



Association Française  
des Sociétés de Services et d'Innovation



Les **membres AFSSI**  
ont la **parole** ”

**WEBINAIRE**



*Le partenaire incontournable de vos innovations*

*Proche de chez vous*





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Les membres AFSSI  
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**WEBINAIRE**

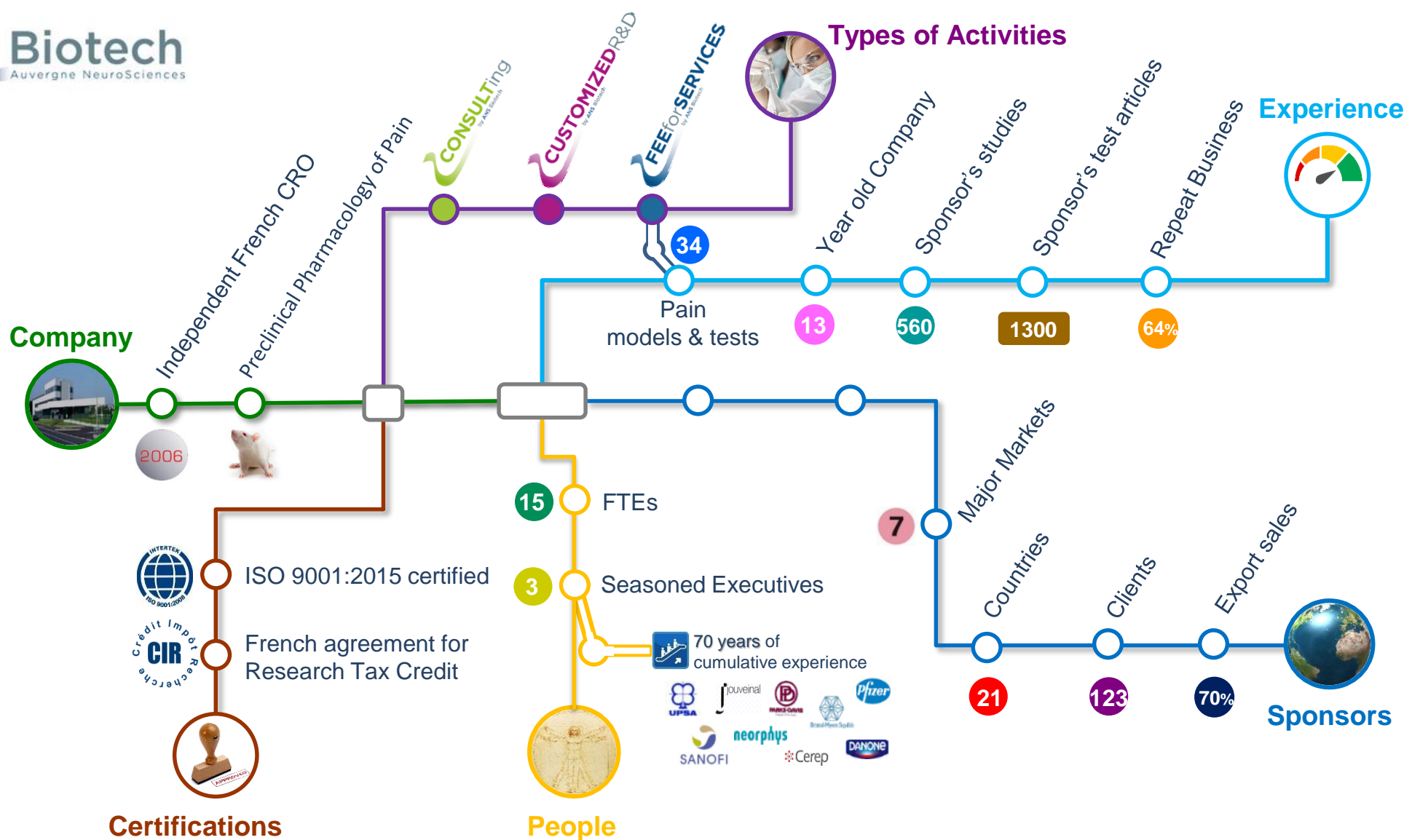
Qui suis-je ?  
La réponse  
en 20 min

AFSSI  
Association Française  
des Sociétés de Services et d'Innovation

### NOTRE ACTIVITÉ

*French CRO fully dedicated to the Preclinical Pharmacology  
of Pain*

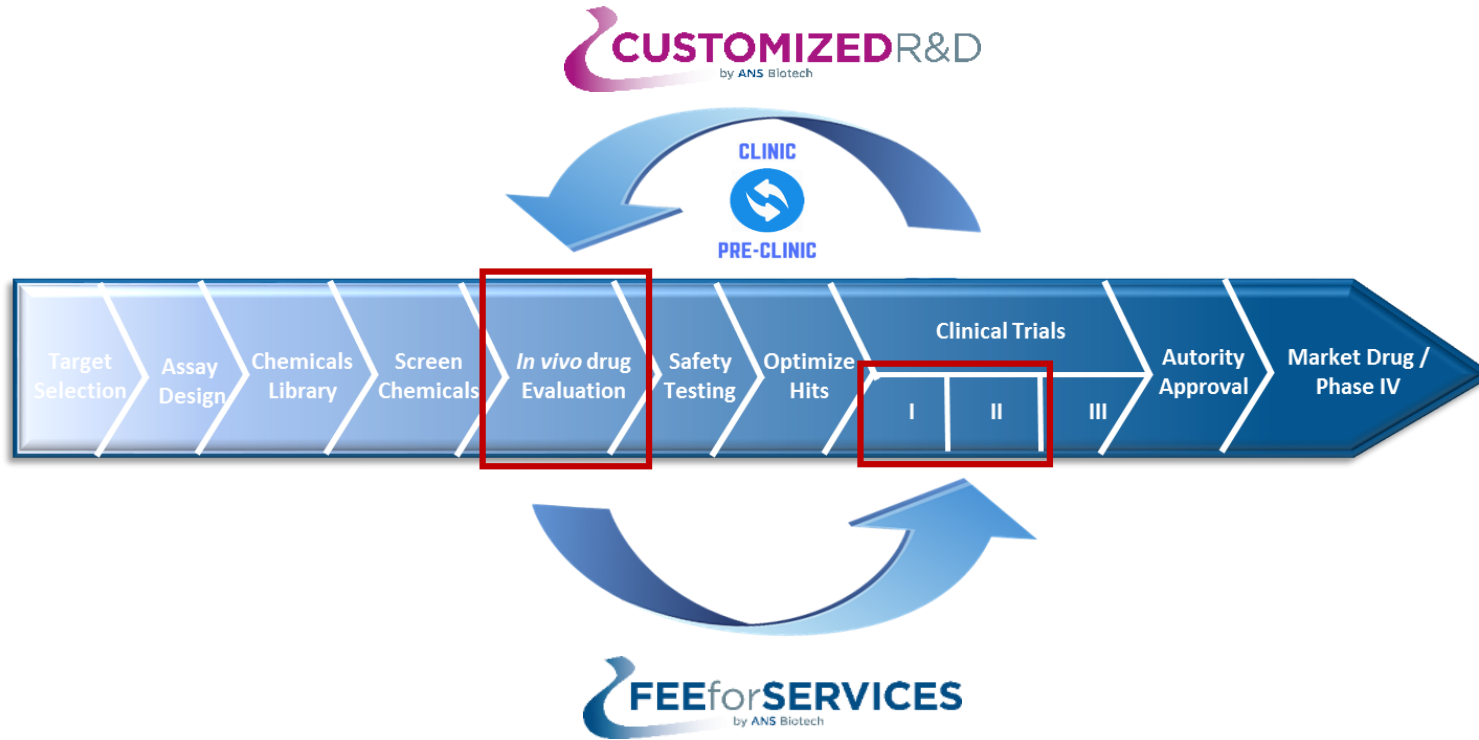
# Les membres AFSSI ont la parole



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## Business model



Pharmacodynamic expertise focused on analgesics





## TRANSLATIONAL RESEARCH *From Bed to Bench & from Bench to Bed*



### 1 Similar pathophysiological MoA



Clinical Cases  
*(hypotheses)*



Clinical Trials  
*(validation of hypotheses)*

Pathophysiological /  
pharmacological MoA  
in *in vivo* models



Clinical POC  
in human

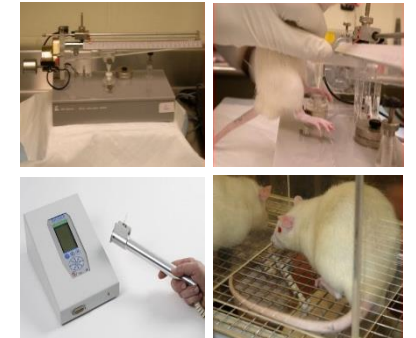


Set-up of  
Animal models



Pharmacological validation  
*(clinically used drugs)*

### 2 Similar methods of investigation



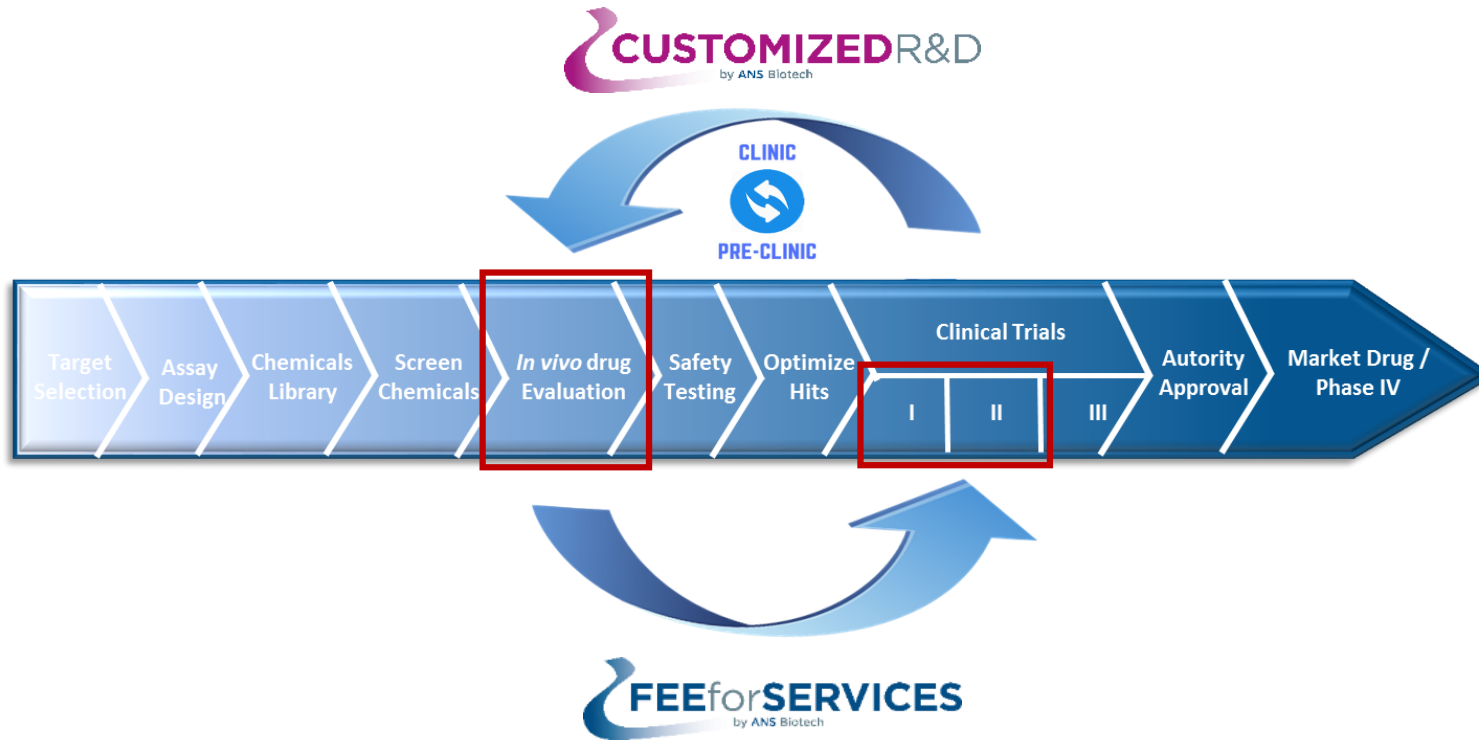
Examples of mechanical stimulations

✓ High Translatability of Animal models

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## Business model



### Pharmacodynamic expertise focused on analgesics

- ✓ Screening of test articles  **ALGOGram™**  
Xpress Screening
- ✓ Proof of concept studies
- ✓ Non-regulatory evaluation of efficacy of drug candidates





## COLLABORATION WITH ANS BIOTECH

*One request, two possibilities!*



1 REQUEST



2 SOLUTIONS



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## MODELS & TESTS



### ACUTE & TONIC PAIN

- Mechanical stimulation  
*Paw pressure test (rat)*  
*Electronic Von Frey test (rat)*
- Thermal stimulation  
*Hot plate test (mouse)*  
*Tail-Flick test (rat, mouse)*  
*Plantar test (rat)*
- Chemical stimulation  
*Acetic acid-induced writhing (rat, mouse)*  
*Formalin test (rat, mouse)*

### CANCER PAIN

- Bone cancer pain  
*Tactile allodynia (electronic Von Frey test - rat)*

### NEUROPATHIC PAIN

- Chronic constriction injury (Bennett model)  
*Mechanical hyperalgesia (paw pressure test - rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*  
*Tactile allodynia (electronic Von Frey test - mouse)*
- Spinal nerve ligation (Chung Model)  
*Tactile allodynia (electronic Von Frey test - rat)*
- Spared nerve injury (SNI model)  
*Mechanical Hyperalgesia (paw pressure test - rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*
- Diabetic neuropathy (STZ model)  
*Mechanical hyperalgesia (paw pressure test - rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*

- Oxaliplatin-induced peripheral neuropathy  
*Cold allodynia (acetone drop test - rat)*

### INFLAMMATORY PAIN

- Carrageenan-induced hyperalgesia or allodynia  
*Mechanical hyperalgesia (paw pressure test - rat)*  
*Thermal hyperalgesia (plantar test - rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*
- CFA-induced hyperalgesia or allodynia  
*Mechanical hyperalgesia (paw pressure test - rat)*  
*Thermal hyperalgesia (plantar test - rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*
- Capsaicin-induced allodynia  
*Tactile allodynia (electronic Von Frey test - rat)*
- Kaolin-induced arthritis  
*Gait score (rat)*  
*Tactile allodynia (electronic Von Frey test - rat)*
- CFA-induced monoarthritis  
*Mechanical hyperalgesia (paw pressure test - rat)*
- MIA-induced osteoarthritis  
*Tactile allodynia (electronic Von Frey test - rat)*
- Partial meniscectomy-induced osteoarthritis  
*Tactile allodynia (electronic Von Frey test - rat)*

### VISCERAL PAIN

- TNBS-induced colonic inflammatory hypersensitivity  
*Mechanical allodynia (colonic distension - rat)*
- Stress-induced colonic hypersensitivity  
*Mechanical allodynia (colonic distension - rat)*

### POSTOPERATIVE PAIN

- Incisional pain (Brennan model)  
*Tactile allodynia (electronic Von Frey test - rat)*

### OPIOID-INDUCED HYPERALGESIA

- Fentanyl-induced hyperalgesia  
*Mechanical hyperalgesia (paw pressure test - rat)*

## OTHER ACTIVITIES

## PROPRIETARY SUPPORT SERVICES

## Offer of Services



Your decision making guide !



*in vivo* high throughput screening in mice



Drug levels in biological tissues



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YOU  
&  
US

Together



## Prerequisites

- Dose range
- Side effects
- PK data
- Drug exposure

CONSULTing  
by ANS Biotech

CUSTOMIZED R&D  
by ANS biotech

TRAINing  
by ANS Biotech

ALGOGram™  
Xpress Screening

NOCIWay™  
Xpress Screening

ANSbioSamples™



## Therapeutic areas

**PAIN IS A TRANSVERSE SYMPTOM!**

- NEUROLOGY
- GASTROENTEROLOGY
- RHEUMATOLOGY
- SURGERY AND ANAESTHESIA
- ONCOLOGY

PPP PRECLINICAL PAIN PROFILING

FEEforSERVICES  
by ANS Biotech

CUSTOMIZED R&D  
by ANS Biotech



Your Pain Program



Your Partner for building step by step  
your Preclinical dossier\* !

- Strategy
- Screening
- Pathophysiology
- Diseases

\* Fully customized to meet Sponsor's needs and priorities

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YOU

- 1. Early data
- 2. Candidate selection
- 3. Proof of concept
- 4. Competitive advantage *vs* reference compound

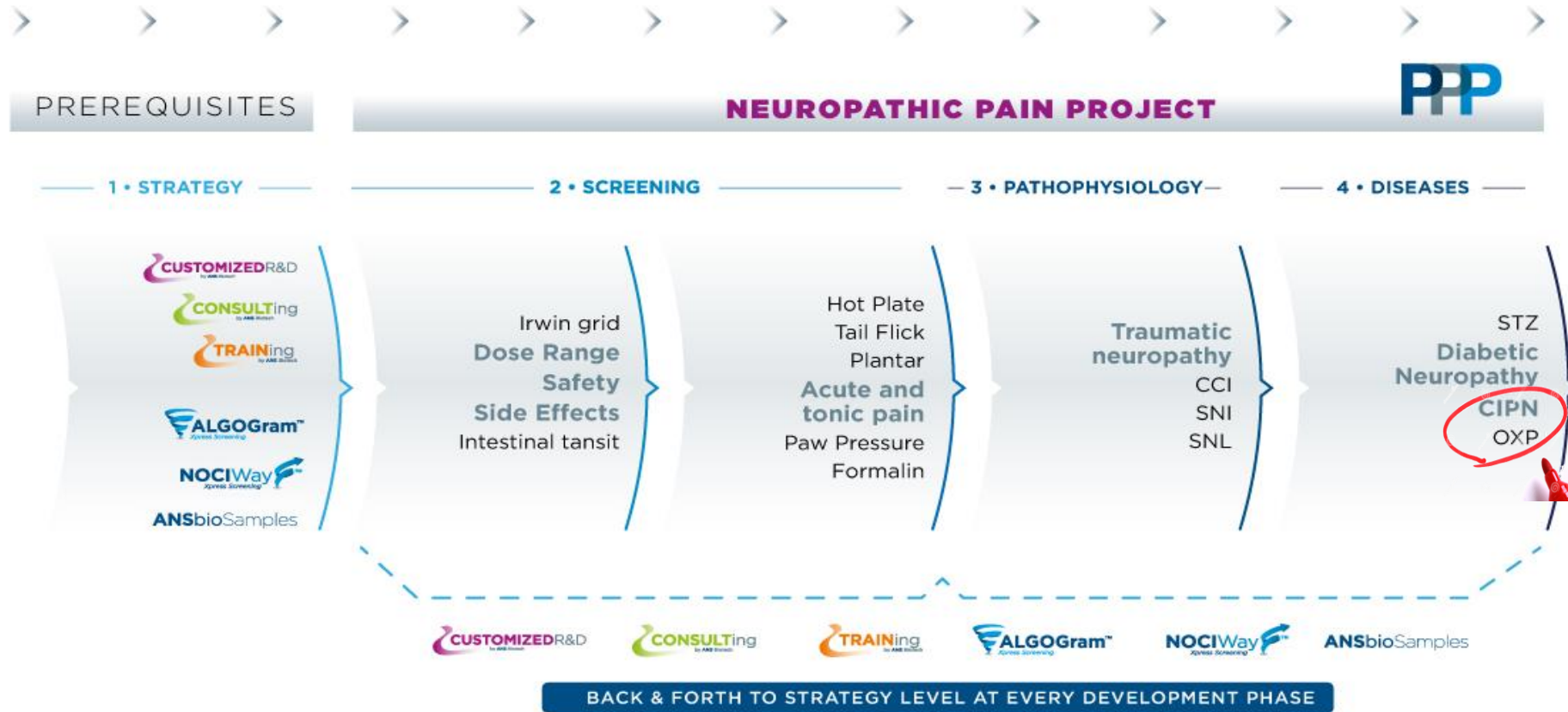
NEUROLOGY



Neuropathic Pain  
Diabetic Neuropathy  
Chemotherapy-Induced  
Peripheral Neuropathy

&

US





## Oxaliplatin-induced Peripheral Sensory Neuropathy

**Oxaliplatin** : Antineoplastic agent used for treatment of colo-rectal cancer

⇒ **Peripheral Neuropathy** : most common of Oxaliplatin-induced neurotoxic adverse effects ( > 90 % patients) with dose-limiting main impact



Patients

✓ **Acute and transient symptoms:**

- Occur from the 1<sup>st</sup> administration
- Cold-related sensitivity
- Hyperexcitability of sensory neurons



✓ **Model of acute intoxication:**

- Cold Hypersensitivity

✓ **Progressive and dose cumulative:**

- Increases progressively in duration and severity with repetition of treatment-cycles
- Impaired sensory nerve conduction (large myelinated A fibers) (proprioception, skin sensation)
- May become persistent (15-20 % of patients )
- Regresses after Oxaliplatin discontinuation



✓ **Model of chronic intoxication:**

- Cold-related Allodynia
- Decrease of Nerve Conduction Velocity
- Decrease of plasmatic NGF level
- Morphometric changes of sensory neurons of DRG correlated to platinum accumulation

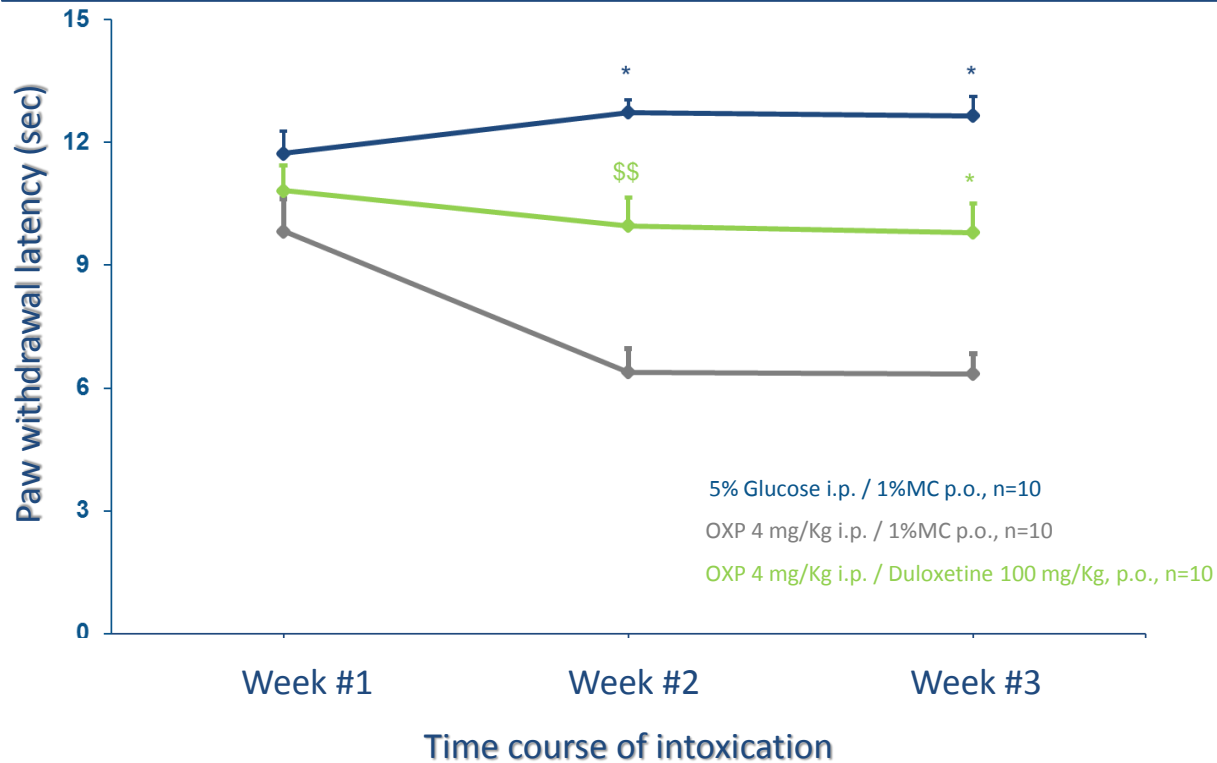


Animal models



## Oxaliplatin-induced Peripheral Sensory Neuropathy

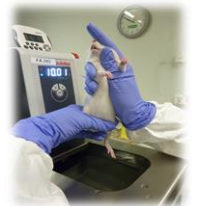
### Antiallodynic effect of a single oral administration of Duloxetine in a chronic model of oxaliplatin-induced neuropathy in rats



\*:  $p < 0.05$  as compared to the vehicle-treated group, Tuckey's test after significant Kruskal-Wallis ANOVA.  
\$:  $p < 0,01$  as compared to the vehicle-treated group, U-Mann Whitney's test.

### Experimental conditions

- ❑ Chronic intoxication with OXP (4 mg/kg, i.p.) twice a week during 3 consecutive weeks / (CD = 24 mg/kg, i.p.)
- ❑ Single oral administration of the vehicle and Duloxetine on testing days (D<sub>4</sub>, D<sub>11</sub> and D<sub>18</sub>).
- ❑ Paw immersion test (cold allodynia) : Latency of both hindpaw withdrawal after immersion into a cryothermostat with a fixed temperature calibrated at 10°C ± 0.5°C.



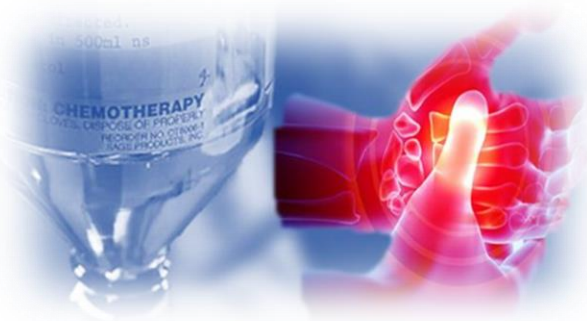
Private 300 sqm animal facility  
Protocols validated by local ethical committee and French Ministry

- ✓ Duloxetine improves the cold allodynia throughout the time course of intoxication with Oxaliplatin.



## Main advantages of the model

- ✓ High translatability to the Clinic
- ✓ Acute and chronic paradigms of intoxication
- ✓ Robust reproducibility & precise measurement of cold allodynia
- ✓ Fully customizable to Sponsor's paradigms of treatment (preventive, curative, chronic, ...)



## ... and to learn more about CIPN

*Save the date!*

**WEBINAR**

17 SEPT

3:00 PM

45 MIN

“Pharmacology and mechanisms of Oxaliplatin-induced neuropathic pain”

by Laurent Diop (Ph.D.) - CSO



# Les membres AFSSI ont la parole



Exclusively dedicated to the behavioral pharmacology of Pain



Animal models close to clinical pain situations (Translational Research)



Client's satisfaction



Lab Operations located in Riom, France (ex-Schering Plough site)



Network of skilled Partners to continue the experience!



The Take Home  
*message*

