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Writing Sample (unedited)

Protocol Synopsis and Table of Schedule of Procedures drafted from unstructured notes

Name of Sponsor/Company: **Name of Investigation Drug:** **Name of Active Ingredient:**	DoloPharma Inc. Nixdolor tablets NIX-123
Study Title:	A Phase 2 Randomized, Double Blind, Placebo-Controlled Study of the Safety and Efficacy of Oral Administration of Analgesic NIX-123 at 100 mg/day in Subjects with Osteoarthritis
Phase of Development:	Phase 2
Objectives:	1. To evaluate the safety of oral administration of NIX-123 (100 mg/day) in tablet format versus vehicle-placebo in subjects with osteoarthritis (OA) 2. To evaluate the efficacy of NIX-123 in subjects with OA
Number of Subjects Planned:	Approximately 80 evaluable subjects with OA
Main Criteria for Inclusion	Be a male or non-pregnant female 18 years of age or older having received a primary diagnosis of OA in the knee (meeting American College of Rheumatology clinical classification), displaying OA symptoms for at least 6 months, ambulatory, reporting knee pain for at least 5 days per week for the previous 3 months at a pain level of ≥5 points on a 0-10 numerical rating scale (NRS), with no knee surgery or corticosteroid injections in the knee in the past 3 months, no use of opioid medication for more than 4 days in the week before screening, and no clinically significant abnormalities in clinical laboratory evaluations and vital signs.
Duration of Study	The study consists of a 3-day screening period, a 7-day washout period A for washout of all prior pain medication, a 7-day dosing period A with Nixdolor or placebo, a second 7-day washout period B for washout of treatment A, a second 7-day dosing period B with Nixdolor or placebo (whichever was not used in dosing period A), and a 7-day follow-up period culminating in an End-of-Study visit. Including the screening period, the maximum study duration for any given subject is 38 days
Investigational Drug, Reference Therapy, Dose, and Mode of Administration:	**Investigational Drug**: Nixdolor analgesic provided as oral tablets for daily ingestion, each containing NIX-123 (active ingredient) **Reference Therapy**: Vehicle placebo lacking Nixdolor will be provided in identical tablets **Dose**: The dosage level to be evaluated will be 100 mg of Nixdolor per day **Administration**: Nixdolor will be administered as one oral tablet. Placebo will be administered as one oral tablet.

Study Design/Methodology:	The study is a phase 2, randomized, double-blind, placebo-controlled crossover design evaluation of safety and efficacy of oral administration of one dosage level of Nixdolor (NIX-123) in subjects with osteoarthritis. As it is a double-blind study, neither subjects nor clinical staff will have knowledge of the treatment allocation. The evaluated dosage level will be 100 mg of Nixdolor per day. A total of 80 subjects will be enrolled; subjects will be randomized to either receive Treatment Sequence I (Nixdolor during dosing period A and placebo during dosing period B) or Treatment Sequence II (placebo during dosing period A and Nixdolor during dosing period B), at a ratio of 1/1. After consent has been obtained, subjects will be screened from Day -10 to Day -8 for eligibility to enter into the study. Study eligibility will be established by medical history, prior medication history, physical examination, vital signs, clinical laboratory tests, urine drug screen for opioids, and pregnancy test. Subjects must meet all entry criteria at screening to be enrolled. Each subject will be provided an adverse events (AE) diary to record any AE that may occur during the study. They will also be provided rescue medication to alleviate any intolerable pain, and a rescue medication diary to record such use. Subjects are instructed not to take more than 2 g of rescue pain medication (acetaminophen/ Tylenol®) per day or any rescue pain medication within 12 hours before each visit. Enrolled subjects will undergo a 7 day washout period A (Day -7 to Day -1) to wash out any prior pain medication. They will be asked to return for baseline and end-of-treatment visits on the day before, and on the last day of, each dosing period. On these visits, safety evaluations will be taken consisting of AE monitoring and vital signs collection, while efficacy evaluations will consist of reporting pain measurement on the 1-10 NRS and monitoring daily rescue medicine consumption. Baseline visits will also be used to confirm ongoing eligibility of subjects. Baseline visits before dosing period A (BL-A) will take place on Day -1. From Day 1 to Day 7, subjects will self-administer treatment A (Nixdolor or placebo) oral tablets for seven consecutive days. They will return to the clinic on Day 7 for End-of-Treatment A (EoT-A) evaluations. Dosing period A will be followed by washout period B (Day 8 to Day 14) to washout treatment A.

	The baseline visit prior to dosing period B (BL-B) will take place on Day 14. From Day 15 to Day 21, subjects will self-administer treatment B (placebo or Nixdolor) oral tablets for seven consecutive days. The subjects will return on Day 21 for the End-of-Treatment B (EoT-B) evaluations. Seven days after the end of dosing period B, on Day 28, subjects will return to the clinic for End-of-Study (EoS) evaluations consisting of safety evaluations, clinical lab tests, and a physical examination.
Safety Evaluations:	Safety will be assessed through physical examination, clinical laboratory tests, and vital signs collection at the screening visit and EoS visit; and through vital signs collection and AE monitoring during the baseline and EoT visits for each dosing period. The relevant data summaries will be presented by Treatment Sequence.
Efficacy Evaluations:	Efficacy will be assessed through monitoring of pain measurements at the screening visit; and through pain measurements and rescue medication consumption at the baseline and EoT visits for each dosing period. The relevant data summaries will be presented by Treatment Sequence.
Pharmacokinetic Evaluations:	There are no pharmacokinetic evaluations in this study

Schedule of Procedures

Study Period		**Washout A**		**Dosing period A**							**Washout B**		**Dosing period B**							
Visits	**1. Screening**		**2. BL-A**							**3. EoT-A**		**4. BL-B**							**5. EoT-B**	**6. EoS**
Study Day(s)	[-10 to -8]	[-7 to -2]	-1	1	2	3	4	5	6	7	[8 to 13]	14	15	16	17	18	19	20	21	28
Informed Consent	X																			
Demographics	X																			
Medical History	X																			
Physical Examination	X																			X
Vital Signs	X		X							X		X							X	X
Clinical Laboratory Tests	X																			X
Entry Criteria (*reconfirm)	X		X*							X*		X*							X*	
Treatment A Administration (NIX-123 or placebo)				←----------X----------→																
Treatment B Administration (Placebo or NIX-123)													←----------X----------→							
Pain Measurement	X		X							X		X							X	
Prior & Concomitant Medication	←----------X----------→																			
Rescue Medication		←----------X----------→																		
Adverse Events		←----------X----------→																		