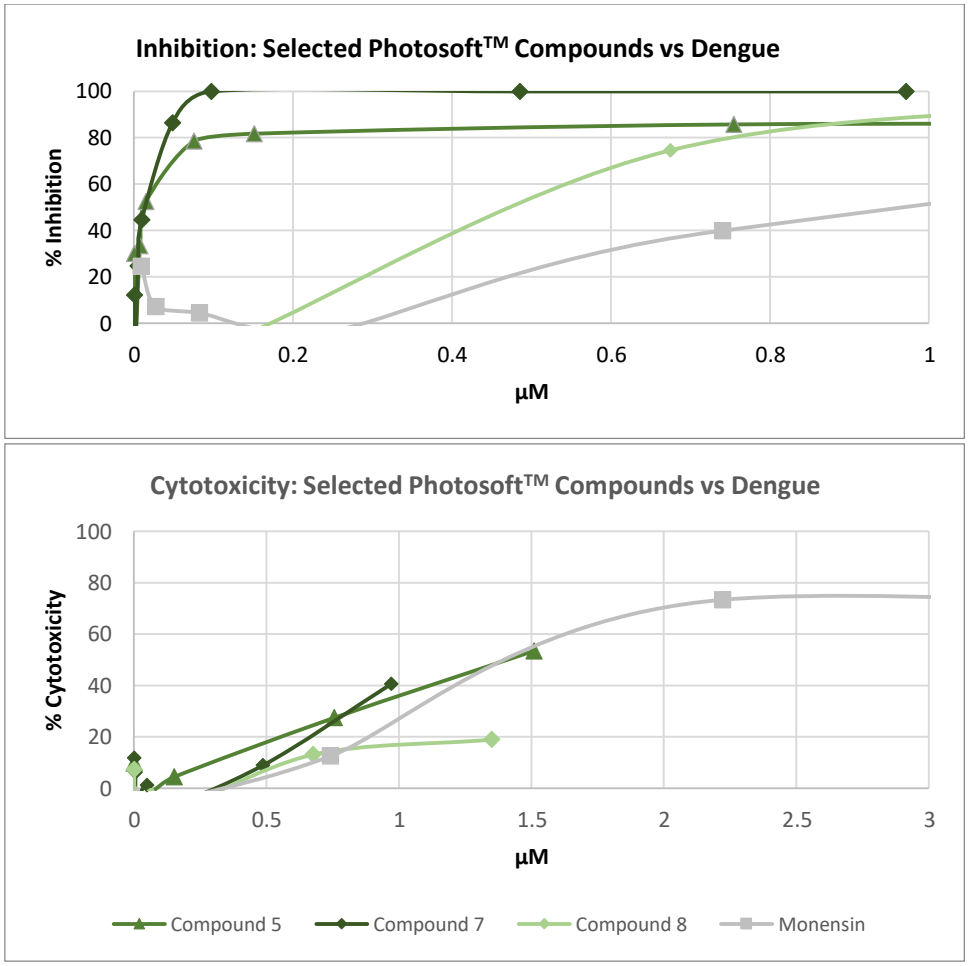

***Figure 1**. The percentage of inhibition of Dengue virus infection (y axis) as a function of the logarithm of compound concentration in µM (x axis). (Right graph) The percentage of cytotoxicity of Vero E6 cells (y axis) as a function of the logarithm of compound concentration in µM (x axis). Data are included for test compounds 5, 7, and 8, and the control drug Monensin, after LED exposure.*

Further, test compound cytotoxicity against the assay cells was low, which together with lower effective concentrations resulted in higher Therapeutic Indexes[1] than Monensin, suggesting higher safety potential for several of the Photosoft™ compounds. In fact, the two most potent anti-Dengue compounds demonstrated insufficient cytotoxicity to determine CC50 (the concentration of the 50% cytotoxic effect) values.

Dengue is spread through the bite of an infected Aedes aegypti mosquito and causes intense pain in joints and muscles, hence its nickname "breakbone fever". The global Dengue treatment market is forecast to hit US$1.3 billion by 2030, reflecting a compound annual growth rate of 11.2%[2].

Methods

Eight dilutions of each test compound were added with virus to the assay cells (Vero E6) and subsequently exposed to a specific wavelength of LED light for 30 seconds or maintained unexposed.

[1] A Therapeutic Index (TI) is frequently determined in viral assays as the dose of a drug that kills 50% of the host cells (CC50) divided by the minimum effective dose to cause 50% inhibition of the virus (EC50). It is generally considered that a drug has a good safety profile if its TI exceeds the value of 10. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4412688/#:~:text=It%20is%20generally%20considered%20that,exceeds%20the%20value%20of%2010)

[2] https://www.biospace.com/article/-dengue-vaccines-market-size-to-reach-us-1-3-billion-by-2030/

Treated cells and virus were then incubated in the dark for 48 hours, and antiviral activity was determined using an immunofluorescence-based assay.

Cytotoxicity was determined by MTT assay on uninfected cells treated with the same concentrations of compounds, after exposure to LED light or maintained unexposed, for the same incubation time.

Results Summary

Of the antiviral test articles, Compound 7 had the lowest EC50 at 11.1nM and Compound 8 had the highest at 539nM.

Compound 1 had the second lowest EC50 (13.5nM) and Compound 5 had the third lowest (18.0nM). Compound 3 and Compound 10 did not display antiviral activity against Dengue under the conditions tested.

	Unexposed			LED exposed		
	EC50 (nM)	CC50 (nM)	TI	EC50 (nM)	CC50 (nM)	TI
Compound 7	>971	>971	-	11.1	>971	>87.7
Compound 1	>1676	>1676	-	13.5	>1676	>204
Compound 5	>1509	>1509	-	18.0	1388	77.0
Compound 4	>1199	>1199	-	27.3	>1199	>43.9
Compound 9	>1082	1015	<0.938	58.1	1072	18.4
Compound 6	>1250	>1250	-	73.7	580	7.88
Compound 2	>1885	>1885	-	89.4	702	7.85
Compound 8	>1350	>1350	-	539	>1350	>2.51
Monensin	1066	2045	1.92	1031	2670	2.59
Compound 3	>1117	>1117	-	>1117	>1117	-
Compound 10	>1331	>1331	-	>1331	>1331	-

***Table 1**: EC50, CC50, and Therapeutic Index (TI) values for test and control compounds against Dengue virus after LED exposure or maintained unexposed ranked in order from lowest EC50 (top) to the highest. TI = CC50/EC50.*

Some cytotoxicity against the assay cells Vero E6, as measured by MTT assay, was observed after light exposure for Compounds 2, 5, and 6, as well as for Compound 9 whether exposed to light or not.

In each instance, greater than 50% cytotoxicity was detected at no more than the highest one or two concentrations tested. The Therapeutic Indices (TI = CC50/EC50) for these compounds after light exposure ranged from 7.85 (Compound 2) to 77.0 (Compound 5).

The two most potent anti-Dengue test articles, Compound 7 and Compound 1 did not demonstrate sufficient cytotoxicity towards Vero E6 to determine CC50 values. Both compounds displayed less than 48% cytotoxicity at the highest concentration tested and little to no cytotoxicity at lower concentrations.

The control drug Monensin displayed antiviral activity against Dengue and demonstrated notable cytotoxicity, both after light exposure and when left unexposed. After light exposure, its EC50 was 1031nM and CC50 was 2670 (TI = 2.59).

Unexposed, its EC50 was 1066nM and CC50 was 2045nM (TI = 1.92). All EC50 determined for the test compounds were lower than the Monensin values, including Compound 7 with an EC50 against Dengue more than 90 times lower than control drug after light exposure.

Next Steps

The Dengue *In Vitro* studies are the third set of successful early-stage tests Invion has undertaken on enveloped viruses, which are viruses with a lipid bilayer membrane on the outer part of the virus.

The other two studies (previously released to the market) where Photosoft™ displayed antiviral activity were on the Zika virus and SARS-CoV-2 (Delta and Omicron variants) viruses.

These tests form part of the testing that Invion is conducting on infectious diseases using the Photosoft™ technology. The results from these and other studies will help the Company decide which infectious disease target(s) have the most promise of advancing to human applications.

This announcement was approved for release by the Board of Directors.

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About Invion

Invion is a life-science company that is leading the global research and development of the Photosoft™ technology for the treatment of a range of cancers, atherosclerosis and infectious diseases. Invion holds the exclusive Australia and New Zealand license rights and exclusive distribution rights to Asia Pacific excluding China (other than Hong Kong, which is included in the Territory), Macau, Taiwan, Japan and South Korea to the Photosoft™ technology for all cancer indications. It also holds the exclusive rights to the technology in Asia Pacific (excluding Greater China) for atherosclerosis and infectious diseases. Research and clinical cancer trials are funded by the technology licensor, RMW Cho Group Limited, via an R&D services agreement with the Company. Invion is listed on the ASX (ASX: IVX). For more information, visit www.inviongroup.com.

About Photodynamic Therapy (PDT)

Invion is developing Photosoft™ technology as a novel next generation Photodynamic Therapy (PDT). PDT uses non-toxic photosensitisers and light to selectively kill cancer cells and promote an anti-cancer immune response. Less invasive than surgery and with minimal side effects, PDT offers an alternative treatment option aimed at achieving complete tumour regression and long-lasting remission.