ISTITUTO RICERCHE APPLICATE

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TO WHOM IT MAY CONCERN
DECLARATION

I.R.A. Istituto Ricerche Applicate S.p.A., Viale delle Industrie 8, 20865 Usmate Velate (MB), Italy, declares that for the medical device **Iradyn** (**REF. 40350** and progenitor medical device: **Iradyn**) the following clinical investigation was performed:

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Summary of Clinical Investigation Report (Iradyn) OPIRA/0121/MD: MEDICAL INTENDED USE

OPEN, NON-COMPARATIVE, MULTICENTRE CLINICAL INVESTIGATION TO EVALUATE THE PERFORMANCE AND SAFETY OF THE MEDICAL DEVICE IRADYN® (POLYMERIZED POLYNUCLEOTIDES) INTRA-ARTICULARLY ADMINISTERED IN SUBJECTS WITH OSTEOARTHRITIS OF THE KNEE

this document is a detailed **Clinical Investigation Report (CIR)** for the medical device **Iradyn**, a gel based polymerised polynucleotides (PDRN) (Class III, CE marked under both MDD and MDR). This specific study, identified by CIP Code OPIRA/0121/MD, is classified as a Post-Marketing Clinical Follow-up (PMCF) study under MDR Article 74, aiming to confirm the performance and safety of an already marketed device without additional invasive procedures.

Study Objective: The primary objective of this clinical investigation was to evaluate the overall performance of the medical device IRADYN gel for intra-articular injection in terms of change in ROM (Range Of Motion) parameters and VAS (Visual Analogue Scale) for pain (at rest) scores assessed by Investigators and patients at 14 weeks (98 days) after the initiation of treatment, compared to Baseline visit (visit 1, day 0).

Study Design: This was an open, non-comparative, multicenter clinical investigation conducted in Romania. It involved **45 patients** over an approximate **14-week (98-day) follow-up period**. Patients received from 1 (mandatory) to 7 intra-articular injections of IRADYN gel (at day 0 and, if needed, at days 7, 14, 21, 28, 35 and 42). The study adhered to ISO 14155:2020 and MDR (EU) 2017/745 guidelines.

Key Findings:

- **Efficacy:** the results of this study confirm the effectiveness of IMD (Investigational Medical Device) administration IRADYN, polymerized polynucleotides (PDRN) gel for intra-articular injection) in patients with knee osteoarthritis. The performance of the IMD was proved by the change in ROM (Range Of Motion) parameters (AKF, PKF, AKE, PKE) and VAS score for pain at rest at 14 weeks (98 ± 4 days) compared to baseline, assessed respectively by the Investigator and the patient. The assessment of performance made by the Investigator through the PEGE (Physician Efficacy Global Evaluation) assessed at week 14 (day 98) indicated a high performance of the IMD as well.

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- **Safety:** IRADYN demonstrated a high safety profile in this trial and therefore as the final conclusion, it can be stated that the administration of IRADYN gel is safe, effective and showed to have lasting effects in improving symptomatology of the patient' s knee OA (Osteoarthritis), thus confirming the IMD' s overall performance.

Conclusion: The clinical investigation confirmed that the administration of Iradyn is **effective and safe**. The results validate the hypotheses formulated in the Clinical Investigation Plan, reinforcing the known favorable risk-benefit profile of the device. The study acknowledges the absence of a control group as a limitation, justified by its non-comparative PMCF nature.

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Clinical Investigation Plan Code	**OPIRA/0121/MD**
ClinicalTrials.gov Identifier	**NCT05206474**
Study type	**Interventional**
Investigational Medical Device	**Iradyn:** Intra-articular gel based on polymerized polynucleotides (PDRN) Investigational product: the medical device Iradyn (class III medical device -Directive 93/42/EEC, already marketed EU and outside EU) is a sterile, injectable, non-pyrogenic, re-absorbable product made of polymerized polynucleotides (PDRN) of animal origin. Iradyn is a class III CE marked medical device (according to Council Directive 93/42/CEE and subsequent modifications and integrations). Iradyn is included in the "legacy" medical devices according to Medical Devices Regulation (EU) 2017/745 – MDR article 120 Regulation (EU) 2023/607.
Indication studied	Intra-articular injection in patients affected by knee osteoarthritis (medical intended use)
Study Title	**OPEN, NON-COMPARATIVE, MULTICENTRE CLINICAL INVESTIGATION TO EVALUATE THE PERFORMANCE AND SAFETY OF THE MEDICAL DEVICE IRADYN® (POLYMERIZED POLYNUCLEOTIDES) INTRA-ARTICULARLY ADMINISTERED IN SUBJECTS WITH OSTEOARTHRITIS OF THE KNEE**
Study Period	Initiation Visit Date: 10-Mar-2022 (centre no. 1) First Patient First Visit: 18-Mar-2022 (centre no. 2) Last Patient Last Visit: 24-Aug-2022 (centre no. 1) Database lock: 14-Oct-2022
Study Duration	14 weeks (98 days)
Number of patients	Planned patients: 45 patients (50 patients considering a drop-out rate equal to 10%). Screened patients: 50 Enrolled patients: 50 Number of dropouts: no dropouts
Results	**The results of this study confirm the effectiveness of IMD administration (IRADYN, polymerized polynucleotides (PDRN) gel for intra-articular injection) in patients with knee osteoarthritis.**

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	The administration of the injections following the first mandatory one was considered optional as per the investigation plan and decided by the Investigator. **IRADYN gel showed to be able to improve the symptomatology of osteoarthritis of the knee from the first IMD administrations.** **The performance was also confirmed by the absolute change in VAS for pain (on moving and on pressing) at all visits compared.**

Usmate Velate, 17th November 2025

I.R.A. Istituto Ricerche Applicate S.p.A.
Dr. Ugo Citernesi
Scientific Director