7 September 2020

Additional information in relation to Opyl's announcement on the 3rd of September 2020

Melbourne, Australia, 7th of September 2020, Opyl Ltd (ASX:OPL) today provides additional information in relation to its announcement titled "***Opyl achieves major milestone with AI platform that forecasts COVID19 clinical trial outcomes"*** released on the 3rd of September 2020 at the request of the ASX.

The original planning of the software platform began in the second half of 2018 and since then Opyl has been actively developing this platform, with it being internally tested and refined over this time. Please refer to Opyl's following previous announcements and investor updates in relation to the 'Clinical Trial Predictor Tool':

1. 19 February 2020;
2. December 2019 Half Year Report;
3. March 2020 Quarterly Activity Report;
4. June 2020 Quarterly Activity Report;
5. June 2020 Investor presentation update; and
6. August 2020 Investor presentation update.

The cost to date has been circa $800K. The software is now functional however the company will continue to further improve and refine the software with future upgrades and expansion of features, which the company anticipates will cost up to another $500K in development. The software platform continues to 'learn' with new information over time and therefore ongoing upgrades are probable. Ongoing developments costs will continue to be funded through current and future revenue, and existing working capital facilities.

The Company will continue to develop its marketing, sales and ongoing customer service support expenditure forecast models as well as revenue models and provides shareholders and the market with updates.

Refer to the Opyl announcement dated 1 May 2020 regarding the R&D tax incentive refund received for the 2019 financial year.

The Company is currently finalising its R&D application for the 2020 financial year.

Opyl's Clinical Trial Predictor Tool/software has been tested internally using standard statistical techniques (AUC, MSE, recall, etc). Internal testing showed that our proprietary techniques have shown strong model predictability (across all trials the AUC is 0.84[1] see Appendix 1)

Opyl defines a 'successful clinical trial' as a trial that completes and achieves its primary endpoint and achieves registration by the regulator. However, there are many other targets/outcomes that the model can predict including time horizons and probability of success for trials to complete each Phase of development (e.g. Phase I, II or III) as well as

[1] For reference, AUC is calculated and interpreted as the following:

1. Take a randomly sampled positive case (successful trial) and a negative case (unsuccessful trial).
2. Use the model to estimate their probability of success.

AUC means that on average the model ranks the positive case higher than the negative case with X% probability, where X is the AUC metric. For all trials (in the validation set), the AUC metric is 0.84, ie 84% probability.

participant drop-out rates, for example to maximise the chance of achieving the primary endpoint and conclusion of each phase.

Machine learning (ML) models have been shown to be good predictors of outcomes in numerous applications across several industries and activities, using historical data as a foundation, when applied to unseen data. For example, ML models can predict the box office success of proposed movies with never seen before plots[2] by examining the characteristics of the proposed movie (the specific actors, producers, runtime, the budget, release dates and so on).

Despite the clinical trial industry expected to grow to USD $69 billion by 2027[3], the use of big data and machine learning techniques to optimise clinical trial design, investment and implementation has been limited, especially in a commercial sense. Some academic research in this field exists[4], this research looks at clinical trial characteristics, however, the Opyl clinical trial predictor tool extends this knowledge and in our opinion improves on accuracy (to better understand and explain and influence clinical trial 'success').

Opyl has developed a prediction system using explainable AI and deep learning. Not only will the prediction tool estimate the chance of a trial's success, but it can also inform trial designers on elements to alter (i.e. opening a specific number of new sites in a selected country or the addition of specific inclusion criteria) within the trial protocol to improve probability of success. The Opyl platform is designed as a decision support tool to augment the role of clinical trial study designers and provide critical information for investors and sponsors.

The platform also uses predictive analytics, a field of artificial intelligence that uses historical publicly available clinical trial data (sole source used by Opyl to date is clinicaltrials.gov) in an internally developed Opyl algorithm (proprietary company technology) to identify patterns of successful completion (i.e. reaching prescribed endpoints or completing a certain clinical Phase) or failure (i.e. failure to meet endpoints or failure to complete the Phase) across a vast number of variables/features (>100) that can make up a clinical trial.

Although the model is not trained specifically on current COVID-19 trials (as no public data is yet available), the clinical trial process has remained relatively universally consistent for decades and provides a reliable foundational model. The Opyl algorithm is trained to recognise patterns and relationships in the clinical trial development process which can help predict outcomes and support decision making.

The Opyl model ingested information from over 300,000 historical trials from ClinicalTrials.gov which forms the training set (see OPL announcement 19 February 2020). The Opyl model examines all sorts of variables and indicators for those trials and weights their impact accordingly. In total, over 21 million data points have been examined across decades of public clinical trial records.

The training data set accesses public data relating to a wide number of therapeutic conditions and trial types, including vaccines and infectious respiratory diseases. A holistic model, which includes data from all trials agnostic to therapeutic area, study candidate or trial design, is best practice, even when predicting COVID-19 associated trials, as trials with unrelated conditions are still likely to contain information that can be generalised to help predict outcomes of COVID-19 trials (e.g. principal investigator experience, number of

[2] https://www.diva-portal.org/smash/get/diva2:1106715/FULLTEXT01.pdf

[3] https://www.grandviewresearch.com/industry-analysis/global-clinical-trials-market#:~:text=The%20global%20clinical%20trials%20market%20size%20was%20estimated%20at%20USD,USD%2049.4%20billion%20in%202020.

[4] https://hdsr.mitpress.mit.edu/pub/ct67j043/release/9

patients, CROs historical performance, number and location of sites, sponsor track record or the success or failure of a vaccine through Phase I, II or III). We believe the Opyl model not only will predict the probability of success, success of not to completion of any Phase and achieving primary endpoint, but also provide insight into the certainty around its prediction and how the study design variables impact the predicted value.

When out-of-sample (unseen) testing of 191 historical respiratory trials and 184 viral trials was conducted, the model produced an AUC of 1.00 for respiratory trials and 0.83 for viral trials demonstrating that accuracy related to viral and respiratory conditions is in line with overall accuracy (see Appendix 1). The model was trained on data from 2005 to 2015. Trials commencing in 2016 where used as the out-of-sample data set, as it was our opinion that this would give a sufficient window for trials to either successfully complete or fail.

In addition to out-of-sample testing, Opyl also conducted out-of-bag[5] testing against the whole clinical trial dataset of 300,000+ trials. Out-of-bag testing provides internal estimates of the likely errors on unseen data (out-of-sample). Out-of-bag testing also allows to test against a much larger dataset, as well as acting as a cross reference point against out-of-sample results. A robust model would expect similar AUC results. Out-of-bag testing produced an AUC of 0.839 which is nearly identical to the out-of-sample AUC (0.04), further validating the results.

As shown by the results above, One of the advantages of machine learning is that out-of-sample forecasts can be made to new data, as the combination of the 21 million data points can be processed using machine learning in a way that the human brain cannot.

Opyl uses a wide range of factors that influence clinical trials, such as clinical sites, clinical stage (Phase I, II or III), prior successes or failures in the area, patient numbers, types, location and patient outcomes in a particular therapeutic area. Currently Opyl inputs over 100 different trial implementation factors into the algorithm to give a 'prediction' on the outcome of a trial or series of trials.

There are currently over 450 vaccines, drugs and treatments in clinical trials for COVID-19. We input all of the publicly available protocol data registered with regulators associated with the COVID-19 studies. From the COVID-19 protocol data set, to date Opyl has identified the probability of success expressed as a percentage, for each trial in completing each Phase of the clinical trial process as well as arriving at a final probability of success score relating to registration of the candidate and achieving market release.

In each of the classes (vaccines and drug therapies), we have identified those drugs and vaccines which returned the highest probability of success score based on the input factors with our algorithm, with ongoing monitoring of the these outgoings as the platform updates with new data.

Clinical trials have many variables, that during the trial may have a substantial impact on the final result. Our predictor score relates to an assessment, based on public data, at that given time and Phase that the drug or vaccine candidate is at. The Opyl model is designed to be repeated regularly to assess the ongoing probability of success as trials progress and new data comes to light.

The Opyl model can be applied to predict the outcome of any trial in any therapeutic area and Opyl has estimates for all current and historical trials across the last two decades.

Stating that COVID-19 is "proof of concept" needs to be corrected in relation to our 3 September Announcement. A more accurate statement is that COVID-19 is the model's first

[5] https://en.wikipedia.org/wiki/Out-of-bag_error

major use case. Opyl has looked at other conditions and individual trials during the development process. Beyond COVID-19 trials, The model has much broader applications and can predict into numerous categories such as, but not limited to:

- Breast Cancer;
- HIV Infections;
- Hypertension;
- Prostate Cancer;
- Asthma;
- Pain;
- Depression;
- Stroke;
- Coronary Artery Disease;
- Cancer;
- Schizophrenia;
- Diabetes;
- Heart Failure;
- Colorectal Cancer;
- Parkinson's Disease;
- Alzheimer's Disease;
- Lung Cancer;
- Cardiovascular Diseases; and
- Rheumatoid Arthritis.

Whilst COVID-19 is a novel condition, from the 300,000+ trials in the database Opyl used, including a vast number of vaccine, virus and respiratory disease trials (7128), the Opyl model is trained using data from related and unrelated conditions and the machine learning algorithm weights each feature according to the importance on predicting the endpoint at the various phases. One of the advantages of machine learning is that once models are trained, they can be generalised and applied into previously unseen data with accuracy providing clarity and ongoing additional evidence, benefiting decision makers.

Several of the Opyl model's features relate to flagging whether a study is related to a viral or respiratory condition. Our internal out-of-sample testing has shown that the model can predict accurately when applied to novel disease conditions, including viruses. In fact, out-of-sample testing (***see Appendix 1***) showed that viral and respiratory conditions perform at least as well as other conditions.

However, there is a large amount of historical publicly available clinical trial data on highly infectious respiratory disease vaccines and therapeutics that is relevant to the COVID-19 use case (ie: Ebola, Influenza, whooping cough, H1N1, H5N1, Enterovirus, Bacterial Pneumonia, Viral pneumonia, Bronchitis, SARS, Rhinovirus and MERS) that were relevant in training the Opyl model and evaluation of ongoing COVID-19 clinical trials.

It is Opyl's expectation that the technology improves clinical trials. The company is responding to a major unmet service need in the global biopharmaceutical and medtech sector in which it is recognised that poor clinical trial designs and recruitment failures need to be reduced and resolved to deliver better returns and that artificial intelligence and predictive analytics is likely to deliver potential solutions. Ref. to Deloitte Insights: *Intelligent clinical trials. Transforming through AI-enabled engagement*. *Feb 2020*.

In 2019, Massachusetts Institute of Technology (MIT) published a clinical trial 'predictor' model which had a number of limitations, identified by the authors. Most notably the MIT paper focused on predicting clinical trial outcomes but did not focus on how the key variables in a clinical trial contribute to the overall prediction. A key feature of the Opyl model is that it uses

explainable AI to not only predict the probability of an outcome, but importantly to provide suggestions as to how variables can be modified to improve outcomes.

A further distinction is that the MIT study only looked at trials that completed. Our model looks at successfully passing the primary endpoint/hypothesis in situ. This approach limits the MIT model to only being applicable to trials at completion, where the Opyl model is applicable at trial outset and throughout, which provides scope to modify protocols, which makes it more commercially applicable in our opinion.

Finally, the Opyl model has an expanded raw feature set of 147, compared to the MIT dataset which, to the best of our knowledge, contains under 30. It is our opinion that missing data and changes in trial protocols once listed, have been handled more appropriately and more reflecting adaptive clinical trial design approaches which is becoming more widespread, particularly during COVID-19, in Opyl's methodology compared to the MIT approach. As part of the ongoing refinement of the platform Opyl will be aiming to increase this raw feature set as part of the improvements and upgrades to the platform, thus continually learning.

It is Opyl's opinion that the model improves on accuracy from previous published work and in the case of the COVID-19 work, provides some insight into the more promising vaccines and therapies. Opyl's model has an overall AUC of 0.84 from internal out-of-sample testing compared to an AUC of 0.78 to 0.81 reported in the MIT paper. Having said that, it should be noted that the targets are different in the two approaches, which does not make them directly comparable and, therefore, it should be noted that this is Opyl's opinion that accuracy is improved on.

In reviewing the publication and the clinical trial influencing factors and the nature of the MIT open source algorithm, Opyl was able to improve, expand and enhance outcomes by developing our own clinical trial predictor model. Opyl makes the statement based on the published data from MIT relative to the Opyl outcomes.

To our knowledge there is no regulatory approvals or authorisations required for the use of this platform. All data accessed is publicly available.

The Board has authorised this announcement for release to the ASX.

-ENDS-

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Opyl is a new generation Australian company that provides leading biopharma and health organisations access to emerging AI-assisted technologies and real-world data insights to understand and improve healthcare design, development and delivery. Opyl works at the intersection of clinical trials, artificial intelligence and social media Our key offering for biopharma, medtech, government and healthcare organisations: • clinical trial recumbent and retention solutions • clinical trial predictive analytics • deep social media insights Our vision is to improve health and wellness by optimising data assets and digital activation to advance technologies for life.

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Appendix 1: Table of model results

Trials	AUC[2]	Number of trials	Actual[3] Successful trials	(Recall[4] at 10%)	(Recall at 20%)	(Recall at 30%)
All trials[1]	0.84	21474	570	329	407	453
Respiratory trials	1.00	191	3	3	3	3
Viral clinical trials	0.83	184	6	3	3	5

1. All trials: Out-of-sample testing is from the 21474 trials that commenced in 2016

2. For reference, AUC is calculated and interpreted as the following:
   1. Take a randomly sampled positive case (successful trial) and a negative case (unsuccessful trial).
   2. Use the model to estimate their probability of success.

   AUC means that on average the model ranks the positive case higher than the negative case with X% probability, where X is the AUC metric. For all trials (in the validation set), the AUC metric is 0.84, i.e. 84% probability.

3. Trials that were reported where primary endpoint was met

4. Recall – the number of successful trials the model ranked in the top x %. For example, the top 10% of trials as ranked by our model included 329 of the 570 successful trials, 3 out of 3 for respiratory conditions and 3 out of 6 for Viral Clinical trials)

Notes

- Model trained on all trials from 2005 to 2015
- Out-of-sample testing is for 2016
- There is a significant lag between trials ending and reported results. If no results are reported after 4 years for the phase that the trial is in, it's assumed that trial failed. In Opyl's opinion late reporting will increase the accuracy of the model, as there is a bias towards reporting trials that successfully completed.