Significant decision made,
Disclosure of the targeted Pain Indication for IRX211

Melbourne, Australia, 10 January 2024 – InhaleRx Ltd (ASX: IRX), ('**IRX** 'or '**the Company'**) an Australian healthcare company developing unique inhaled drug-device products to address unmet medical needs in the pain management and mental health sectors, is pleased to announce that it has nominated Breakthrough Cancer Pain (**'BTcP'**) as the primary area of focus for its proposed Phase 2 clinical trial of IRX211.

- Following pre-IND meeting feedback from the US Food & Drug Administration ('**FDA'**) in March 2023, the Company undertook a detailed and careful evaluation process which has resulted in the decision to promote BTcP as the primary indication of focus for the proposed Phase 2 trial of IRX211.
- The established path to registration for BTcP offers a significant commercial opportunity for IRX211 and is also expected to significantly reduce the overall amount of exploratory work and better mitigate regulatory uncertainty (compared to the Complex Regional Pain Syndrome ('**CRPS'**), with resulting time and cost savings.
- An Australian provisional patent application for the Treatment of BTcP was filed at the Australian Patent Office on 21 December 2023 as application number 2023904186.
- There are many aspects that make BTcP a more attractive acute pain candidate versus CRPS. These include, but are not limited to:
    - BTcP is a well-established condition compared to the paroxysmal pain episodes in CRPS;
    - BTcP has advantageous defined primary endpoints which are expected to improve the probability of data being useful to the FDA in the pursuit of a NDA;
    - Lower placebo response rates are expected for BTcP versus CRPS;
    - BTcP has a very large Total Addressable Market ('**TAM'**); and
    - BTcP has a large potential patient population leading to expected faster recruitment rates.

IRX211 is a cannabinoid derived drug (dronabinol) delivered via inhalation in a fixed dose designed to provide rapid onset analgesia for patients suffering with acute episodic bursts of breakthrough pain, which are generally of short duration, typically lasting minutes to hours, including BTcP and aspects of CRPS.

IRX recently completed its Phase 1 clinical trial for IRX211 and reported pleasing preliminary results for pharmacokinetics (PK), safety and tolerability in healthy male and female subjects. There were also no serious adverse events throughout the duration of the study, the results of which have provided the necessary data to inform the dose required for the next stage of the drug development pipeline - the proposed Phase 2 trial.

IRX conducted a pre-IND meeting with the FDA in March 2023, which provided valuable feedback on IRX's roadmap to an NDA for IRX211 as a treatment for CRPS. Whilst supportive overall, some of the feedback received encouraged the Company to reconsider pain indications for which the path to registration required

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less exploratory work and for which the IRX211 formulation was a closer fit, based on the recent Phase 1 pharmacokinetic ('**PK**') results.

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The Company aims to provide therapeutic solutions to market in a cost-effective and time-efficient manner. In contrast to CRPS, the current drugs approved for BTcP are mainly fentanyl-based (opioids). This means that the known registration strategy employed for these products presents a clearer pathway for IRX211 towards a New Drug Approval ('**NDA**').

The Company's overarching goal remains to achieve a NDA with the FDA. IRX is committed to driving cost efficiencies while delivering outcomes in the shortest time frame possible.

Breakthrough Cancer Pain

According to the 11th revision of the International Classification of Diseases, chronic cancer pain is defined as pain caused by primary cancer itself, metastases or its treatment. BTcP is described as a temporary intensification of such pain that arises either spontaneously or in connection with a particular predictable or unpredictable trigger, even when the background pain is relatively stable and well-controlled.

While the current (mainly opioid-based) therapeutic options play a crucial role in managing pain, their prescription and use requires careful monitoring and adherence to established guidelines to mitigate the significant risks of tolerance, dependence, and opioid-related adverse events. As a result, there is a significant unmet need in the BTcP space for a non-opioid-based rapid-onset analgesic.

It is estimated that approximately half of the adult cancer population experiences BTcP at some point, this can vary based on disease progression, ranging from 39.9% in outpatient clinics to 80.5% in palliative care units[1].

There are an estimated 18.1m cancer survivors living in the US alone[2], with approximately one to two-thirds of patients with advanced cancer and chronic pain experiencing BTcP[3].

IRX211 is aiming to capture a significant share of this market due to its non-opioid nature and rapid onset of action.

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[1] Deandrea S, Corli O, Consonni D, Villani W, Greco MT, Apolone G. Prevalence of breakthrough cancer pain: a systematic review and a pooled analysis of published literature. J Pain Symptom Manage [Internet]. 2014 [cited 2023 Apr 11];47(1):57–76. Available from: https://pubmed.ncbi.nlm.nih.gov/23796584/

[2] https://cancercontrol.cancer.gov/ocs/statistics

3 Davis MP. Breakthrough Pain in Cancer Patients – Characteristics, Impact, and Assessment. US Oncology Hemat 7(1):12, 2011.

Pivot to BTcP as Primary Indication for Phase 2 trial of IRX211

Key points supporting the pivot are:

1. **Established indication:** BTcP is an established indication compared to the new and exploratory nature of breakthrough pain in CRPS, which requires additional discovery work and increased expenditure.

2. **FDA Vouchers:** IRX may be eligible for three FDA vouchers for BTcP, including Fasttrack, Breakthrough and Accelerated vouchers, providing various advantages such as accelerated approval and market access.

3. **Multiple approvals:** BTcP has multiple existing approvals allowing for a clearer trial design, making the path to approval more apparent.

4. **Single pivotal phase 3 trial:** Given BTcP is an established indication with approved treatments, IRX211 may be able to seek FDA approval for a single pivotal Phase 3 trial (as opposed to the standard pathway which often requires multiple phase 3 trials), potentially resulting in time and cost savings.

5. **Larger patient population for BTcP:** BTcP has a significantly larger estimated patient population compared to CRPS, potentially making recruitment for clinical trials faster and more cost-effective. The increased patient population may make it easier to conduct large-scale clinical trials and gather sufficient evidence to support the drug's efficacy and safety.

6. **Commercial opportunity for BTcP drug:** The commercial opportunity for an approved BTcP drug is substantial. IRX has completed an assessment of this opportunity and the IRX Board is satisfied that the potential value creation opportunity justifies the adoption of BTcP as the target pain indication for the proposed IRX211 Phase 2 clinical trial programme.

The Company previously completed a formal tender process for its Phase 1 and 2 clinical trial requirements for IRX211 on the basis of CRPS as the primary pain indication ('**the Tender'**). This ultimately led to shareholders approving the appointment of Ingenu CRO Pty Ltd (a subsidiary of major shareholder, Cannvalate Pty Ltd) as the Contract Research Organisation ('**CRO'**) to oversee the trials at an Extraordinary General Meeting on 17 February 2023.

While the pivot to BTcP (as outlined above) provides the potential for overall significant time and cost savings across the entirety of the clinical development timeline for IRX211 (versus CRPS), the change of focus to BTcP as the primary indication for the Phase 2 trials is initially expected to result in a change in scope for the proposed IRX211 phase 2 trial. This change in scope is currently being evaluated by IRX management, but is expected to require an increase in the number of trial participants versus what was included in the Tender. Accordingly, it is expected that the cost of this trial and its duration will likely exceed what was included in the Tender. A further up-date will be provided once this evaluation process has been completed.

To increase the probability of success, it is critical that the Company remains agile so that it can mitigate risks, as well as take advantage of new opportunities. It does this by carefully considering study data, regulatory feedback and market dynamics in context and as they eventuate to ensure value is maximised for the Company and its shareholders.

Notwithstanding the above, CRPS remains a viable supplementary pain indication for IRX211 and it is the Company's intention that opportunities for the application of IRX211 for CRPS will be explored further once the BTcP indication pathway is more thoroughly investigated and developed.

CEO, Mr Darryl Davies said; "IRX's ability to be nimble has served as a significant advantage in this particular case. Feedback from the FDA from earlier in 2023 resulted in a comprehensive review of potential alternative pain indications. This work has provided us with confidence that BTcP will provide a combination of primary endpoints that are better suited to the characteristics of IRX211 (compared with those of CRPS), resulting in a better-established pathway with a resultant increase in the probability of success."

IRX's Chief Scientific Officer, Dr Rob Jenny, said "We are excited to apply the learnings made while exploring the orphan disease CRPS as a drug development target to the much larger BTcP patient population. We believe IRX211 will find its way to market more rapidly via a clinical programme involving the BTcP population and will underpin further product extensions targeting other similar pain indications, including CRPS."

Authorised by the Board of Directors.

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About InhaleRx Limited (ASX: IRX) – www.inhalerx.com.au

InhaleRx Limited is an Australian healthcare company which is developing unique medicinal drug-device products to address unmet medical needs in pain management and mental health sectors.

The overarching goal is to pursue U.S. FDA approval and registration to treat Panic Disorder and pain using rapid and cost effective regulatory pathways, such as 505(b)(2). A 505(b)(2) application is a NDA that contains full reports of investigations of safety and effectiveness where at least some of the information required for approval comes from studies available in the public domain.

There is a significant economic opportunity for IRX and the Company's shareholders as these carefully selected medical indications under investigation currently have extremely limited treatment options, whilst also offering a low side effect profile.

IRX holds an innovation patent and provisional patents for the nominated indications and the Company plans to continue to strengthen this position.