



GLOBAL INTERSTITIAL CYSTITIS
BLADDER PAIN SOCIETY

Volume 8 Issue 9 || September 2026

GIBS NEWSLETTER

The Dawn of NOP Agonism: Does it signal a Paradigm Shift in the Pharmacological Management of IC/BPS?

Latest Announcement

**12th Annual Congress on
IC/BPS - GIBS 2027**

**Lock the Date :
28th-29th August 2027**

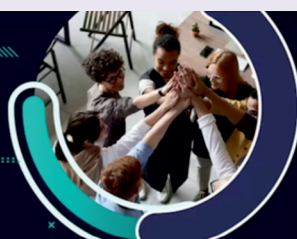
**Venue :
Soon to be Announced**

**Theme: Phenotype, Pathways
and Precision in IC/BPS**

BECOME GIBS LIFETIME MEMBER

BECOME
A LIFETIME MEMBER

GRAB THE BENEFITS



SCAN HERE!

Introduction:

1. The Failure of Conventional Therapy

The treatment of Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) has historically been an exercise in frustration. Current oral therapies—Pentosan Polysulfate Sodium (PPS), Amitriptyline, Hydroxyzine, Gabapentin etc, primarily target the urothelial barrier or provide generalized neuromodulation. However, they frequently fail to address the core pathophysiology: a hyper-sensitized nervous system and an "irritable" bladder motor profile.

As we progress through 2026, the urological community is pivoting toward the Nociceptin/Orphanin FQ (NOP) receptor system, a pathway that offers the precision we have lacked for decades.

2. Understanding the opioid receptors

The opioid system is governed by a family of G-protein coupled receptors (GPCRs) located throughout the central and peripheral nervous systems. While classically known for three main receptors, the modern consensus recognizes **four distinct types**.

a. Mu (μ) Opioid Receptor (MOP)

The Mu receptor is the "heavyweight" of the system and the primary target for most clinical painkillers like morphine, fentanyl, and oxycodone.

Primary Functions: Supraspinal and spinal analgesia, sedation, and slowed gastrointestinal motility.

The "Double-Edged Sword": It is the receptor most responsible for the euphoric effects and the subsequent high potential for addiction, as well as dangerous respiratory depression.

Location: High density in the brain (cortex, thalamus) and the dorsal horn of the spinal cord.

b. Delta (δ) Opioid Receptor (DOP)

Delta receptors often work in synergy with Mu receptors but have a slightly different therapeutic profile.

Primary Functions: Analgesia and, notably, mood regulation. Research suggests DOP agonists may have antidepressant and anxiolytic properties.

Clinical Interest: They generally carry a lower risk of respiratory depression and constipation than Mu agonists.

+91 80972 53466

info@gibsociety.com

www.gibsociety.com



- **Location:** Predominantly found in the cerebral cortex and the olfactory bulb.

c. Kappa (κ) Opioid Receptor (KOP)

The Kappa receptor is unique because its activation often produces effects opposite to those of the Mu receptor.

- **Primary Functions:** Spinal analgesia and diuresis (increased urination).
- **Psychological Impact:** Unlike the euphoria of Mu receptors, Kappa activation often causes dysphoria, hallucinations, and intense discomfort.
- **Clinical Interest:** Because they provide pain relief without the "high," they have been studied for chronic pain, though the side effects on mood are a major barrier.

d. Nociceptin/Orphanin FQ Receptor (NOP)

Previously known as the ORL-1 (Opioid-Receptor-Like 1), this is the "non-classical" fourth member.

- **Primary Functions:** Modulation of pain, anxiety, and the micturition reflex.
- **Unique Pharmacology:** It does not bind to traditional opioid ligands like naloxone. It is functionally "anti-opioid" in the brain but highly analgesic in the spinal cord.
- **Clinical Interest:** It is the only receptor in this family that shows significant promise for treating bladder-centric pain and urgency without the baggage of addiction or respiratory failure.

3. The Nociceptin/Orphanin FQ Receptor (NOP)

a. Molecular Pharmacodynamics

The NOP receptor (encoded by the OPRL1 gene) is a G-protein coupled receptor (GPCR) that primarily couples with Gi/o proteins.

The Signalling Cascade:

- **Adenylyl Cyclase Inhibition:** Binding of the endogenous ligand (Nociceptin) inhibits adenylyl cyclase, reducing intracellular cAMP levels.
- **Ion Channel Modulation:** It activates G protein-coupled inwardly rectifying potassium (GIRK) channels and inhibits N-type voltage-gated calcium channels (Cav2.2).

The Result: This hyperpolarizes the neuron and inhibits the release of excitatory neurotransmitters like Substance P and Glutamate, which are the primary drivers of pain transmission in the bladder.

b. The "Anatomical Dichotomy" of Pain

The NOP system is unique because its effect on pain depends entirely on where the receptor is activated. This "site-specific" behaviour is critical for drug design:

- **Spinal Level (Antinociceptive):** Activation in the dorsal horn of the spinal cord inhibits the "upward" transmission of pain signals. This produces a potent analgesic effect similar to classical opioids but without the same respiratory risks.
- **Supraspinal Level (Pronociceptive):**
Interestingly, activation in the brain can sometimes counteract morphine and actually increase pain sensitivity.
- **Peripheral Level (Bladder):** NOP receptors are located on the sensory afferent fibres of the bladder. Activation here directly raises the threshold for the micturition reflex, effectively telling the brain the bladder is "less full/ less painful" than it actually is.



c. Comparison: NOP vs. Classical Opioids (MOP)

Feature	Classical Opioids (MOP)	NOP Agonists
Primary Effect	Potent Central Analgesia	Neuromodulation & Desensitization
Addiction Risk	High (Dopamine surge in the Ventral Tegmental Area)	Low/None (No Ventral Tegmental Area involvement)
Respiratory Depression	Significant risk	Minimal to None
Tolerance	Develops rapidly	Develops much slower
Naloxone Effect	Fully Antagonized	Not affected by Naloxone

4. Sunobinop (V117957): The Vanguard of NOP Agonism

a. Pharmacodynamics: Selective Partial Agonism

Sunobinop is a potent, small-molecule, selective partial agonist at the human NOP receptor. Its brilliance lies in its high degree of functional selectivity:

- **Receptor Selectivity:** It binds to NOP with nanomolar affinity (K_i). Crucially, it acts as a low-affinity antagonist at μ and κ opioid receptors and a weak partial agonist at δ receptors.
- **The "Ceiling Effect":** As a partial agonist, Sunobinop activates the receptor enough to achieve therapeutic desensitization of the bladder sensory nerves without reaching the "full" activation levels that might lead to profound sedation or motor impairment.
- **Renal Target:** Unlike many urological drugs that undergo heavy hepatic metabolism, Sunobinop is primarily excreted unchanged via the kidneys. This ensures that the active compound reaches high concentrations in the urine, potentially allowing for a "topical-from-within" effect on the bladder urothelium.
- **Non-Addictive Profile:** Crucially, NOP receptors are not expressed on the dopamine neurons of the ventral tegmental area (the brain's reward centre). This explains why NOP agonists do not carry the high abuse potential that has sidelined traditional opioids in chronic pain management.

b. Mechanism of Action: Silencing the Sensory Impulse

In the context of IC/BPS, Sunobinop functions as an "Electronic Filter" for the bladder.

- **Peripheral Desensitization:** In the bladder wall, NOP receptors are located on the C-fiber and A-delta sensory afferents. When activated, the agonist inhibits the release of pro-inflammatory neuropeptides (Substance P and CGRP (Calcitonin Gene-Related Peptide)). This effectively raises the "pain threshold" of the bladder, meaning the patient can tolerate more volume before the sensation of "painful urgency" begins. By slowing the rate of sensory firing during bladder filling, Sunobinop increases the Functional Bladder Capacity. The brain receives "fullness" signals much later, directly addressing the frequency-urgency cycle.
- **Central Modulation (The Spinal Gate):** In the dorsal horn of the spinal cord, NOP agonists inhibit the transmission of nociceptive (pain) signals from the bladder to the brain. This "gates" the pain, preventing the central sensitization that often leads to the chronic, "all-over" pelvic pain characteristic of late-stage IC/BPS.
- **Motor Control:** Unlike anticholinergics which paralyze the detrusor, NOP agonists modulate the micturition reflex centrally, increasing bladder capacity without necessarily causing the urinary retention seen with older medications.

GIBS NEWSLETTER

c. Present Clinical Status (2025-2026)

Following successful Phase 1b results, Sunobinop has demonstrated significant efficacy in recent studies:

- **The 41% Response Rate:** In trials specifically targeting female IC/BPS patients, 41% of participants reported "marked or moderate" improvement in symptoms, compared to only 9% in the placebo arm.
- **Pain Reduction:** Data showed a statistically significant reduction in the Numerical Rating Scale (NRS) for "Worst Pain" both during the day and overnight.
- **Nocturia Improvement:** Because it is dosed at bedtime, it leverages its mild sedative secondary effect to help patients stay asleep, while its NOP-driven mechanism prevents the bladder from triggering the micturition reflex mid-sleep.

4. Future Scope: Who are the Ideal Candidates?

As we move toward the final regulatory approval phases, we can identify three specific patient profiles where Sunobinop will likely become the First-Line Systemic Choice:

Patient Profile	Why Sunobinop?
The "Refractory Non-Hunner"	For the 90% of patients without lesions who fail PPS/Elmiron, Sunobinop offers a non-urothelial, neural-pathway solution.
The Nocturia-Dominant Patient	Patients whose quality of life is destroyed by 5+ nightly voids will benefit from the drug's rapid absorption and bedtime dosing.
The "Centralized" Pain Patient	Patients exhibiting signs of Allodynia (where light bladder filling feels like intense burning) require the spinal "gating" that only an NOP agonist provides.

5. Conclusion: A New Standard of Care

The rise of NOP agonists represents more than just a new drug; it represents our success in finally decoding the neuro-urolgy of bladder pain. For the patients we treat, this may be a transition from "managing" symptoms to "modulating" the disease.

References

1. Hanno PM, et al. (2025). The Changing Landscape of IC/BPS: From Urothelial Barriers to Neuro-Modulation. Journal of Clinical Urology.
2. Candelieri, A. & Ko, J. (2026). NOP Receptor Agonism: A New Frontier in Non-Opioid Analgesia for Chronic Pelvic Pain. Frontiers in Pharmacology.
3. Global Interstitial Society White Paper (2025). Sunobinop: Summary of Phase 2b Results and Path to Market.
4. Andersson KE. (2024). Pharmacological Treatment of the Overactive Bladder and IC/BPS. Urological Clinics.
5. Whiteside G, Stamford, CT, Auge C, Lluell P. PD05-09 Effects of Sunobinop (V117957) In A Model Of Acute Cystitis Induced By Cyclophosphamide. Journal of Urology 2023 Apr 1;209(Supplement 4):e152.

AUTHOR



Col (Dr.) Amit Agrawal

Commanding Officer, Field Hospital, Bhuj

BE THE NEXT NEWSLETTER AUTHOR

Please send your contributions to INFO@GISBOCIETY.COM

GIBS 2026 - 11th Annual Congress Post Event Highlight



GIBS NEWSLETTER

Beyond the Bladder:Decoding Subtypes, Delivering Solutions

22nd - 23rd August 2026 | Hotel Clarks Amer, Jaipur

Two Days. Seven Sessions. One Shared Mission.

We are delighted to share the successful completion of the 11th Annual Congress of the Global Interstitial Cystitis / Bladder Pain Society (GIBS 2026), held on 22-23 August 2026 at Hotel Clarks Amer, Jaipur. The congress opened with warm welcome addresses by Organising Chairman Dr. Shivam Priyadarshi, GIBS Chairman Dr. Rajesh Taneja, and GIBS Secretary Dr. Sanjay Pandey, who reflected on "A Decade of Learning & Journey" for the GIBS community before the scientific proceedings began. Over two inspiring days, more than 100+ delegates including faculty from 8 countries (Myanmar, Nepal, Russia, Malaysia, UAE, Iran, Israel, Iraq, USA & across Europe via Online Platform) came together across seven scientific sessions, creating a warm and vibrant platform for exchange, learning and collaboration in the field of Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS).

100+ Delegates	~80 Faculty Members	2 Days	7 Scientific Sessions
--------------------------	-------------------------------	------------------	---------------------------------

Day 1 - A Scientific Journey Beyond the Bladder

Session 1, "The Unseen Inhabitants: Unravelling the Microbiome's Role in IC/BPS" (convened by Dr. Syed Sajjad Nazir), opened the scientific programme with a deep dive into the urinary, genital and gut microbiomes. Dr. Syed, Dr. Eman, Dr. Neelanjana, Dr. Latika and Dr. Shivam guided delegates through dysbiosis, the gut-bladder axis and emerging microbiome-directed therapies, from probiotics to bacteriophage therapy.

Session 2, "Clinical Management: On and Beyond the Horizon" (convened by Dr. Latika Chawla), brought together Dr. Manish Man, Dr. Amit, Dr. Apeksha, Dr. Navita, Dr. Neeraj, Dr. Sanjay, Dr. Ng Poh and Dr. Ekaterina for a candid conversation on evidence versus real-world practice, gender-based approaches, immunomodulatory therapy, interventional pain strategies and personalised medicine.

Session 3, "Advances in Molecular Biology of IC/BPS" (convened by Dr. Amit Agrawal), took the discussion deeper into emerging science, mesenchymal stem cells, PRP, and urinary, blood-based, neurogenic and genomic biomarkers with insights from Dr. Aashee, Dr. Himmat Singh, Dr. Siti Nur, Dr. Mohan, Dr. Hemant and Dr. Karishma. Delegates also heard from Two Industry-Sponsored Sessions over Lunch: Dr. Sanjay Pandey on Sacral Neuromodulation (Medtronic), and Dr. Rajesh Taneja on Methamphetamine Hippurate for UTI Prevention and Antibiotic Stewardship (Dr. Reddy's).

Understanding the Patient Through Phenotyping

Session 4, "Phenotypes in IC/BPS" (convened by Dr. Ankur Sharma), was one of the True Highlights of the Congress. Dr. Ankur, Dr. Vikky, Dr. George, Dr. Poongodi, Dr. Suman, Dr. Mohini and Dr. Monika explored why phenotyping matters, the shift from bladder-centric to systemic pain phenotypes, and how technology can support phenotype-guided management. The Session Closed with the Engaging Case-Based Panel Discussion, "Which Phenotype Is This?" - Presented by Dr. Vikky with Expert Panelists Dr. Eman, Dr. Ng Poh, Dr. Sanjay, Dr. Ranjana and Dr. Latika bringing these ideas to life through real clinical cases. "IC/BPS does not look the same in every patient - and understanding the patient may change how we understand the disease."

Celebration, Reflection & Renewal (Inaugural Ceremony)

Day 1 closed on a joyful and inspiring note with the Inauguration Ceremony, formally welcoming the GIBS 2026 delegation. We were deeply honoured to have Dr. Pramod Yeole, Vice-Chancellor of Rajasthan University of Health Sciences (RUHS), grace the occasion as Chief Guest. In his address, Dr. Yeole spoke warmly of the importance of dedicated scientific platforms like GIBS in advancing patient-centred urological care, and commended the congress for bringing together such a distinguished community of clinicians and researchers.

The ceremony was further enriched by an address from Mrs. Swati Jajodia, CMD of Swati Spentose, who shared inspiring words on the spirit of collaboration between science and industry in driving better outcomes for IC/BPS patients, and extended her warm wishes for a successful and impactful congress.

The evening continued with a relaxing Yoga Session led by Mrs. Tanya Saxena, and a memorable Gala Dinner where faculty and delegates came together to celebrate the shared journey, the kind of moments that stay with us long after a conference ends.

Celebration, Reflection & Renewal (Inaugural Ceremony)

Day 2 began early and energetically with the Best Abstract / Paper Competition, where young scientists presented original research judged by Prof. Dr. Phone Myint, Dr. Manish Man, Dr. George, Dr. Aparna, Dr. Ng Poh and Dr. Eman. Topics ranged from clinical predictors of symptom severity to paraurethral filler injections, intravesical Pentosan Polysulfate therapy and even a phenotypic variability, a genuine showcase of the fresh ideas shaping the future of IC/BPS research.

Session 5, "Reading the Evidence Right: A Critical Discussion" (convened by Dr. Latika Chawla), invited Dr. Dheera, Dr. Sarthak, Dr. Abhishek, Dr. Nihal and Dr. Ushma to critically appraise recent literature spanning surgical approaches, intravesical cell therapy, the urinary viral spectrum and pelvic floor physiotherapy encouraging delegates to look closely at what the evidence really tells us.

A Strong Focus on the Future

The congress concluded its scientific journey with Session 7, "Future Directions" (convened by Dr. Shivam Priyadarshi), featuring Dr. Plekhanova on current and future clinical trials and Dr. Sanjay on the future vision for IC/BPS. A Rich Panel Discussion on "Gaps in the Path to the Future," Moderated by Dr. Shivam with Country Head Expert Panelists - Prof. Dr. George, Prof. Dr. Phone, Dr. Ng Poh, Dr. Manish Man, Dr. Eman, Dr. Aparna, Dr. Rajesh and Dr. Rohit, brought together diverse perspectives on where GIBS should focus in the next decade..

The Congress Closed with a Heartfelt Closing Ceremony Recognition and Recap led by Dr. Sanjay, followed by Closing Remarks from Organising Chairman Dr. Shivam, Before Delegates gathered for a final lunch together.

More Than Science - It Was About People

While the scientific programme was at the heart of GIBS 2026, its true strength came from the people who made it possible. Across two days, the meeting created warm opportunities to share experiences, ask questions, challenge perspectives and build lasting professional connections from the lecture halls to the coffee breaks in between.

Every question added value. Every discussion opened a new perspective.
Every interaction strengthened the GIBS community.

GIBS 2026 in the News

[illegible]

GIBS 2026 travelled well beyond the walls of Hotel Clarks Amer. The congress was featured across newspapers and media publications, with journalists and health reporters covering the scientific proceedings and the growing conversation around IC/BPS care in India. We are proud that this platform for science and collaboration also became a platform for public awareness.

Celebrating the GIBS Community

We extend our heartfelt gratitude to all our faculty members, chairpersons, convenors, panelists, judges, abstract presenters and delegates for their valuable contribution to GIBS 2026. Your expertise, enthusiasm and willingness to share knowledge made the scientific programme truly meaningful.

A special word of appreciation for our young researchers, who brought fresh ideas and scientific curiosity that will help shape the future of IC/BPS research and to everyone who travelled to Jaipur and became part of these two memorable days: thank you for making GIBS 2026 what it was.

Announcing GIBS 2027 - The Journey Continues!

As we close the chapter on an inspiring GIBS 2026, we're excited to look ahead. Jaipur gave us two unforgettable days of learning, connection and discovery and now, the GIBS family is on its way to a different city

GIBS 2027 - COMING TO MUMBAI!

28th – 29th August 2027 | Mumbai, India

"A New Conversations. New Perspectives. One Shared Mission. See You in Mumbai!"



GLOBAL INTERSTITIAL CYSTITIS
BLADDER PAIN SOCIETY

GIBS 2027

ANNOUNCING

 **28th-29th AUGUST 2027**

Theme:

Phenotypes, Pathways to Precision in IC/BPS



VENUE : MUMBAI, INDIA

(Location To Be Announced)



Become a Lifetime Member and
Avail Discounts on GIBS 2027 Registration

 info@gibsociety.com