

# Single- and Repeat-Dose Pharmacokinetics of Sublingual Sufentanil NanoTab™ in Healthy Volunteers

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# Sufentanil: A Superior Opioid

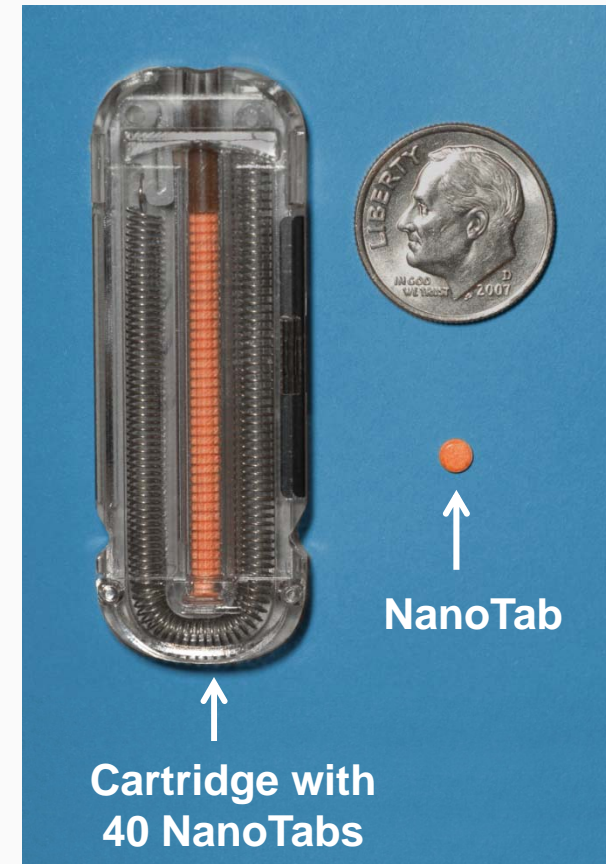
- Approved for intravenous (IV) and epidural administration<sup>1</sup>
- High therapeutic index<sup>2</sup>
- No active metabolites<sup>3</sup>
- Rapid transmucosal uptake

Opioid	Therapeutic index <sup>2</sup>
Methadone	12
Meperidine	28
Morphine	70
Hydromorphone	232
Fentanyl	300
<b>Sufentanil</b>	<b>25,000</b>

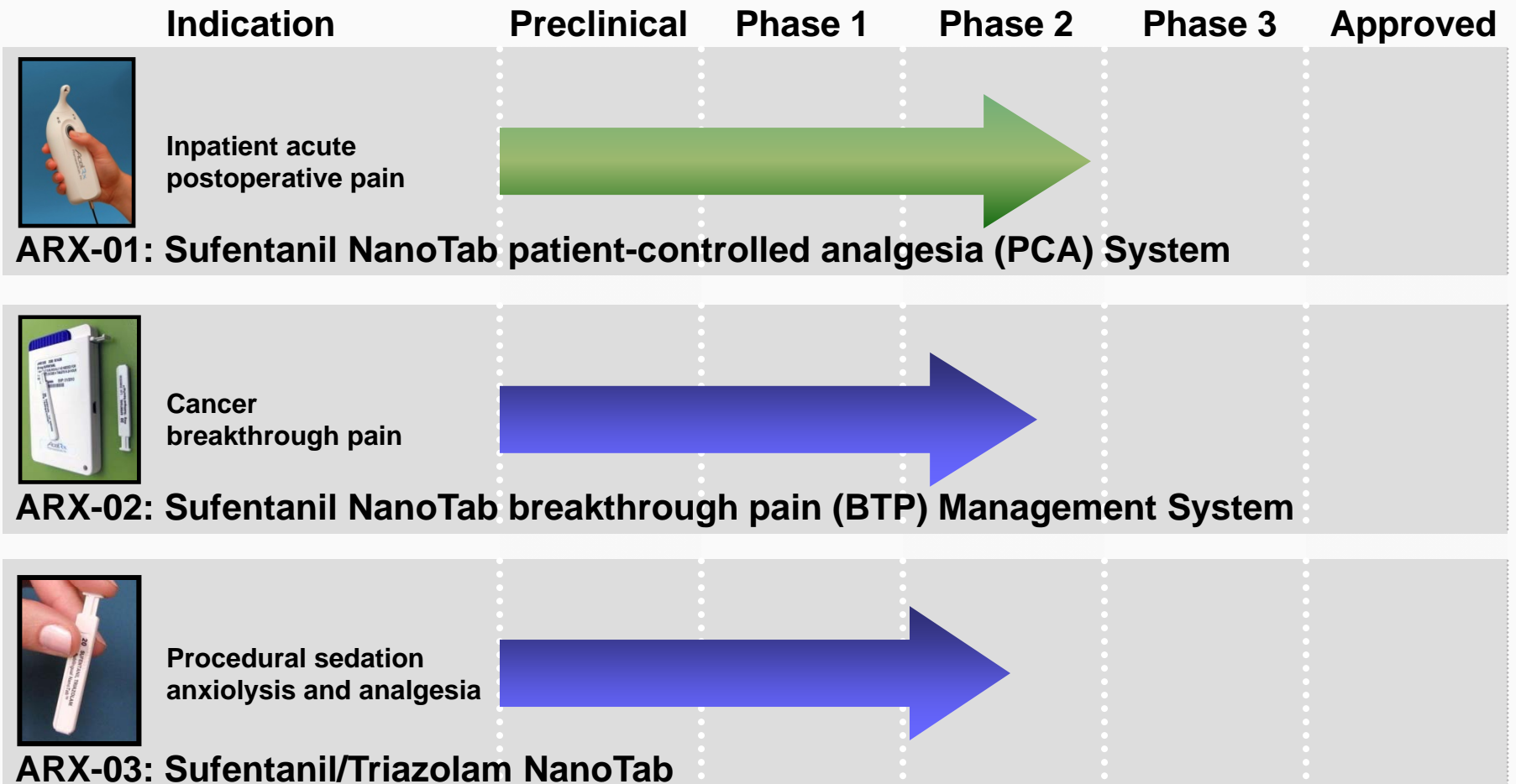
Therapeutic index = median lethal dose (LD<sub>50</sub>) / lowest median effective dose (ED<sub>50</sub>)

# NanoTab: Efficient Transmucosal Delivery

- NanoTab: a novel oral transmucosal dosage form
- Key attributes:
  - Bioadhesive
  - Low saliva response
    - Minimal swallowed drug
    - Enhanced transmucosal uptake
  - Consistent pharmacokinetics
  - High bioavailability
  - Lower maximum concentration ( $C_{max}$ ) than IV infusion



# AcelRx Development Programs



# Noninvasive Handheld Sublingual PCA System

## IV PCA Pump



## Sufentanil NanoTab PCA System



### Key potential benefits

- No programming errors
- No IV-related complications
- Improved patient mobility
- High patient and caregiver satisfaction

# Objective and Methods

## Objective:

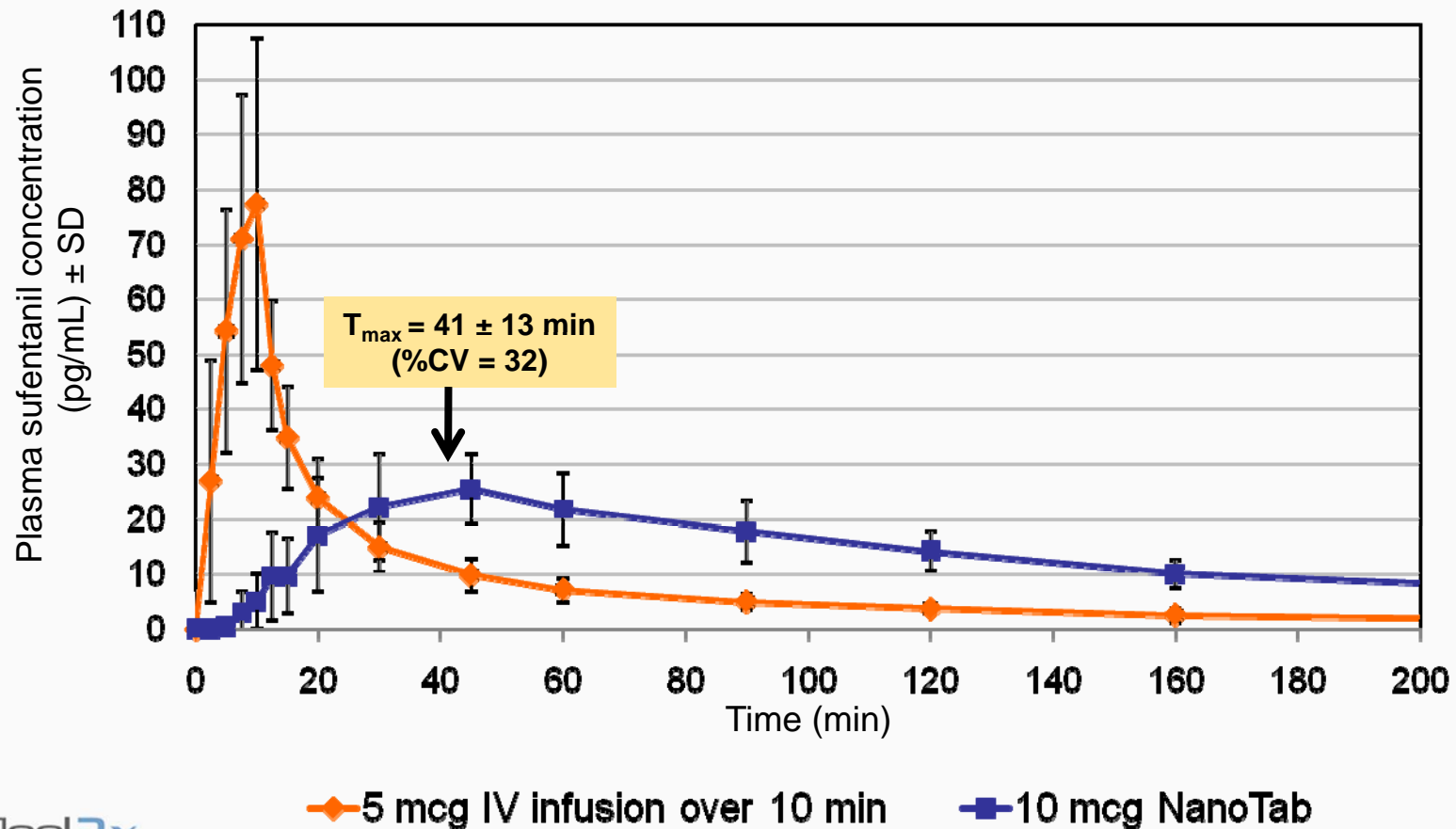
- To evaluate overall Phase 1 pharmacokinetic data from both single- and multiple-dose sublingual administrations of Sufentanil NanoTab (10 mcg)

## Methods:

- Two Phase 1 studies (ARX-F01-01 and ARX-C-002) evaluated healthy young subjects aged 18 to 45 years
- 33 subjects (17 male, 16 female) from both studies combined received a single 10 mcg NanoTab
- 12 of these subjects in a separate arm of the study also received a 10 mcg NanoTab every 20 minutes for a total of 4 doses
- All subjects received IV sufentanil 5 mcg as a comparator

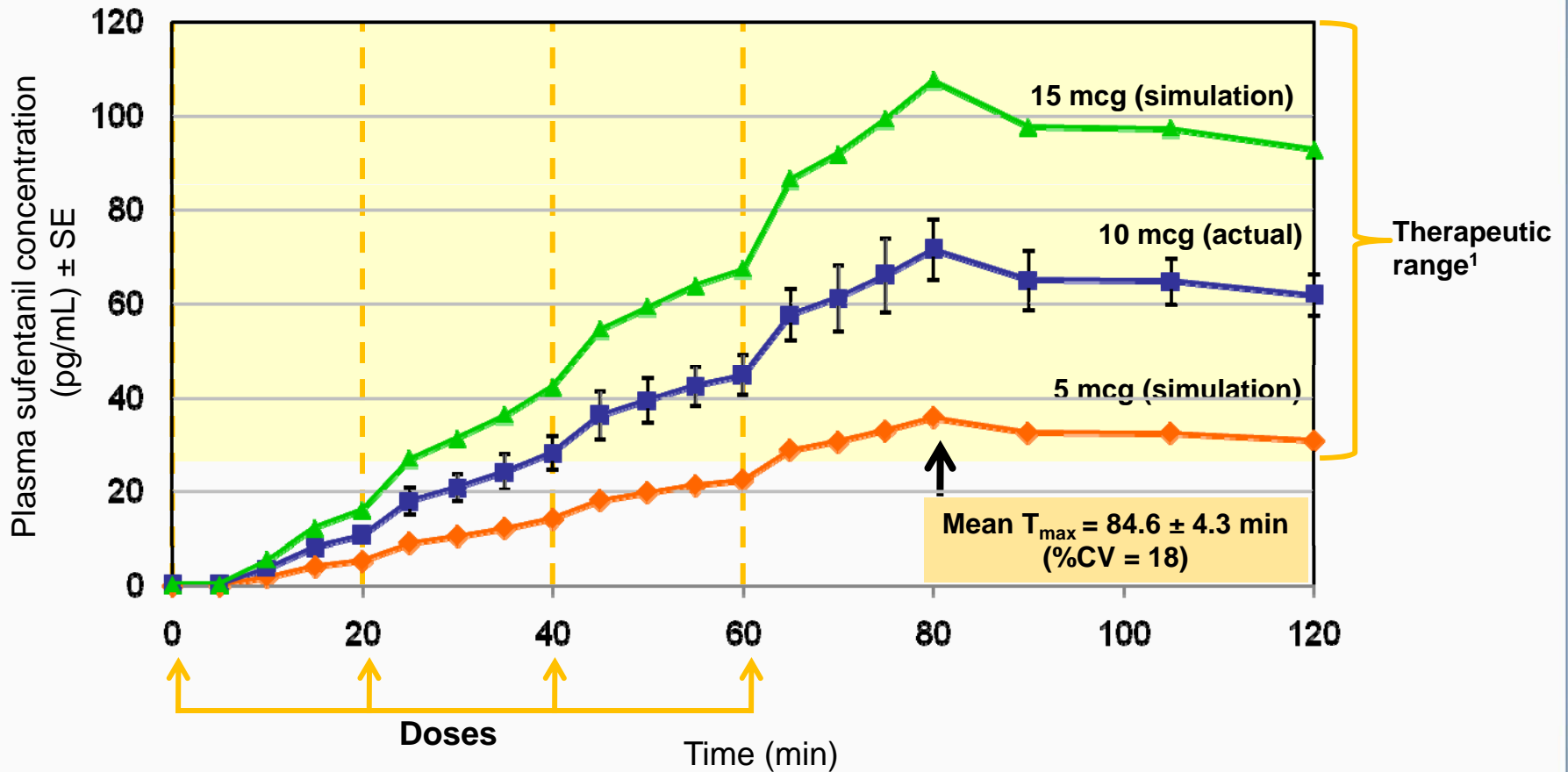
# NanoTab Oral Transmucosal Delivery: Consistent and Therapeutically Useful Plasma Profile

Sufentanil plasma concentration: single sublingual NanoTab 10 mcg  
versus IV infusion 5 mcg (over 10 minutes)



# Repeat Dosing at 20 Minute Intervals: Titrating to an Effective Concentration

Sufentanil plasma concentration with repeat dosing



# Sufentanil NanoTab Pharmacokinetics

PK parameters	NanoTab single dose 10 mcg (n = 33*)	NanoTab repeat dosing 10 mcg every 20 min x 4 (n = 12)
Bioavailability	78%	88%
C <sub>max</sub> (%CV)	21.4 pg/mL (36%)	78.7 pg/mL (26%)
T <sub>max</sub> (%CV)	43.8 min (34%)	84.6 min [24.6 min after last dose] (18%)
Half-life (%CV)	2.1 h (38%)	3.5 h (29%)

\*Results of the two Phase 1 studies are combined for 10 mcg single dose analysis.

# Sufentanil NanoTab PCA System: Development Update

- Completed three Phase 2 studies, including major orthopedic and major abdominal surgeries (158 patients received active drug)
- The Sufentanil NanoTab 15 mcg dose was the most efficacious, with no difference in adverse events versus 5 or 10 mcg strengths
- Median usage was 10 NanoTabs over 12 hours
- Very low adverse event profile for sedation and oxygen desaturation



**Sufentanil NanoTab  
PCA System**

**Thank You**