

Expanding Treatment Landscape for Inborn Errors of Immunity

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ABSTRACT Inborn errors of immunity (IEI) encompass a rapidly growing spectrum of genetic disorders affecting immune development and function and resulting in susceptibility to infection, immune dysregulation, autoimmunity and malignancy. The therapeutic approach to IEI has evolved considerably over recent decades. The cornerstones of management include antimicrobial prophylaxis, immunoglobulin replacement, and treatment of immune dysregulation and lymphoproliferative complications. For patients with severe IEI, hematopoietic stem cell transplantation offers potentially curative therapy, with early transplantation associated with improved outcomes in appropriately selected patients. The therapeutic landscape is expanding through the development of gene therapy and an increasing number of disease-specific, targeted treatments directed at defined molecular and immunological pathways. These advances are shifting the paradigm from predominantly supportive management toward increasingly definitive and precision-based therapies. As therapeutic opportunities continue to evolve, broadening awareness of these advances across medical disciplines will be critical to ensuring that patients with IEI can benefit from the full range of available therapies and achieve the best possible outcomes.

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KEY WORDS: biological treatment, inborn errors of immunity (IEI), hematopoietic stem cell transplantation (HSCT), treatment

Colonel Ogden Bruton first described a patient with congenital immunodeficiency in 1952. His patient was a young boy with recurrent bacterial infections and absent serum gamma globulin. [1]. Treatment options were scarce and included only repeated courses of antibiotics, a novel treatment at the time, and symptomatic relief. Clinical outcomes were poor.

While infection control remains the cornerstone of care

for many conditions, during the past two decades there has been a paradigm shift toward disease-specific and potentially curative strategies. The integration of immunoglobulin replacement, hematopoietic stem cell transplantation (HSCT), gene therapy, and targeted biologic agents has transformed outcomes for many forms of primary immunodeficiency, previously considered fatal [2].

As our understanding of inborn errors of immunity (IEI) has deepened, it has become clear that these disorders extend far beyond recurrent infections, encompassing immune dysregulation, autoimmunity, and malignancy. These new aspects of IEI present different challenges to both patients and caregivers. Treatments for over-activation of the immune system may worsen immunodeficiency [3]. Insights into the diverse genetic and mechanistic pathways underlying IEI have not only reshaped our view of immune system biology but have also transformed the therapeutic landscape, driving the development of increasingly precise and effective treatments.

Additional challenges persist. Access to advanced therapies remains uneven globally, long-term outcome data are limited for many novel interventions, and therapeutic decision-making is often complicated by overlapping immune phenotypes and co-morbidities. A comprehensive understanding of current and emerging treatment modalities is essential for clinicians and researchers involved in the care of immunodeficient patients.

In this review, I outline the tenets of treating patients with

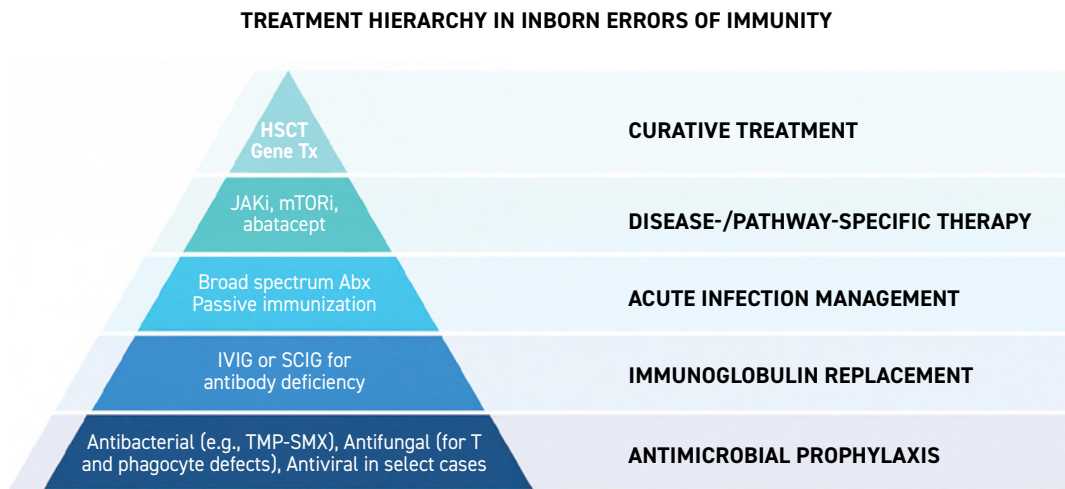
THE MAINSTAYS OF INBORN ERRORS OF IMMUNITY TREATMENT INCLUDE PROPHYLACTIC ANTIMICROBIAL TREATMENT, IMMUNOGLOBULIN REPLACEMENT FOR HUMORAL DEFECTS, AND MONITORING FOR AUTOIMMUNITY AND LYMPHOPROLIFERATION.

immune deficiencies, integrating established therapeutic modalities with emerging curative and experimental approaches [Figure 1]. Emphasis is

placed on the underlying rationale and evidence guiding each strategy, as well as on recent innovations and future directions in the evolving field of IEI management.

Figure 1. Treatment hierarchy in inborn errors of immunity

ABx = antibiotics, HSCT = hematopoietic stem cell transplantation, JAKi = Janus kinase inhibitors, mTORi = mTOR inhibitors, IVIG = intravenous immunoglobulin, SCIG = subcutaneous immunoglobulin, TMP-SMX = trimethoprim/sulfamethoxazole



GENERAL PRINCIPLES OF MANAGEMENT

Early diagnosis and supportive care

Early recognition and accurate diagnosis of immune deficiencies are critical for improving outcomes. Delayed diagnosis often leads to irreversible organ damage, chronic infections, or immune dysregulation. Like therapeutics, diagnostics have greatly improved in recent years, with functional assays and genetic testing able to more accurately pinpoint the exact IEI [4]. Once identified, management should begin with stabilization of the patient’s immune status, infection control, and prevention of secondary complications. A multidisciplinary approach including immunologists, infectious disease specialists, hematologists, and genetic counsellors is essential for comprehensive care and for tailoring therapy according to disease severity and individual risk factors.

Infection prevention and prophylaxis

Prevention of infection remains a central pillar of management across all forms of immune deficiency. Prophylactic antimicrobials are frequently employed to reduce the incidence of bacterial, viral, and fungal infections. Trimethoprim-sulfamethoxazole is commonly used for *Pneumocystis jirovecii* prophylaxis, while azoles may be indicated for patients at risk of invasive fungal disease. Antiviral prophylaxis, such as acyclovir or valganci-

clovir, is considered in selected settings, particularly post-transplant or during profound lymphopenia [5,6].

Prompt and aggressive management of infections is crucial in immune-deficient patients, as infection progression can be rapid and life-threatening. Empiric antimicrobial regimens should initially be broad and guided by local epidemiology and prior culture data. For chronic viral infections, antiviral agents and passive immunization may be used as adjunctive measures.

Vaccination strategies require individualization. Live-attenuated vaccines are contraindicated in many patients with severe T-cell or combined immunodeficiencies, whereas inactivated vaccines may be administered but often yield suboptimal responses. Household contacts should be appropriately immunized to provide herd protection, with the exception of oral polio and live influenza vaccines.

Monitoring and long-term follow-up

Long-term care in IEI extends well beyond infection surveillance. Serial assessment of lymphocyte subsets, immunoglobulin levels, and vaccine responsiveness provides actionable data on immune recovery or decline, particularly after HSCT or gene therapy. Organ-specific monitoring, such as pulmonary function tests for chronic lung disease or liver imaging for nodular regenerative hyperplasia, can detect complications before they become

irreversible. Equally important is structured surveillance for autoimmunity and malignancy, now leading causes of morbidity in survivors.

Management of secondary immunodeficiencies

Secondary immune deficiencies, arising from human immunodeficiency virus infection, malignancy, protein loss, or iatrogenic immunosuppression, require treatment of the underlying cause when possible. In selected cases, immunoglobulin replacement or prophylactic antimicrobials may be indicated. As the use of biologics and targeted anticancer therapies expands, awareness of associated immune deficits and appropriate mitigation strategies is increasingly important [7].

SPECIFIC TREATMENT MODALITIES

Immunoglobulin replacement therapy

Immunoglobulin replacement remains the standard of care for patients with significant antibody deficiencies, including X-linked agammaglobulinemia and common variable immunodeficiency (CVID). Both intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG) routes are effective for infection prevention and quality-of-life improvement [8]. However, as the spectrum of IEI manifestations widens, it is important to remember that many disease manifestations, such as inflammatory bowel disease-like symptoms and interstitial lung disease, are unaffected by immunoglobulin replacement.

Dosing is based on trough IgG levels and clinical response, with typical replacement doses ranging from 400–800 mg/kg monthly for IVIG or 100–150 mg/kg weekly for SCIG.

Adverse effects are generally mild but include headache, infusion reactions, and, rarely, thromboembolic events or renal dysfunction. Novel formulations with facilitated subcutaneous delivery and higher concentrations have improved convenience and adherence [8].

Hematopoietic stem cell transplantation

HSCT remains the only curative option for many severe primary immunodeficiencies, including most forms of severe combined immunodeficiency (SCID), Wiskott–Aldrich syndrome, and chronic granulomatous disease.

CURATIVE TREATMENT WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION IS WARRANTED FOR SEVERE INBORN ERRORS OF IMMUNITY, AND THE SOONER IT IS PERFORMED, THE BETTER.

The cardinal rule of HSCT in primary immunodeficiencies is the earlier, the better. Newborn screening programs for T-cell defects, primarily but not exclusively SCID, now enable HSCT within mere months of birth, with much greater success rates. Advances in donor selection, conditioning regimens, and graft manipulation have also markedly improved survival. Reduced-intensity conditioning and haploidentical transplantation protocols have expanded eligibility to patients lacking matched donors. Post-transplant immune reconstitution should be carefully monitored, and complications

such as graft-versus-host disease require prompt management. Long-term outcomes are generally excellent when transplantation is performed early in life, before irreversible infections or organ damage occur [9].

HSCT in adult IEI patients, once considered almost taboo due to poor outcomes, has improved significantly in recent years and is now a viable option for selected cases with poor prognosis on conservative therapy. Better understanding of the natural history of specific IEI and advances in transplant practice continue to improve success rates [10].

Gene therapy has emerged as a transformative approach for monogenic immune deficiencies. Early trials using γ -retroviral vectors for adenosine deaminase (ADA)-SCID and X-linked SCID established proof of concept but were complicated by insertional mutagenesis. Despite these challenges, γ -retroviral gene therapy for ADA-SCID ultimately led to the regulatory approval of Strimvelis. Subsequently, the development of self-inactivating lentiviral vectors substantially improved the safety profile while maintaining high efficacy, resulting in several additional gene therapy products receiving regulatory approval.

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GENE THERAPY IS EMERGING AS A POSSIBLE REPLACEMENT FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SELECTED CASES.

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Targeted biologic and small-molecule therapies

As understanding of immune signaling pathways deepens, targeted immunomodulation has become increasingly important. In many immune dysregulation syndromes, overactivation of T or B cells leads to autoimmune manifestations and must be curtailed.

Autoimmunity driven by autoantibodies, such as refractory cytopenias in CVID, sometimes warrant B-cell

depletion with monoclonal antibodies targeting CD20 (e.g., rituximab), CD19 (e.g., inebilizumab), or CD38 (e.g., daratumumab). The use of these agents often requires concurrent immunoglobulin replacement therapy due to iatrogenic hypogammaglobulinemia. This therapy is even used in cases where the original IEI does not include a humoral defect [11].

For an expanding spectrum of inborn errors of immunity, pathway-specific therapies are now available that directly modulate the underlying defect. These targeted approaches mitigate immune over-activation while avoiding the profound immunosuppression associated with prolonged corticosteroid use or hematopoietic stem cell transplantation.

CTLA-4 haploinsufficiency, LRBA deficiency, and DEF6 deficiency are disorders of immune regulation characterized by impaired checkpoint signaling, leading to uncontrolled lymphocyte activation, autoimmunity, and lymphoproliferation. Abatacept, a CTLA-4-Ig fusion protein, restores inhibitory signaling by competing with CD28 for binding to CD80/CD86 on antigen-presenting cells [12]. Clinical experience has shown that abatacept can reduce autoimmune cytopenias, enteropathy, and lymphoproliferation in these patients, offering a rational, mechanism-based therapy.

Gain-of-function mutations in STAT1 and STAT3 lead to hyperactive cytokine signaling, resulting in chronic mucocutaneous candidiasis (in STAT1 GOF), autoimmunity, and lymphoproliferation. Janus kinase (JAK) inhibitors block upstream JAK activity, thereby dampening excessive STAT phosphorylation and downstream transcriptional activity. Clinical reports demonstrate that JAK inhibition can ameliorate autoimmunity, improve fungal control, and normalize inflammatory markers in affected patients [13].

Activated PI3K δ syndrome is caused by gain-of-function mutations in *PIK3CD* or *PIK3R1*, leading to hyperactivation of the PI3K-AKT-mTOR pathway. Patients present with recurrent infections, lymphoproliferation, and autoimmunity. mTOR inhibitors have been successfully used by dampening downstream signaling [14]. More recently, leniolisib, a selective inhibitor of the PI3K δ enzyme, was approved by the U.S. Food and Drug Administration (FDA) as a treatment to address the root cause of the disorder. Leniolisib treatment showed promising clinical benefits [15].

Dysregulated complement activation has emerged as a therapeutic target in a subset of IEI characterized

by excessive complement-mediated inflammation and tissue injury. Complement inhibitors, such as the anti-C5 monoclonal antibody eculizumab, block terminal complement activation by preventing C5 cleavage and subsequent membrane attack complex formation. Clinical experience in selected complement-driven disorders has demonstrated the potential of complement blockade to ameliorate inflammatory manifestations. As complement dysregulation in IEI continues to be elucidated, therapies targeting different components of the complement cascade may represent an expanding approach for patients with complement-mediated immune pathology [16].

EMERGING AND EXPERIMENTAL THERAPIES

The rapid pace of innovation in immunology and genetics continues to generate new therapeutic possibilities for immune deficiencies. Most of these therapies remain experimental, but early results suggest immune deficiencies may be corrected at their molecular roots rather than managed symptomatically.

Engineered T cells from induced pluripotent stem cells

Patient-derived induced pluripotent stem cells (iPSCs) can be differentiated into antigen-specific T cells engineered with defined T cell receptors or chimeric antigen receptors, offering a renewable source of antigen specific lymphocytes for IEI patients when faced with chronic viral infections such as cytomegalovirus and adenovirus. While still in the early stages and limited in scope, iPSCs could provide immune protection against important pathogens until the patient undergoes corrective HSCT [17].

Gene and base editing for precision correction

Gene editing technologies such as CRISPR-Cas9 offer the potential for precise correction of disease-causing mutations at their native loci, preserving endogenous regulation. Ongoing trials are exploring applications in SCID variants, chronic granulomatous disease, and Wiskott-Aldrich syndrome. Challenges include ensuring durable engraftment of corrected stem cells, manufacturing scalability, and cost [18,19]. Base editing enables single-nucleotide correction without double-strand breaks, making it especially relevant for monogenic IEI caused by point mutations in genes like *STAT1* or *STAT3*. Pre-clinical studies show promising accuracy and safety compared to CRISPR-Cas9 [20].

**PRECISE GENETIC DIAGNOSIS IS
IMPERATIVE AS THE TOOLBOX OF
DISEASE-SPECIFIC TREATMENTS GROWS.**

Thymus transplant

Thymus transplantation has been attempted since the late 1970s for congenital athymia, but early efforts rarely achieved durable immune reconstitution. More recent protocols, particularly for complete DiGeorge anomaly and FOXP1 deficiency, have shown improved long-term survival and functional T-cell recovery. A distinct regenerative approach was introduced with Rethymic, an allogeneic cultured thymus tissue therapy approved by the U.S. FDA in 2021 for patients with congenital athymia. Together, these advances have transformed thymus transplantation from an experimental procedure into a clinically established treatment for selected patients with congenital athymia [21].

Autologous stem cell-derived immune reconstitution

Genetically corrected autologous hematopoietic stem cells can be reinfused to bypass donor HSCT limitations, avoiding graft-versus-host disease and donor scarcity. Lentiviral and CRISPR-based platforms show encouraging early results in ADA-SCID, X-linked SCID, and X-CGD [22].

Cellular therapies

Engineered immune cell products, including virus-specific T cells, CAR-T cells, and regulatory T-cell infusions, aim to provide functional immunity or tolerance in ICI. These strategies remain experimental but represent a shift toward precision cellular interventions [23,24].

Microbiome modulation

Targeted probiotics, fecal microbiota transplantation, and engineered microbial consortia are being explored to correct dysbiosis in ICI. Animal models suggest benefits for inflammation and mucosal immunity, although translation to human care requires careful validation [25].

CONCLUSIONS

The purpose of this review was not to list all novel ICI therapies in existence. Such a list would be too long to remember by heart and outdated as soon as it would be released. Rather, the point was to reiterate the basic tenets of ICI treatment and to reflect the giant leaps in the field in mere decades.

The management of immune deficiencies has evolved from generic, one-size-fits-all infection prevention and supportive care toward precision and potentially curative therapies. Advances in transplantation, gene therapy, and targeted biologics have dramatically improved survival and quality of life for many patients who once faced fatal outcomes.

These successes highlight new challenges, such as ensuring long-term safety, affordability, and global accessibility of advanced treatments.

In the future, the practice of immunology will demand not only technical expertise but also imagination and adaptability. The expanding repertoire of therapies for ICI calls for clinicians who can chart individualized paths, embrace discoveries as part of daily care, and anticipate the evolving needs of their patients. Ultimately, the future challenge lies in translating innovation into sustained well-being, making the promise of modern immunology a reality for patients worldwide.

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References

1. Bruton OC. Agammaglobulinemia. *Pediatrics* 1952; 9 (6): 722-8.
2. Perez E. Future of therapy for inborn errors of immunity. *Clin Rev Allergy Immunol* 2022; 63 (1): 75-89.
3. Notarangelo LD, Bacchetta R, Casanova JL, Su HC. Human inborn errors of immunity: an expanding universe. *Sci Immunol* 2020; 5 (49): eabb1662.
4. IJspeert H, Edwards ESJ, O'Hehir RE, Dalm VASH, van Zelm MC. Update on inborn errors of immunity. *J Allergy Clin Immunol* 2025; 155 (3): 740-51.
5. Yao Z, Kido T, Hosaka S, et al. Infection prevention in patients with inborn errors of immunity: Insights from Japan's nationwide study. *Pediatr Int* 2025; 67 (1): e70093.
6. Kuruvilla M, de la Morena MT. Antibiotic prophylaxis in primary immune deficiency disorders. *J Allergy Clin Immunol Pract* 2013; 1 (6): 573-82.
7. Otani IM, Lehman HK, Jongco AM, et al. Practical guidance for the diagnosis and management of secondary hypogammaglobulinemia: A Work Group Report of the AAAAI Primary Immunodeficiency and Altered Immune Response Committees. *J Allergy Clin Immunol* 2022; 149 (5): 1525-60.
8. Sil A, Basu S, Joshi V, et al. Immunoglobulin replacement therapies in inborn errors of immunity: a review. *Front Pediatr* 2024; 12: 1368755.
9. Anchoo C, Lev A, Simon AJ, et al. Outcome of hematopoietic stem cell transplantation for severe combined immunodeficiency and impact of newborn screening on overall survival: a single referral center study. *J Allergy Clin Immunol* 2025; 155 (6): 1800-12.
10. Burns SO, Morris Emma C. How I use allogeneic HSCT for adults with inborn errors of immunity. *Blood* 2021; 138 (18): 1666-76.
11. Elmoursi A, Barmettler S. Therapeutic B-cell depletion: mechanisms, clinical applications, and implications for secondary immunodeficiency. *J Allergy Clin Immunol* 2025; 156 (3): 597-603.

12. Lo B, Zhang K, Lu W, et al. Patients with LRBA deficiency show CTLA4 loss and immune dysregulation responsive to abatacept therapy. *Science* (1979). 2015 Jul 24; 349 (6246): 436-40.
13. Fischer M, Olbrich P, Hadjadj J, et al. JAK inhibitor treatment for inborn errors of JAK/STAT signaling: an ESID/EBMT-IEWP retrospective study. *J Allergy Clin Immunol* 2024; 153 (1): 275-286.e18.
14. Coulter TI, Cant AJ. The treatment of activated PI3K δ syndrome. *Front Immunol* 2018; 9: 2043.
15. Rao VK, Webster S, Annašediv AA, et al. A randomized, placebo-controlled phase 3 trial of the PI3K δ inhibitor leniolisib for activated PI3K δ syndrome. *Blood* 2023; 141 (9): 971-83.
16. Brodzski N, Frazer-Abel A, Grumach AS, et al. European Society for Immunodeficiencies (ESID) and European Reference Network on Rare Primary Immunodeficiency, Autoinflammatory and Autoimmune Diseases (ERN RITA) Complement Guideline: Deficiencies, Diagnosis, and Management. *J Clin Immunol* 2020; 40 (4): 576-91.
17. Netsrithong R, Garcia-Perez L, Themeli M. Engineered T cells from induced pluripotent stem cells: from research towards clinical implementation. *Front Immunol* 2024; 14: 1325209.
18. Fischer A. Gene therapy for inborn errors of immunity: past, present and future. *Nat Rev Immunol* 2023; 23 (6): 397-408.
19. Torrance R, Orf K, Fox TA. Gene therapy for inborn errors of immunity: past progress, current status and future directions. *Rare Dis Orphan Drug J* 2025; 4 (4): rdodj.2025.42.
20. McIvor RS, Eaton EJ, Webber BR, Moriarity BS. Advancing gene targeting for primary immune deficiencies: Adenine base editing of the human IL2RG locus for correction of SCID-X1. *Mol Ther* 2024; 32 (6): 1606-8.
21. Kreins AY, Bonfanti P, Davies EG. Current and future therapeutic approaches for thymic stromal cell defects. *Front Immunol* 2021; 12: 655354.
22. Kohn LA, Kohn DB. Gene therapies for primary immune deficiencies. *Front Immunol* 2021; 12: 648951.
23. Keller MD, Bollard CM. Virus-specific T-cell therapies for patients with primary immune deficiency. *Blood* 2020; 135 (9): 620-8.
24. Bluestone JA, Burnett BK, Crute CE, et al. Regulatory T cell therapies to treat autoimmune diseases and transplant rejection. *Nat Immunol* 2025; 26 (6): 819-24.
25. Cortés M, Olate P, Rodriguez R, et al. Human microbiome as an immunoregulatory axis: mechanisms, dysbiosis, and therapeutic modulation. *Microorganisms* 2025; 13 (9): 2147.

Live your life as an experiment.

Pema Chödrön (Born 1936), American-born Tibetan Buddhist

Capsule

Immediate ambulatory electrocardiographic monitoring in syncope

In a randomized ASPIRED trial, **Reed** and colleagues investigated whether immediate ambulatory ECG monitoring improves the diagnostic evaluation of patients presenting with unexplained syncope. Early monitoring substantially increased the detection of clinically important arrhythmias compared with conventional diagnostic pathways and shortened the time to diagnosis.

Earlier rhythm identification allowed faster initiation of appropriate therapy, including pacemaker implantation or antiarrhythmic treatment when indicated. The findings support early ambulatory ECG monitoring as a valuable first-line strategy for patients with unexplained syncope.

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Eitan Israeli

Capsule

Ovoporexton for narcolepsy type 1: results from two phase 3 trials

Dauvilliers and colleagues evaluated ovoporexton (TAK-861), an oral selective orexin receptor-2 agonist designed to address the underlying orexin deficiency in narcolepsy type 1. Two randomized, placebo-controlled phase 3 trials: First Light and Radiant Light included 168 and 105 participants, respectively. Patients aged 16–70 years received twice-daily ovoporexton (1 or 2 mg) or placebo for 12 weeks. The primary outcome was the change in mean sleep latency on the Maintenance of Wakefulness Test (MWT). Ovoporexton increased MWT sleep latency by 14.3–19.8 minutes, versus changes of -0.4 to -0.8 minutes with placebo ($P < 0.001$). Epworth Sleepiness Scale scores improved by 9.7–11.8 points, compared

with only 1.5–1.7 points with placebo. Weekly cataplexy frequency decreased by 79.0–88.8%, versus 27.7–39.1% with placebo. Both objective wakefulness and subjective daytime sleepiness improved substantially. Adverse events occurred in 86–89% of ovoporexton recipients versus 43–54% receiving placebo. The most frequent adverse effects were increased urinary frequency and transient insomnia. These trials provide strong evidence that direct restoration of orexin signaling can improve several core manifestations of narcolepsy type 1.

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Eitan Israeli