Chronix Biomedical Study Demonstrates Its Blood Test Can Predict Response to Cancer Immunotherapy

- *First study of a liquid biopsy to predict response to immunotherapy*
- *Highly accurate with a PPV of 92% and 100% for progression after one and two cycles respectively*
- *Early discovery of treatment-induced hyper-progressive disease*
- *Published in the peer-reviewed journal, Clinical Cancer Research*

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SAN JOSE, Calif. & GÖTTINGEN, Germany--(BUSINESS WIRE)--Chronix Biomedical, Inc., a developer of novel cancer blood-based molecular diagnostics, announces the publication of positive results of a study using its circulating cell-free tumour DNA-based test as a means to predict therapeutic response to immunotherapy in multiple solid tumour types. The paper, by lead author Dr Glen J Weiss *et al*, was published online today in the journal *Clinical Cancer Research*[1].

"The key finding is the ability of the test to make an early prediction of response and disease control, just three to four weeks after initiation of immunotherapy. The flexibility to switch treatments early on based on an accurate prediction has great potential to improve the treatment of many cancers."
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Immunotherapy has become prominent in recent years as a result of remarkable response rates seen in previously unresponsive cancers and overall survival benefits seen in patients. However, there are several issues with the approach. First, only a minority of patients usually respond or have disease control with treatment. Second, there can be serious adverse effects with immunotherapy, including an acceleration of cancer growth referred to as hyper-progression. Third, immunotherapy is in general very expensive and consequently there is a high cost to healthcare payers given that many patients do not respond.

The publication describes a blinded, prospective study designed to validate an algorithm, based on changes in Chronix's proprietary genomic copy number instability (CNI) score, for predicting response to treatment after one or two cycles of immunotherapy in a range of cancers. The study was conducted using blood samples from 56 patients with different tumour types including lung, kidney, breast, pancreatic, colorectal cancers and melanoma. All patients were undergoing treatment with immunotherapy, mostly anti-PD1 immune checkpoint inhibitors with concurrent chemotherapy[2].

Three important points were observed in this study:

- The study showed Chronix's test provided an 83% overall prediction accuracy in predicting response and disease control/progression, with a positive predictive value for progression of 92% after one cycle of immunotherapy. After a second cycle of

immunotherapy, the CNI-score yielded a 100% positive predictive value for progression.

- Six cases of hyper-progression were observed, five of which could be identified by CNI-score at a significantly earlier time point than by the current practice of imaging (six- nine weeks earlier).
- One patient with progressive disease who had been misclassified as stable on the basis of imaging assessments was able to be identified by the CNI score.

The Clinical Cancer Research paper is the first peer-reviewed publication describing Chronix's CNI-based approach with immunotherapy and may be the first for any therapeutic monitoring strategy based on a liquid biopsy with this class of drug[3].

The study demonstrates that Chronix Biomedical's CNI-based therapeutic monitoring test can identify progressing and hyper-progressive patients earlier than with currently available technologies. This could allow treating physicians to switch progressing or hyper-progressive patients to alternative therapies sooner and achieve better treatment outcomes, as identifying these patients through imaging or other methods can take several months. Furthermore, the fact the study showed accurate prediction of response and disease control with different cancers and with patients undergoing various treatments suggests the test should have broad applicability.

The paper's lead author Dr Weiss commented:

"*The key finding is the ability of the test to make an early prediction of response and disease control, just three to four weeks after initiation of immunotherapy. The flexibility to switch treatments early on based on an accurate prediction has great potential to improve the treatment of many cancers*."

An interim dataset from the study was presented at the *American Society of Clinical Oncology Annual Meeting* last year[4]. Chronix and its collaborators have now published and/or presented results of pilot studies the CNI therapeutic monitoring tests in patients receiving immunotherapy, chemotherapy[5], and radiotherapy. Results of recently completed pilot studies in pancreatic cancer and head and neck cancer have also been submitted for presentation at a scientific meeting later this year.

Chronix intends to conduct a number of larger studies in individual cancers to validate CNI-based testing in specific therapeutic monitoring applications and support regulatory submissions. The first such study in metastatic pancreatic cancer, where the standard assessment of treatment is particularly insufficient, is already well underway.

Chronix Biomedical's CEO, Dr Howard B. Urnovitz, commented:

"*We are pleased to be able to share fully the details of this study with the oncology community, and highlight the performance of our CNI-based test, with the publication in Clinical Cancer Research. With advances occurring almost daily in the treatment of cancer with immunotherapy, we expect therapeutic monitoring of response to gain additional importance*."

About Chronix Biomedical

Chronix Biomedical, Inc. is a US-based molecular diagnostics company developing blood tests for the screening and monitoring of cancer. Chronix's tests use proprietary algorithms to derive a copy number instability (CNI) score from sequencing of circulating cell-free tumour DNA (cfDNA), which can be used in the prognosis, diagnosis and monitoring of therapeutic response to cancer. Chronix already offers supplemental screening evaluation tests based on copy number instability

for diagnosis of breast and prostate cancer. For more information visit www.chronixbiomedical.com.

References

[1] Tumor Cell-Free DNA Copy Number Instability Predicts Therapeutic Response to Immunotherapy, Weiss *et al*. CCR 2017. The publication can be searched on http://clincancerres.aacrjournals.org/content/early/recent

[2] All patients were treated with an approved immunotherapy per the label or under a clinical trial protocol. Patients received anti-PD1 therapy, either pembrolizumab (Merck & Co's Keytruda(R)) or nivolumab (Bristol-Myers Squibb's Opdivo(R)), almost all in combination with chemotherapy. Patients with renal cancer or melanoma received interleukin-2, aldesleukin (Nestle's Proleukin(R)). One patient with melanoma received a combination of an anti-PD1 combined with ipilimumab (Bristol-Myers Squibb's Yervoy(R)), an anti-CTLA4 antibody.

[3] Based on a literature search conducted on behalf of Chronix Biomedical.

[4] "Tumor cell-free DNA copy number instability (CNI) predicts therapeutic response to immunotherapy prior to cycle 2" http://meetinglibrary.asco.org/content/166601-176

[5] Changes in tumor cell-free DNA copy number instability (CNI) predict therapeutic response in metastatic cancers, Weiss *et al*, American Association for Cancer Research 2016 Annual Meeting (see link).

Contacts

Chronix Biomedical, Inc
Dr Howard Urnovitz, CEO, +1-408-960-2307
hbu@chronixbiomedical.de
or
Shard Capital Partners LLP
(Corporate Adviser and Broker)
Dr Wang Chong, +44 20 7186 9948
wang.chong@shardcapital.com