



**The Italian R&D excellence at the
American Urological Association's 2019 Annual Meeting**

Preliminary data show Oncofid®P-B is very well tolerated and has promising efficacy when administered for up to 12 consecutive weeks in BCG unresponsive/intolerant patients with bladder carcinoma *in situ* (CIS)

- Eighteen out of 20 enrolled patients completed the 12-week intensive course. Instillations were very well tolerated; no patients withdrew from the study.
- Of the 18 patients who completed the 12-week intensive course, 13 (72.2%) showed a complete response, defined as negative cystoscopy including urothelium biopsy and negative cytology, and entered the 12-months maintenance phase. Of these, 3 are still disease-free after 12 months, 7 are still in maintenance phase, 2 relapsed after 3 months and 1 discontinued due to concomitant disease.
- Oncofid®P-B is a Paclitaxel-Hyaluronic Acid conjugate developed and patented by Fidia farmaceutici, a leading Italian pharmaceutical multinational company.

Chicago, May 3, 2019 – Fidia farmaceutici today announced the positive preliminary results from an open-label, single-arm, multicenter clinical trial evaluating safety, tolerability and efficacy of Oncofid®P-B, an innovative Paclitaxel-Hyaluronic Acid conjugate, in patients with carcinoma *in situ* (CIS) of the bladder, unresponsive or intolerant to BCG (Bacillus Calmette-Guérin) and unwilling or unfit for cystectomy. Oncofid®P-B showed excellent tolerability for a prolonged treatment schedule and good efficacy, with 72.2% (13/18) complete response in patients who completed the 12-week induction phase.

*“CIS of the bladder is still an unmet medical need and the excellent safety profile and positive preliminary efficacy results obtained with Oncofid®P-B when administered according to a prolonged treatment schedule support the further clinical development of this innovative drug - said **Dr. Rodolfo Hurle, Principal Investigator at Humanitas Research Hospital, Italy** – providing a potential pharmacological alternative to cystectomy for these high risk patients”.*

The study evaluated Oncofid®P-B administered in 12 consecutive intravesical weekly instillations (intensive phase), followed in responsive patients by 12 monthly instillations (maintenance), in patients with bladder CIS, unresponsive or intolerant to BCG and unwilling or unfit for cystectomy. The primary endpoint was the overall safety profile. Secondary endpoints included efficacy after the intensive phase and after the entire treatment period, compliance, systemic absorption. Complete response (CR) was defined as negative cystoscopy, including urothelium biopsy and negative cytology. Patients who achieved a CR after intensive phase were followed up every 3 months for up to 1 year during maintenance, by flexible cystoscopy and urine cytology. For pharmacokinetic assessment, blood samples were collected after the 1st and 12th instillation.

As per today, the rate of complete response at the end of the intensive phase is 72.2% (13/18 patients), with excellent safety and tolerability profile. Drug related adverse events are limited in number and severity, and so far, no patient discontinued the treatment.



"We are excited by these results, which indicate how tolerated and effective Oncofid®P-B may be in addressing bladder CIS- said Dr. Carlo Pizzocaro, President and CEO of Fidia farmaceutici – We are closer to potentially offer these seriously ill patients an effective pharmacological treatment as an alternative to cystectomy. This study allowed us to acquire further information on the safety, tolerability and efficacy of Oncofid-P-B, and the data presented at AUA 2019 demonstrate the ability of this approach to achieve complete responses in patients with limited or no pharmacological treatment options."

Bladder Carcinoma *in Situ* – CIS

Bladder cancer is the 5th most common malignant disease in Western countries, the 2nd most prevalent urologic cancer after prostate cancer in men¹. Approximately 75-85% of patients with bladder cancer present with a disease confined to mucosa or submucosa (non-muscle invasive bladder carcinoma – NMIBC)^{2,3}. Carcinoma *in situ* (CIS) is a flat, high-grade, non-invasive urothelial carcinoma that can be missed or misinterpreted as an inflammatory lesion during cystoscopy, if not biopsied. CIS is often multifocal and can occur in the bladder, but also in the upper urinary tract, prostatic ducts, and prostatic urethra⁴. Molecular biology techniques and clinical experience have demonstrated the highly malignant potential of CIS lesions⁵. The standard of care for CIS is intravesical BCG⁶. In BCG-unresponsive patients, the only therapeutic option is radical cystectomy, an invasive procedure with important consequences on the patient's quality of life.

ONCOFID®P-B

Oncofid®P-B is an innovative conjugate of Hyaluronic Acid (HA) and paclitaxel, a cytotoxic drug with poor water solubility. The conjugation of paclitaxel with HA makes the drug easily water soluble, thereby improving tolerability and allowing more intensive treatment schemes.

Fidia farmaceutici

Fidia farmaceutici is an Italian multinational company, with R&D, manufacturing and sales capabilities, and an extensive product portfolio mainly based on natural and functionalized hyaluronic acid (over 700 patents), in joint care, wound healing, ophthalmology, aesthetics and regenerative medicine. Manufacturing operations are FDA-inspected and approved, and the company extends its global reach through wholly-owned subsidiaries and partners in over 100 countries worldwide.

¹ Cumberbatch MG, Rota M, Catto JW, La Vecchia C The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol.* 2016;70(3):458-66.

² Smith, A. B. et al. Muscle-invasive bladder cancer: evaluating treatment and survival in the National Cancer Data Base. *BJU Int.* 2014; 719–26.

³ Burger, M. et al. Epidemiology and risk factors of urothelial bladder cancer. *Eur. Urol.* 2013; 63:234–41.

⁴ Sylvester, R.J., et al. High-grade Ta urothelial carcinoma and carcinoma in situ of the bladder. *Urology*, 2005. 66: 90.

⁵ Tang, DH, Chang SS. Management of carcinoma in situ of the bladder: best practice and recent developments. *Ther Adv Urol.* 2015 7(6): 351–364.

⁶ AUA/SUO Joint Guideline: Published 2016