Beqalzi (Sonrotoclax) FDA Approval: BCL-2 Inhibitor for MCL

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Executive Summary

Beqalzi (generic name **sonrotoclax**) is a novel, *next-generation* BCL-2 inhibitor that earned accelerated FDA approval on May 13, 2026 for adult patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two prior therapies including a Bruton's tyrosine kinase inhibitor (BTKi) ([1] www.fda.gov) ([2] www.nasdaq.com). This represents the **first and only FDA-approved BCL-2 inhibitor for MCL** ([3] www.fiercepharma.com) (venetoclax, the prior first-in-class BCL-2 inhibitor, had been used only off-label in MCL). In its pivotal Phase 1/2 trial (BGB-11417-201), sonrotoclax monotherapy produced an overall response rate (ORR) of 52% (95% CI 42–62%) and a median duration of response (DOR) of 15.8 months ([4] www.fda.gov) ([5] www.nasdaq.com). The drug's design emphasizes *greater potency and selectivity* than venetoclax, with preclinical studies showing roughly **14-fold higher potency** and **6-fold greater BCL-2 selectivity** ([6] www.fiercepharma.com). Moreover, sonrotoclax has a **shorter systemic half-life** than venetoclax (enabling easier dose ramp-up and reduced tumor-lysis monitoring) ([7] www.fiercepharma.com) ([8] www.onclive.com). Clinicians and advocacy groups herald the approval as a significant advance: for example, MD Anderson's Michael Wang, M.D., praised sonrotoclax's ability to deliver "robust disease control" where options were scarce ([9] www.nasdaq.com), and the Lymphoma Research Foundation's CEO called it "significant progress…offering renewed hope" to MCL patients ([10] www.nasdaq.com).

This report provides an in-depth analysis of Beqalzi/sonrotoclax: its discovery and clinical development (including trial results and safety profile), the regulatory milestones (FDA accelerated approval and global status), and its projected role in the hematologic oncology landscape. We compare sonrotoclax to existing therapies—especially venetoclax ("Venclexta")—and outline BeOne Medicines' ambition to challenge venetoclax's dominance. We also examine the broader implications for treatment sequencing in MCL, the dynamics of the BCL-2 inhibitor class, and potential future applications (such as in CLL, Waldenström's, etc.) ([11] www.fiercepharma.com) ([12] www.marketscreener.com). This analysis incorporates clinical data, expert commentary, patient-impact perspectives, and market context to form a comprehensive picture of Beqalzi's promise and challenges.

Introduction and Background

Mantle cell lymphoma (MCL) is a rare, aggressive subtype of non-Hodgkin lymphoma arising from B cells in the mantle zone of lymph nodes. It typically harbors the t(11;14) translocation, leading to cyclin D1 overexpression and dysregulated proliferation. MCL accounts for roughly 5% of NHL cases worldwide, with about 3,300 new cases diagnosed annually in the U.S. ([13] www.nasdaq.com) ([14] www.marketscreener.com). Globally, an estimated ~28,000 people have MCL ([14] www.marketscreener.com). Unlike indolent lymphomas, MCL often presents at an advanced stage and follows a relapsing course. First-line regimens (e.g. chemoimmunotherapy, sometimes with consolidative autologous stem-cell transplant in younger patients) commonly induce remissions, but relapses are expected. Five-year survival rates hover around 50% ([14] www.marketscreener.com), underscoring the unmet need for effective salvage treatments as the disease evolves.

Current management of R/R MCL usually involves agents with targeted mechanisms, reflecting the paradigm that alternating modes of action may improve outcomes. Bruton's tyrosine kinase inhibitors (BTKi) such as ibrutinib (Imbruvica) and acalabrutinib (Calquence) markedly improved outcomes in the post-chemotherapy setting ([15] www.fiercepharma.com). The first CAR T-cell therapy for MCL, brexucabtagene autoleucel (TECARTUS), was FDA-approved in 2020 for relapsed disease after ≥1 prior therapy, achieving high response rates (e.g. ZUMA-2 trial: CR ~67%, ORR ~93% ([16] www.onclive.com)). Nonetheless, a significant fraction of patients either cannot access or eventually progress after CAR-T or BTKi therapy. Waldenström's macroglobulinemia, chronic lymphocytic leukemia (CLL), and other B-cell malignancies overlap therapeutically with MCL. BCL-2 family proteins, key regulators of apoptosis, have emerged as attractive targets across these cancers. In particular, BCL-2 overexpression (anti-apoptotic "guardian" of cells) is common in B-cell cancers, enabling malignant cells to survive. Thus, pharmacologic inhibitors of BCL-2 ("BH3 mimetics") aim to release the apoptotic brakes and induce tumor cell death.

AbbVie/Roche's venetoclax (Venclexta) validated BCL-2 as a therapeutic target. Approved in 2016–2017, venetoclax is highly effective in CLL/SLL (with or without certain chemotherapies) and acute myeloid leukemia (AML), and has since gained multiple indications ([17] www-cdn.pharnexcloud.com). Globally approved in 80+ countries ([17] www-cdn.pharnexcloud.com), venetoclax achieved blockbuster status: sales grew from ~$344 million in 2018 to over $2.0 billion in 2022 ([18] www-cdn.pharnexcloud.com). However, venetoclax was not explicitly approved for MCL, and its use in MCL had been investigational or off-label. Importantly, venetoclax has a long half-life and requires a careful multi-week ramp-up to mitigate tumor lysis syndrome (TLS) risk ([7] www.fiercepharma.com). These PK and safety considerations, along with occasional resistance development, have constrained its convenience and broad use.

BeOne Medicines (through its U.S. entity BeOne Medicines USA, Inc.) developed **sonrotoclax** (BGB-11417) as a "second-generation" BCL-2 inhibitor intended to build on and surpass venetoclax. Preclinical data indicated that sonrotoclax has higher potency and selectivity: in biochemical assays it demonstrated roughly 14-fold greater potency against BCL-2 and a 6-fold higher BCL-2 vs BCL-XL selectivity compared to venetoclax ([6] www.fiercepharma.com). Crucially, sonrotoclax's pharmacokinetics feature a **shorter half-life** and no evidence of accrual, meaning dose escalation should be easier and TLS management simplified ([7] www.fiercepharma.com). These characteristics promise greater convenience and a potentially better safety profile (especially less prolonged cytopenia or risk of TLS) than venetoclax, which historically required inpatient observation during ramp-up ([7] www.fiercepharma.com).

The development program for sonrotoclax has spanned multiple hematologic malignancies. In December 2025, data from a Phase 1/2 study in R/R MCL (after BTKi) were presented at ASH ([19] www.onclive.com). These results formed the basis of the FDA submission, and were also filed with Chinese regulators. In fact, sonrotoclax gained "first-in-world" approval in China on January 6, 2026 for R/R MCL and for R/R CLL/SLL ([20] www.marketscreener.com). The U.S. FDA granted Breakthrough Therapy, Fast Track, and Orphan Drug designations to sonrotoclax in MCL. The May 2026 accelerated approval in the U.S. was conducted under Project Orbis (international review collaboration) ([21] www.fda.gov). Continued approval for MCL will require confirmatory evidence, e.g. from the ongoing Phase 3 CELESTIAL-RRMCL trial (sonrotoclax plus zanubrutinib vs zanubrutinib alone in R/R MCL, projected completion 2028) ([22] www.oncologypipeline.com).

Alongside regulatory steps, BeOne is advancing sonrotoclax in clinical trials across B-cell cancers. Notably, combination trials in chronic lymphocytic leukemia (CLL) with fixed-duration regimens (e.g. with BTKi or anti-CD20 antibodies) are underway ([23] www.oncologypipeline.com) ([24] www.nasdaq.com). Early data in front-line CLL plus zanubrutinib show extremely high rates of undetectable minimal residual disease (uMRD) – 91% at 48 weeks, rising to 98% by 96 weeks ([25] www.fiercepharma.com) – signaling that sonrotoclax could eventually rival venetoclax's dominance in CLL. Moreover, sonrotoclax is in development for Waldenström's macroglobulinemia (Phase 2), relapsed multiple myeloma (planned Phase 3 combo), and front-line CLL vs standard-of-care in Phase 3 ([26] www.oncologypipeline.com). The drug's flexible profile (oral, potent, targeted) positions it as a *foundational BCL-2 inhibitor* for BeOne's portfolio.

In summary, the FDA nod for Beqalzi/sonrotoclax updates the MCL treatment paradigm by adding a new targeted mechanism of action (MOA) option post-BTKi ([10] www.nasdaq.com). This report will examine the comprehensive evidence surrounding sonrotoclax's entry into the clinic, its performance vs. established therapies, anticipated impact on patient care, and strategic implications in oncology.

Mantle Cell Lymphoma: Epidemiology and Unmet Needs

Mantle cell lymphoma (MCL) is a distinct B-cell lymphoma historically considered incurable with standard therapies. According to the American Cancer Society, MCL incidence in the U.S. is about 3,000–4,000 cases per year – roughly 3,300 new cases annually ([13] www.nasdaq.com). Globally it comprises about 5% of non-Hodgkin lymphoma cases – on

the order of 25,000–30,000 people living with MCL ([14] www.marketscreener.com). The median age at diagnosis is in the mid-60s, with a male predominance.

MCL has a characteristic immunophenotype (CD19+, CD20+, CD5+, cyclin D1+). It can present as leukemic (circulating lymphocytes) or nodal/organ involvement. Patients often present with high tumor burden (e.g. bulky lymphadenopathy, splenomegaly, bone marrow infiltration) ([14] www.marketscreener.com). Thanks to modern therapies, many patients achieve remission after initial therapy (often combination chemoimmunotherapy, e.g. R-CHOP/R-hyperCVAD or bendamustine-R〈rituximab〉). However, despite aggressive front-line treatment (and sometimes consolidative autologous stem cell transplant for fit patients), relapse is almost inevitable. Even with novel agents, nearly all patients will eventually develop refractory or relapsed disease ([14] www.marketscreener.com).

The prognosis for relapsed MCL is generally poor. Before CAR-T, median overall survival in second-line and beyond was often measured in a couple years at best. The introduction of BTK inhibitors transformed this outlook: in relapsed MCL after chemo, ibrutinib yielded ORRs of ~68–77% and median progression-free survivals (PFS) around 13–20 months depending on the study. Acalabrutinib, a second-generation BTKi, also showed high activity (ORR ~81%, median PFS ~20 months). Pirtobrutinib (non-covalent BTKi, Jaypirca) gained accelerated approval in 2023 for R/R MCL after ≥2 prior therapies (≥1 must have been BTKi); in the pivotal ROTOR-1 trial it achieved an ORR of ~52% and median DOR ~9 months ([15] www.fiercepharma.com). Nonetheless, resistance and long-term outcomes remain suboptimal: most patients eventually progress on BTKi therapy (due to BTK binding site mutations or downstream pathway changes), and effective options after BTKi are limited.

Aside from BTK inhibitors, other approved or commonly used therapies for R/R MCL include lenalidomide (an immunomodulatory agent), bortezomib (a proteasome inhibitor), chemotherapy backbones (sometimes with bendamustine), and anti-CD20 monoclonal antibodies (rituximab-ofatumumab). The only CAR T-cell therapy, brexucabtagene autoleucel (Tecartus), has shown remarkable efficacy (in ZUMA-2, ORR ~93%, CR ~67%) even in heavily pretreated patients. However, CAR-T is logistically complex, not universally accessible, and has unique toxicities (CRES, cytopenias). Xenogeneic stem cell transplant and allo-transplant remain high-risk options for some younger patients.

In summary, post-BTKi MCL is a challenging setting. In the words of an authority in the field, “therapy choices are limited and outcomes are poor” for patients with relapsed/refractory MCL ([9] www.nasdaq.com). This dire situation has motivated the search for alternative targets. One logical target is BCL-2: MCL cells often express high BCL-2, reflecting their reduced apoptotic priming. A potent BCL-2 inhibitor could therefore drive cell death in MCL clones that have become resistant to other mechanisms. Until now, however, no BCL-2 inhibitor was formally available for MCL. Venotoclax had not been approved in this disease, rendering sonrotoclax’s FDA approval the first of its kind ([3] www.fiercepharma.com).

The BCL-2 Pathway and Inhibitors

BCL-2 (B-cell lymphoma-2) is an anti-apoptotic protein that plays a key role in the intrinsic (mitochondrial) cell death pathway ([17] www-cdn.pharnexcloud.com). Under normal physiology, BCL-2 binds and sequesters pro-apoptotic proteins like Bax and Bak, thereby preventing them from inducing mitochondrial outer membrane permeabilization. In many cancers, especially hematologic malignancies, BCL-2 is overexpressed, which helps malignant cells evade death. Targeting BCL-2 thus aims to restore the apoptotic program in cancer cells. The first drug to exploit this was *navitoclax* (ABT-263), a BCL-2 family inhibitor developed by Abbott/Lilly. Navitoclax saw clinical activity but caused dose-limiting thrombocytopenia (because it also inhibited BCL-xL, a platelet survival factor).

The breakthrough came with *venetoclax* (Venclexta), an oral BH3 mimetic developed by AbbVie/Roche that selectively binds **BCL-2** with high affinity, sparing BCL-xL ([17] www-cdn.pharnexcloud.com). Venetoclax induces apoptosis in BCL-2–dependent cells and was first approved in CLL/SLL (2016) and later in AML (2018, in combination with hypomethylating agents) ([17] www-cdn.pharnexcloud.com). It has since achieved indications in several B-cell malignancies: in CLL (including with rituximab or obinutuzumab), in SLL, in AML, and (outside USA) in Waldenström’s macroglobulinemia and multiple

myeloma contexts. Extensive clinical trials (>230 trials) have evaluated venetoclax in myriad settings ([27] www-cdn.pharnexcloud.com). As of the mid-2020s, crude numbers indicate that more than one-third of new adult leukemias/lymphomas involve BCL-2 pathway targeting.

Venetoclax's success turned it into a $2+ billion product, but it also highlighted important lessons. Because venetoclax can cause very rapid tumor cell death, careful dosing schedules were needed. In CLL, a 5-week dose ramp-up is required (starting from 20 mg daily, doubling weekly up to target dose of 400 mg daily) to minimize TLS risk. In practice, this often means frequent lab checks (electrolytes) and even inpatient care during ramp-up for high-risk patients. The high potency of venetoclax means most rapidly proliferating tumors respond with cytolysis, which is good (de-bulking) but must be managed. Additionally, venetoclax's long half-life (circa 19–26 hours at steady state) means plasma levels remain high after each dose, further increasing TLS risk ([7] www.fiercepharma.com). Common blood-related toxicities include neutropenia (up to ~40-50% in CLL trials), anemia, and thrombocytopenia. Nonetheless, intensive prophylaxis protocols (hydration, allopurinol, slow dose titration) allowed venetoclax to be safely administered across many centers.

No approved BCL-2 inhibitor besides venetoclax existed prior to 2026. Apart from the limited navitoclax, other BCL-2–targeting candidates were mostly preclinical or early-phase (e.g. APG-1252, a stapled BCL-2/BCL-XL inhibitor, was investigated in solid tumors). In China, domestic companies had been developing their own BCL-2 inhibitors (for instance, Ascentage's Lisaftoclax/APG-2575, Fosun's FCN-338), but none had entered global trials by early 2026. Thus, BeOne's sonrotoclax represents the **first next-generation BCL-2 inhibitor to reach major approvals**.

Table 1 compares key features of sonrotoclax and venetoclax:

Feature	Sonrotoclax (Beqalzi)	Venetoclax (Venclexta)
Developer/Company	BeOne Medicines (BeiGene)	AbbVie/Roche
FDA Approval (MCL)	Accelerated (May 13, 2026) for R/R MCL (post-BTKi and rituximab) ([1] www.fda.gov) ([2] www.nasdaq.com)	Not approved for MCL (used off-label)
Mechanism	Selective BCL-2 inhibitor (BH3 mimetic) ([2] www.nasdaq.com) ([28] www-cdn.pharnexcloud.com)	Selective BCL-2 inhibitor (BH3 mimetic)
Selectivity (vs BCL-XL)	~6-fold greater selectivity for BCL-2 (vs Venclexta) ([6] www.fiercepharma.com)	Benchmark (shipped; less selective to BCL-XL)
Potency	In vitro assays ~14× more potent than venetoclax ([6] www.fiercepharma.com)	Proven potent at clinical doses; reference agent
Half-life	Shorter; rapid clearance (enables easier dose titration) ([7] www.fiercepharma.com)	Long (~19–26 hr); long accumulation can prolong TLS risk
Dosing/Ramp-Up**	4-week ramp-up (to 320 mg daily) ([29] www.fda.gov)	5-week ramp-up (to 400 mg daily in CLL)
Main Indication (US)	R/R MCL after ≥2 lines (incl. BTK-inhibitor) ([1] www.fda.gov)	CLL/SLL (various settings), AML (with azacitidine), etc.
Other Approved Indications	(China: R/R CLL/SLL, ≥1 prior line) ([30] www.nasdaq.com)	CLL/SLL, AML, frontline AML (with azacitidine), etc.
Breakthrough/ Orphan	FDA Breakthrough (MCL), Orphan (MCL, AML, etc) ([31] www.nasdaq.com)	FDA Breakthrough (some combos), Orphan (for CLL etc)
Monitor/TLS Risk	Lower (due to short half-life); routine blood checks soon after dose ([7] www.fiercepharma.com)	Higher; extended observation (6–8 and 24 hr) needed during ramp-up
Major Trials / Pivotal Data	BGB-11417-201 (Phase 1/2 MCL): ORR 52%, DOR 15.8 mo ([4] www.fda.gov) ([5] www.nasdaq.com)	MCL: limited data; CLL/SLL pivotal: ORR ~92% (CLL-14, MURANO); AML: CR ~36% in Combo (VIALE-A)
Global Launch (Date)	2026 (US, China)	2016 (US) in CLL; multi-indication since, globally

Notes: Table data are drawn from FDA, press releases, and literature sources ([1] www.fda.gov) ([5] www.nasdaq.com) ([6] www.fiercepharma.com). Clinical data for venetoclax vary by trial and disease setting.

The table highlights that sonrotoclax enters with a highly competitive profile: notably, being roughly an order of magnitude more potent in vitro and having a shorter half-life should, in theory, translate to equal or better efficacy with a simpler

administration. Moreover, sonrotoclax adds MCL to BCL-2's clinical reach; this may allow vectored treatment sequences (e.g. BTKi → BCL-2i → CAR-T) that were not previously possible.

Clinical Development of Sonrotoclax (Beqalzi)

Preclinical and Early Development: Sonrotoclax's origin traces to BeiGene's medicinal chemistry efforts to "build a better venetoclax." Preclinical research demonstrated that sonrotoclax (BGB-11417) has extremely high BCL-2 binding affinity and does not accumulate significantly in plasma ([32] www.fiercepharma.com) ([33] www.nasdaq.com). Experimental models suggested it could induce apoptosis in cancer cells resistant to venetoclax (for example, cell lines harboring the G101V BCL-2 mutation that confers venetoclax resistance) ([28] www-cdn.pharnexcloud.com) ([34] pubmed.ncbi.nlm.nih.gov). These attributes justified advancing sonrotoclax into human studies.

Phase 1/2 Mantle Cell Trial (BGB-11417-201, NCT05471843): The pivotal clinical trial for FDA approval was a single-arm, multicenter Phase 1/2 study enrolling 103 adult patients with relapsed or refractory MCL. Key eligibility criteria included at least one prior anti-CD20 therapy and a BTK inhibitor (ibrutinib or acalabrutinib) ([35] www.fda.gov). The protocol used a ramp-up dosing schedule to mitigate TLS: sonrotoclax was escalated weekly to a target dose of 320 mg daily by week 5, followed by maintenance 320 mg daily until progression or unacceptable toxicity ([36] www.fda.gov).

An independent review committee (using Lugano criteria) assessed efficacy. The confirmed overall response rate (ORR) was **52%** (95% confidence interval 42–62%) ([4] www.fda.gov) ([5] www.nasdaq.com). This comprised a complete response (CR) rate of 16% ([5] www.nasdaq.com). The median time to first response was brief (~1.9 months) ([5] www.nasdaq.com). Durability was notable: at a median follow-up of 11.9 months, the median duration of response (DOR) was **15.8 months** (95% CI, 7.4–not estimable) ([4] www.fda.gov) ([5] www.nasdaq.com), indicating many responses were still ongoing. By comparison, pirtobrutinib in a similar post-BTKi MCL setting reported an ORR of ~50% and shorter median DOR (~8.3 months) ([15] www.fiercepharma.com), suggesting that sonrotoclax's anti-tumor activity was at least comparable if not more durable.

Subgroup analyses (reported in abstracts) indicated similar response rates regardless of certain high-risk features (e.g. TP53 mutation status or blastoid histology), although small numbers limit firm conclusions. Time-to-response was generally rapid, implying most responders had significant tumor burden reduction even at early evaluation.

Safety Profile: Among 115 patients evaluable for safety in the MCL trial, treatment-emergent adverse events were generally consistent with the BCL-2 class ([37] www.fda.gov) ([38] www.oncologypipeline.com). About **37%** of patients experienced serious adverse events (SAEs) ([37] www.fda.gov) ([38] www.oncologypipeline.com). The most frequent SAE was pneumonia (occurring in ~10% of patients) ([37] www.fda.gov). There were 4% fatal adverse reactions (as noted in BeOne's safety dataset), predominantly due to infections ([38] www.oncologypipeline.com). Neutropenia was common, reflecting potent myeloid suppression typical of BCL-2 inhibitors (though exact rates not yet fully disclosed). The rates of tumor lysis syndrome (TLS) appear low; the company reported it as an "important identified risk" but with only 1% actual cases in similar populations. OncLive commentary noted "a low rate of TLS" and overall moderate toxicity ([8] www.onclive.com). Sonrotoclax's shorter half-life likely contributes to this (post-dose drug levels fall more quickly, reducing sustained TLS risk).

No new safety signals emerged beyond those expected. Unlike venetoclax, sonrotoclax's label was issued **without a boxed warning** (the FDA-required warning) ([39] www.oncologypipeline.com), though it does list TLS, serious infections, and neutropenia as warnings. (By contrast, venetoclax's U.S. prescribing information includes a black-box warning for TLS.) By press time, over 2,200 patients had been treated with sonrotoclax across trials ([33] www.nasdaq.com), and no unexpected cumulative toxicity patterns were reported. Importantly, one patient in the trial died from infection while on sonrotoclax ([40] www.fiercepharma.com); BeOne has stated there were no other signals of liver damage, cardiac toxicity, or renal failure beyond what would be expected.

Table 2 (below) summarizes the key ongoing Sonrotoclax trials:

Trial Name (NCT)	Indication	Design	Status/Results
BGB-11417-201 (NCT05471843)	R/R MCL (post-BTKi & anti-CD20)	Phase 1/2, single-arm monotherapy	Primary basis for US accelerated approval (ORR 52%, DOR 15.8m) ([4] www.fda.gov)
Celestial-TNCLL (301, NCT057XXX)	1st-line CLL	Phase 3: sonrotoclax + zanubrutinib vs obinutuzumab + venetoclax	Enrollment ongoing; MRD endpoint data expected 2026, potential AA support ([41] www.oncologypipeline.com)
Celestial-203 (NCTXXXXX)	Waldenström's macroglobulinemia (WM)	Phase 2: open-label (sonrotoclax ± zanubrutinib)	Enrollment complete (Nov 2025); pending results, likely registration enabling ([26] www.oncologypipeline.com)
Celestial-RRMCL (NCT06742996)	R/R MCL (prior anti-CD20 only)	Phase 3: sonrotoclax + zanubrutinib vs zanubrutinib	Confirmatory trial for MCL (completion ~Aug 2028) ([22] www.oncologypipeline.com)
Celestial-RRCLL (NCTXXXXX)	R/R CLL/SLL (post-BTKi)	Phase 3: sonrotoclax + rituximab vs venetoclax + rituximab	Ongoing (primary completion ~Sep 2029) ([42] www.oncologypipeline.com)
Celestial-TNCLL (304, NCT057XXX)	1st-line CLL	Phase 3: sonrotoclax + zanubrutinib vs calquence + venetoclax	Started Jan 2026; MRD data by 2029 ([43] www.oncologypipeline.com)
Unnamed trial (planned)	R/R multiple myeloma	Phase 3: sonrotoclax + anti-CD38 mAb + dex	Planned H2 2026 (BeOne pipeline) ([44] www.oncologypipeline.com)
Unnamed trial (planned)	R/R CLL	Phase 3: sonrotoclax + BGB-16673 (BTK degrader) vs ?	Planned (combination with BTK degrader) ([45] www.oncologypipeline.com)

Table 2. Selected Sonrotoclax clinical trials as of mid-2026. (LN: BeOne data compiled from press release and pipeline summaries ([46] www.oncologypipeline.com) ([24] www.nasdaq.com).)

Collectively, these trials indicate that sonrotoclax is being positioned as both a monotherapy and backbone in combinations. The front-line CLL trials (Celestial-TNCLL 301/304) pit sonrotoclax + BTKi against standard regimens, signifying intent for label expansion into the far larger CLL market. The relapsed Waldenström's trial could yield a novel targeted option for that disease. The confirmatory MCL study (Celestial-RRMCL) combines sonrotoclax with zanubrutinib, reflecting an expectation that pairing the new BCL-2 inhibitor with a potent BTKi may further deepen responses.

Efficacy Outcomes and Comparative Analysis

The hallmark of accelerated approval is demonstration of a meaningful surrogate endpoint – in this case, response rate and durability – in a serious disease setting with unmet need. Sonrotoclax's Phase 1/2 data fulfilled this. The **overall response rate (ORR)** of ~52% in the MCL cohort was consistent across independent review and investigator assessments ([4] www.fda.gov). The **complete response (CR) rate** was 16% ([5] www.nasdaq.com). The **median time to response** was rapid (1.9 months) ([5] www.nasdaq.com), indicating that responders tended to show tumor shrinkage after just a couple of cycles. The **duration of response** (median 15.8 months, not diminished at data cutoff) suggests that many patients enjoyed prolonged remissions on sonrotoclax monotherapy ([4] www.fda.gov). At data cutoff, more than half of responders were still in response.

For context, the MCL patient population in this trial was heavily pretreated, had failed BTKi therapy, and had likely exhausted other targeted agents. The experience with venetoclax in MCL is limited, but historic studies suggested response rates in the range of 25–75% in smaller series, often when combined with other drugs. The purely single-agent design and robust ORR of 52% positions sonrotoclax favorably. Notably, the responses appear **durable**; median DOR of 15.8 months exceeds that seen with pirtobrutinib in a similar line of therapy (8.3 months) ([15] www.fiercepharma.com) and suggests that BCL-2 inhibition may induce longer-term control even after BTKi failure.

Also illustrative is a comparison highlighted by BeOne's CMO: sonrotoclax monotherapy in the Phase 1/2 setting achieved similar ORR but notably longer DOR than pirtobrutinib (Brukinsa's competitor). Specifically, in a head-to-head media statement, BeOne noted that pirtobrutinib's label reports ORR ~50% with median DOR ~8.3 months, whereas sonrotoclax got ORR 52% with median DOR 15.8 months in analogous patients ([15] www.fiercepharma.com). (Cross-trial

comparisons are always cautioned, but these figures suggest at least equivalence and possibly superiority in response durability.) BeOne also emphasized that physicians, when switching therapy modes, might prefer a targeted small molecule (like a BCL-2 inhibitor) over another BTKi, potentially favoring sonrotoclax in some salvage scenarios ([47] www.fiercepharma.com).

The assembled data convinced regulators that sonrotoclax provides a clinically meaningful benefit. Michael Wang, M.D. (from MD Anderson Cancer Center and Global PI on the trial) applauded that the data "confirm its role as a *foundational therapy* for mantle cell lymphoma in the post-BTK inhibitor setting," and that it "can deliver robust disease control when treatment choices are limited and outcomes are poor." ([9] www.nasdaq.com) He further noted that sonrotoclax offers physicians "an important new option grounded in both efficacy and tolerability, fundamentally changing how we think about sequencing therapy in this disease." This expert perspective highlights how the drug may shift the treatment algorithm for MCL.

From the patient viewpoint, the CEO of the Lymphoma Research Foundation stated: "For people living with relapsed or refractory mantle cell lymphoma, each progression can bring uncertainty… The FDA approval of sonrotoclax represents significant progress … offering renewed hope for patients and families who have exhausted other available therapies." ([10] www.nasdaq.com) This sentiment underscores the real-world impact – sonrotoclax gives new cause for optimism in a setting that had few good options beyond cytotoxic salvage.

Quantitatively, approximately **3300 new MCL cases** occur yearly in the U.S ([48] www.nasdaq.com). If roughly 40–50% of these patients eventually exhaust at least two lines (including BTKi), the potential U.S. label population may be on the order of a couple thousand patients per year. Globally, with 28,000 prevalent cases of MCL ([14] www.marketscreener.com), and substantial use of BTKi, sonrotoclax's addressable market in MCL is limited but significant for an orphan disease. Importantly, by being the first BCL-2 agent approved in this niche, BeOne can set pricing at a premium (akin to venetoclax's high pricing for CLL). Initial speculation suggests a cost comparable to venetoclax (which, in U.S., is roughly $18,000 per month for a 400 mg dose before discounts), though official pricing has not yet been announced (as of May 2026).

Safety and Tolerability

Sonrotoclax's safety profile largely reflects on-target effects of BCL-2 inhibition. In the MCL trial, the label lists key warnings for **tumor lysis syndrome (TLS), serious infections, and neutropenia** ([38] www.oncologypipeline.com). The ramp-up schedule (4 weeks to reach 320 mg) is designed to manage TLS risk; routine laboratory monitoring (e.g. electrolytes) is recommended around initial dosing, but prolonged hospital stays are typically unnecessary. In contrast to venetoclax's multi-week ramp in CLL (which often required patients to be observed up to 24 hours after each dose increase), sonrotoclax's shorter half-life permits a simpler monitoring scheme. Dr. Agarwal (BeOne's Hematology CMO) noted that for sonrotoclax, patients could take the drug and then have blood drawn **4 or 6 hours later** to check for TLS – a schedule far less burdensome than venetoclax's requirement of 6–8 hour and 24-hour checks after each dose escalation ([49] www.fiercepharma.com).

Indeed, in the Phase 1/2 MCL study, TLS was reported in only 1% of patients (a very low incidence). OncLive's Michael Wang remarked that sonrotoclax monotherapy was "generally well tolerated with manageable safety and a **low rate of tumor lysis syndrome**" ([8] www.onclive.com). This suggests that, with prophylaxis, sonrotoclax's TLS risk can be controlled in practice.

Hematologic toxicities were expected: nearly half of patients developed neutropenia (any grade) on venetoclax in CLL trials, and similar or slightly lower rates occurred with sonrotoclax. BeOne's reports indicate about 37% experienced Grade 3–4 neutropenia (consistent with a non-trivial but expected risk) ([38] www.oncologypipeline.com). Infectious complications were the other major concern. Approximately 37% of patients in the MCL trial had serious adverse events, the most common being pneumonia (10%) ([37] www.fda.gov). There were several treatment-related deaths: 13 of 42 total deaths in the trial were not attributed to disease progression ([50] www.fiercepharma.com), but only one death was explicitly

infection-related ([51] www.fiercepharma.com). Overall, no unexpected organ toxicities were noted. There were no signals indicating significant hepatotoxicity or cardiotoxicity distinct from class effects.

Table 3 below compares adverse event highlights for sonrotoclax versus venetoclax (in their respective trials):

Adverse Effect	Beqalzi (Sonrotoclax)	Venclexta (Venetoclax)
Tumor Lysis Syndrome	<1–2% (with ramp-up; low rate reported) ([8] www.onclive.com)	6–8% (with careful prophylaxis; can be fatal)
Serious Infections	37% of patients had SAEs (most commonly pneumonia) ([37] www.fda.gov)	Infections in ~20–30% of patients (varies by study)
Neutropenia (Grade 3/4)	~30–40% (BeOne report) ([38] www.oncologypipeline.com)	~40–50% (common in CLL trials)
Other Hematologic AEs	Anemia, thrombocytopenia (common, ~moderate)	Anemia (30-40%), thrombocytopenia (~10-15%)
Hepatotoxicity	No unusual signal reported	Elevated LFTs in some AML pts (monitor LFTs)
Black Box/TLS Warning	**No black box** (label includes TLS warning) ([38] www.oncologypipeline.com)	**Boxed warning** for TLS on label
Monitoring Requirement	Blood tests at ~4-6h post-dose during ramp	Blood tests at 6-8h and ~24h post-dose required
Fatal Reaction Rate	~4% of treated patients (mostly infections) ([38] www.oncologypipeline.com)	~2-5% (varies by series)

Table 3. Selected safety/tolerability comparisons for sonrotoclax vs venetoclax.

Overall, sonrotoclax's safety appears **comparable or modestly improved** relative to venetoclax, driven primarily by the shorter half-life and lack of severe TLS. The FDA noted that serious adverse drug reactions in MCL patients were "generally consistent" with the known class effects ([37] www.fda.gov). BeOne asserts that across all trials (2,200+ patients to date), no major new concerns have emerged. Continued pharmacovigilance and the confirmatory trial will further define long-term safety. For now, sonrotoclax's tolerability is viewed as manageable – roughly two-thirds of patients in the trial were able to remain on therapy without discontinuing for toxicity. Aminoglycosides, antiepileptics, or other drugs affecting metabolism would need caution (as with venetoclax, sonrotoclax is metabolized by CYP3A4). Finally, BeOne's communications emphasize that sonrotoclax could reduce the clinical burden: Dr. Agarwal noted that the goal is to require "probably one or two at most" monitoring visits during ramp-up in CLL – a far cry from venetoclax's typical three or more inpatient days ([11] www.fiercepharma.com).

Regulatory Status

United States (FDA): On May 13, 2026, the U.S. FDA granted *accelerated approval* to sonrotoclax (Beqalzi) for R/R MCL in adult patients after ≥2 prior lines including BTKi ([1] www.fda.gov). The label indication reads: *"Beqalzi is indicated for adult patients with relapsed or refractory mantle cell lymphoma who have received at least two prior lines of systemic therapy, including a Bruton's tyrosine kinase inhibitor."* ([52] www.drugs.com). This approval was based on the ORR and DOR endpoints from BGB-11417-201. Under accelerated approval rules, continued approval may depend on verification of clinical benefit in confirmatory trials (here, CELESTIAL-RRMCL). The recommended dosing is a four-week ramp to 320 mg daily, then 320 mg daily maintenance ([36] www.fda.gov). Physicians must monitor blood chemistries before and during initiation, consistent with TLS precautions. Notably, the FDA's announcement explicitly mentioned that the review was done via Project Orbis (an international collaboration) with the EMA as an observer ([21] www.fda.gov). The agency granted priority review and recognized sonrotoclax with Breakthrough Therapy, Fast Track, and Orphan Drug designations for MCL (and other hematologic cancers) ([53] www.fda.gov) ([54] www.nasdaq.com).

China: Sonrotoclax achieved **first-in-world approval** in the People's Republic of China on January 6, 2026 ([55] www.marketscreener.com). This Chinese approval covered two indications: (1) R/R MCL after ≥1 prior therapy including BTKi; and (2) R/R chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after ≥1 prior systemic therapy including BTKi ([20] www.marketscreener.com). The Chinese decision was based on parallel review of the same daughter Phase 1/2 study (for MCL) and a separate Phase 2 study (100 pts) for CLL/SLL ([56] www.marketscreener.com). In these

trials, ORRs were 52.4% in MCL and 77% in CLL/SLL ([57] www.marketscreener.com). BeOne described this as “first-in-world” and signaled a global strategy (awaiting FDA review, which indeed came through).

Europe (EMA and others): Sonrotoclax is under review in the European Union as of mid-2026, with submissions based on the same clinical data ([30] www.nasdaq.com). The EMA has not yet announced a decision (typical timelines would target late 2026 or early 2027). Other regions (e.g. Australia, Canada, Japan) have not had published updates by May 2026, but it is likely BeOne will seek approvals globally. The FDA’s use of Project Orbis suggests coordination is ongoing. For now, the U.S. and China approvals represent the lead regulatory markets.

Regulatory Designations: In addition to Breakthrough for MCL, the FDA has granted **Fast Track** status for sonrotoclax in Waldenström’s macroglobulinemia (reflecting the Celestial-203 trial) ([54] www.nasdaq.com). Orphan Drug status was issued for sonrotoclax in multiple indications: MCL, Waldenström’s, multiple myeloma, AML, MDS ([54] www.nasdaq.com). These designations confer various benefits (e.g. fee waivers, market exclusivity incentives). The confirmatory trial (CELESTIAL-RRMCL) is a requirement to convert accelerated approval to full approval; interim analyses or external evidence may also influence the final MCL labeling.

Competition and References: For perspective, Venclexta’s FDA approval history is useful. For instance, venetoclax’s accelerated approval in AML (as compared to trial endpoints of remission rate) and full approvals in CLL were similar processes. Sonrotoclax’s accelerated approval in MCL sets a milestone as “first BCL-2 inhibitor in MCL”. The *Drugs.com* approval history page confirms sonrotoclax’s first FDA approved date as May 13, 2026 ([58] www.drugs.com), and summarizes the label indication. ([52] www.drugs.com).

In sum, sonrotoclax’s regulatory journey was swift once data matured. FDA’s emphasis on Project Orbis and on international observation hints that both U.S. and other agencies found the evidence compelling. The company’s communications emphasize that Beqalzi is “the first new BCL2 inhibitor approved in a decade in the U.S.” ([59] www.nasdaq.com), since venetoclax’s initial approval. This suggests the door is open for a new class, of which sonrotoclax is currently the sole representative in MCL.

Comparison with Venetoclax (Venclexta) and Other Therapies

The advent of sonrotoclax naturally invites comparison with venetoclax, the incumbent BCL-2 inhibitor. Although both drugs target the same protein, their clinical contexts and pharmacology differ. Table 1 earlier outlined the high-level distinctions. Here we delve deeper:

Mechanistic and Pharmacologic Differences: Preclinical research showed sonrotoclax binds BCL-2 very potently, with roughly 14× the in vitro potency of venetoclax ([6] www.fiercepharma.com). It also is more selective (reducing off-target BCL-xL blockade). In the press release, BeOne emphasizes that sonrotoclax was “designed to enhance BCL2 inhibition – with greater potency, selectivity, and a pharmacologic profile with potential to improve efficacy, tolerability, and convenience” over other BCL-2 inhibitors ([2] www.nasdaq.com). The shorter half-life of sonrotoclax (exact numeric half-life is not public, but described as “much faster clearance” ([49] www.fiercepharma.com)) was touted as a clinical advantage. In practice, venetoclax’s long half-life forces sustained tumor lysis monitoring, while sonrotoclax’s quick drop-off allows simpler dosing checks. Importantly, as Dr. Agarwal noted, sonrotoclax could allow “next day” monitoring after dose, versus venetoclax’s prolonged 24-hour observation requirement ([49] www.fiercepharma.com).

These PK differences may translate into safety benefits. The “no box warning” on sonrotoclax underscores that the FDA did not find TLS unmanageable under the new regimen ([38] www.oncologypipeline.com). By contrast, venetoclax labels include a black-box warning for TLS, necessitating hospitalization in high-risk CLL. Both drugs carry risks of neutropenia and infections; BeOne claims that extensive patient exposure (>2,200 pts) has shown no unexpected long-term safety issues with sonrotoclax ([33] www.nasdaq.com).

Clinical Efficacy: Head-to-head efficacy in trials is lacking. The key data for venetoclax in MCL come from small studies or combination trials (often with ibrutinib or obinutuzumab). For instance, one phase 2 trial of venetoclax + ibrutinib in relapsed MCL reported CRs in 21% of patients, ORR ~71%. However, venetoclax as monotherapy in MCL was never rigorously studied or approved. Sonrotoclax's ORR 52% (monotherapy) and median DOR ~16 months ([4] www.fda.gov) stand in line with, or perhaps exceed, expectations from these small datasets. In related settings, venetoclax ORRs in CLL hover in the 90% range for certain regimens, but it's a different disease context.

Sai comparison: In CLL, venetoclax (with obinutuzumab in first-line CLL-14) had ORR 93%. Sonrotoclax's reported combinations (with BTKi) have shown surprisingly deep remissions (uMRD rates of 91–98% in early trials ([25] www.fiercepharma.com)). But those are different trial designs. It is in CLL that sonrotoclax is pitched as a direct rival: BeOne says "the real battle with Venclexta lies in CLL" ([60] www.fiercepharma.com). Their goal is to reduce monitoring visits dramatically. Early data (BGB-11417-101) suggest sonrotoclax+zanubrutinib in frontline CLL achieved >90% uMRD, a vindication of the concept ([25] www.fiercepharma.com). Whether these effects exceed venetoclax's regimen will await phase 3 readouts, but the implication is that sonrotoclax could become another option in the fixed-duration, MRD-driven CLL paradigm.

In Waldenström's macroglobulinemia, venetoclax has activity (ORR ~80% in some series) and is used off-label or in trials. Sonrotoclax's story in WM is just beginning (Phase 2 completing), but given the accelerated designation, regulators see it as potentially filling a niche (WM is a rare disease, FDA orphan). Similarly, in relapsed myeloma, venetoclax (in combination with dexamethasone) showed benefit in t(11;14) patients; sonrotoclax might be tested there too via BeOne's planned study.

Market Positioning: Venetoclax currently holds a virtual monopoly on market share among BCL-2 inhibitors. Its multi-billion dollar revenues underscore its success in CLL/AML. Sonrotoclax enters a smaller initial market (MCL, only a few thousand patients/year in the U.S.), but with exclusive status and a favorable profile, analysts expect it to command a premium. More importantly, sonrotoclax aims for label expansions into CLL/SLL and other diseases where venetoclax is already established (and possibly beyond, like AML or myeloid diseases). If approved in first-line CLL (and eventually replacing one of venetoclax's uses), sonrotoclax could tap into the much larger CLL market (over 20,000 newly diagnosed cases in U.S. annually ([14] www.marketscreener.com)). However, AbbVie has deep pockets and established habitat: it may push back competitively (for example, venetoclax is often paired with anti-CD20s like rituximab, whereas sonrotoclax has trials with zanubrutinib). Nevertheless, having a "new-for-old" competitor generally forces innovation – possibly lower prices or novel combos – benefiting patients.

Other Competitors: Beyond venetoclax, the immediate competitor in R/R MCL is not another BCL-2 inhibitor but rather alternate MOAs. As pointed out by FiercePharma, Lilly's pirtobrutinib (Jaypirca) is a competing oral agent with a different target (BTK). As of 2026, Jaypirca has an orphan label for post-BTKi MCL (based on its 2022 approval) with ORR 50% ([15] www.fiercepharma.com). Sonrotoclax enters with similar ORR but longer DOR, as noted above ([15] www.fiercepharma.com). Thus for physicians, the choice might be: after failing a BTKi, do I switch to another BTKi (pirtobrutinib) or go to a BCL-2 inhibitor (sonrotoclax)? BeOne suggests many doctors will opt for a new mechanism (as some surveys indicate "copied mechanism" often yields cross-resistance), favoring sonrotoclax in many cases ([47] www.fiercepharma.com).

Immunotherapy (CAR-T) is also competition; however, sonrotoclax offers an outpatient small-molecule approach that may be more accessible to patients who cannot do CAR-T due to comorbidities or logistics. Moreover, patients may take sequential therapies over many lines, so sonrotoclax does not preclude eventual CAR-T. On the contrary, a robust response with sonrotoclax might be able to induce remission that can carry patients toward a more curative option or at least longer survival.

BCL-2 Inhibitor Landscape: The FDA approval of sonrotoclax likely energizes interest in other BCL-2 inhibitors in development. Chromatographic/clinical research shows several agents in Phase 2/3, including: Ascentage's APG-2575 (Lisaftoclax) in Phase 3 in CLL ([61] www-cdn.pharnexcloud.com), Fosun's FCN-338 (in Phase 2), and others. Preclinical work suggests potential for pan-BCL-2 inhibitors and for agents tackling BCL-2 with resistance mutations (BeOne's own

other candidate BGB-21447 targets venetoclax-resistant mutations ([62] www-cdn.pharnexcloud.com)). The global pipeline is crowded, especially in China where many companies view BCL-2 as a lucrative and "proven" target. However, sonrotoclax's first-to-market advantage (at least initially in US and China) gives it a head start.

In summary, sonrotoclax's strengths — high potency, proven single-agent efficacy, and first approval in MCL — give it a strong footing. Its main threat is venetoclax's entrenched position, but if sonrotoclax can prove equal or superior convenience/efficacy, it will truly become a "challenger" in the BCL-2 class. ([32] www.fiercepharma.com) ([60] www.fiercepharma.com).

Case Example: Sonrotoclax in Clinical Context

To illustrate the potential impact of sonrotoclax, consider a hypothetical scenario reflecting a typical patient journey in R/R MCL. A 65-year-old man with MCL was initially treated with chemoimmunotherapy (bendamustine plus rituximab) and achieved remission. Two years later, he relapses and receives ibrutinib (a BTK inhibitor). After another remission, he relapses again on ibrutinib. At this point – R/R MCL after ≥2 lines including BTKi – historically one might offer pirtobrutinib or chemotherapy (with modest expected outcomes) or pursue clinical trial/CAR-T if available. Without an approved BCL-2 inhibitor, venetoclax might be tried off-label, but insurers might not reimburse it for MCL, and physicians have limited experience with it in this disease.

Now imagine sonrotoclax is available. The patient is started on a four-week ramp of sonrotoclax (20→40→80→160→320 mg daily). Day 1 labs show no TLS; the patient has a brief outpatient clinic blood draw 6 hours after the 160 mg dose with no abnormalities, so the ramp continues. By week 6, the patient is on 320 mg daily maintenance. At week 8 restaging scans show a >60% reduction in lymph node bulk, meeting partial response criteria. By month 4, bone marrow biopsy is negative and PET scan is clear (a CR). His response is durable; at one year he remains progression-free, with only manageable neutropenia (treated by periodic growth factor and intermittent dose holds) and no severe infections. He describes a logistical experience much simpler than his prior therapy: he did outpatient labs for ramp-up and has monthly lab checks now, without any hospitalizations for TLS.

This case aligns with trial data: in BGB-11417-201, over half of patients responded and many remained in response at ~one year ([4] www.fda.gov). Dr. Wang's observation ("robust disease control when…outcomes are poor" ([9] www.nasdaq.com)) is exemplified here. The patient's 1-year progression-free interval (~12 months) matches the trial's median DOR (~15.8 months) ([4] www.fda.gov). Without sonrotoclax, such a patient might have expected a few months of survival; with sonrotoclax, he has a durable remission (potentially prolonging life and quality of life). Of course, each patient varies, but this hypothetical reflects the *potential* difference sonrotoclax makes in clinical practice.

Another illustrative angle is therapy sequencing. Before sonrotoclax, a physician might have considered continuing BTKi therapy (e.g. switching ibrutinib to acalabrutinib) or high-intensity chemotherapy (e.g. high-dose methotrexate/cytarabine) for second relapse. Sonrotoclax offers a non-chemotherapy target switch. As Dr. Agarwal suggested, many doctors "prefer to switch mechanism of action" after BTK failure ([47] www.fiercepharma.com). In practice, this patient "Switched" from a BTK-targeted agent to a BCL-2 inhibitor, a strategy not available prior.

Such case examples, though anecdotal, are supported by the trial evidence and expert commentary ([47] www.fiercepharma.com) ([8] www.onclive.com). They underscore that sonrotoclax can fill a critical gap: it is effective enough to put patients into remission, and safe enough to be feasible, after exhausting other targeted options.

Implications and Future Directions

Patient Care Impact: In the immediate term, Beqalzi offers a new line of defense for MCL after standard therapies fail ([10] www.nasdaq.com). For oncologists, it adds a targeted oral option akin to the well-known venetoclax, which may improve patient acceptance. The easier management (shorter ramp, less TLS monitoring) should reduce treatment

burden. For patients and families, the psychological effect – “renewed hope” as phrased by the Lymphoma Research Foundation ([10] www.nasdaq.com) – can be significant, given the emotional toll of few alternatives. Over time, routine incorporation of sonrotoclax may shift MCL treatment guidelines: for example, NCCN guidelines will likely include it as a standard option in third-line.

Clinical Sequencing: One open question is where sonrotoclax will fit relative to other therapies. Possibilities include: (a) after ibrutinib and rituximab (as studied); (b) after any BTKi (ibrutinib, acalabrutinib, or zanubrutinib); © possibly even before CAR-T in patients who are transplant-eligible. If sonrotoclax proves highly effective, some clinicians might delay CAR-T until later, using the ease of oral therapy first. Conversely, patients not eligible for CAR-T will have a strong new option. How to sequence BCL-2 with other therapies (e.g. should venetoclax ever be used after sonrotoclax fails, or vice versa?) will require clinical judgement and future studies. For now, switching from BTK inhibition to BCL-2 inhibition is an obvious shift given available data.

Broader Oncology Landscape: The BCL-2 class just became more vibrant. Other companies developing BCL-2 inhibitors will accelerate efforts to prove themselves against venetoclax and now sonrotoclax. In the near term, BeOne will focus on demonstrating sonrotoclax’s value in CLL (the “real battle” described by Agarwal ([60] www.fiercepharma.com)). By showing that sonrotoclax can achieve deep remissions with minimal monitoring, BeOne hopes to carve out a niche even in diseases where venetoclax is entrenched. The blitz of upcoming data (e.g. Celestial-TNCLL results, likely by late 2026) will clarify sonrotoclax’s candidacy in CLL. If successful, it might compete in first-line CLL, at which point venetoclax might feel pressure.

BeOne’s strategy of combining sonrotoclax with its own Bruton’s-targeted agents (zanubrutinib, the BTK degrader BGB-16673) reflects the modern paradigm of targeted therapy cocktails. The initial “foundation therapy” concept suggests that sonrotoclax is envisioned as a backbone that can synergize with many other agents. For instance, in Waldenström’s, a disease often driven by MYD88/NF-κB and reliant on BCL-2 for cell survival, adding sonrotoclax to zanubrutinib (a potent BTK inhibitor) could produce exceptional responses – an approach now being tested ([24] www.nasdaq.com).

Market Forecasts: While detailed market research is proprietary, one can estimate that the new MCL indication will yield modest revenue initially (given the small patient population), but approvals in larger diseases could multiply sales. If sonrotoclax gains in CLL, even capturing a fraction of the CLL population would equate to thousands more patients. By comparison, venetoclax’s revenue nearly doubled year-over-year in the early ’20s ([18] www-cdn.pharnexcloud.com) as indications expanded. BeOne is a much smaller company than AbbVie, but with nimble management (it splits time between California, Switzerland, China) and partnerships (BeOne USA, formerly BeiGene USA), it has global reach. The company’s stock and investor communications have likely positioned sonrotoclax approval as a crucial value inflection, which might drive additional investment into both the drug’s rollout and ongoing trials.

Healthcare System Impact: BeOne will need to expand manufacturing to meet demand. The company’s press release highlights a new biologics facility in New Jersey (though sonrotoclax is a small molecule, not biologic) ([63] www.nasdaq.com), suggesting they are scaling up capacity. Insurers and health systems will evaluate cost-effectiveness. Given the orphan drug status and lack of alternatives, sonrotoclax may be reimbursed at a premium price. Any negotiations will consider the drug’s high response rate and duration relative to prior therapies. Health economic studies will join for refractory populations where survival is short without targeted therapy.

Research Directions: The approval of sonrotoclax likely prompts new research questions. For example, what resistance mechanisms might emerge? Some patients inevitably relapse on venetoclax due to mutations (e.g. BCL-2 G101V, P53 co-mutations). Will sonrotoclax face the same mutations, or are different clones dominant? BeOne’s pipeline includes a BGB-21447 that targets some resistant BCL-2 mutants (currently Phase 1), suggesting preemptive thinking about resistance ([28] www-cdn.pharnexcloud.com).

Additionally, researchers will investigate optimal combination partners. The synergy between BCL-2 and BTK inhibitors is mechanistically plausible; BTKi kills some MCL clones while BCL-2 inhibitors mop up others. Data from ASH 2025 and upcoming ASCO 2026 on zanubrutinib+sonrotoclax showed deep MRD remissions in CLL, hinting that sequential or

concurrent use of these might one day become standard. Other combo trials (e.g. with CD20 antibodies, lenalidomide, PI3K inhibitors) might emerge.

Finally, long-term follow-up will show whether sonrotoclax monotherapy truly prolongs survival. Accelerated approval is based on response, but convincing overall survival (OS) data or PFS would cement its benefit. The confirmatory CELESTIAL-RRMCL trial may provide a comparative outcome (vs zanubrutinib alone) to quantify survival gain. If that shows a significant PFS improvement, a full approval will likely follow.

Conclusion

The FDA's accelerated approval of **Beqalzi (sonrotoclax)** on May 13, 2026 heralds a new chapter in mantle cell lymphoma therapy: for the first time, patients have an FDA-sanctioned BCL-2 inhibitor to deploy in this aggressive disease. Sonrotoclax's approval is built on solid clinical evidence of efficacy (ORR 52%, median DOR ~16 months) and a manageable safety profile ([4] www.fda.gov) ([8] www.onclive.com). It complements existing options (BTK inhibitors, CAR-T) by introducing a distinct mechanism. Its design improvements over venetoclax (greater potency, shorter half-life) promise enhanced convenience and potentially broader applicability.

From a broader oncology perspective, sonrotoclax positions BeOne Medicines as a rising challenger in the BCL-2 inhibitor class. With blockbuster-like ambitions, BeOne aims to leverage this first victory in MCL to pursue larger markets in CLL, WM, and beyond. The initial data in CLL are striking, and forthcoming trial results will test whether sonrotoclax can indeed "reshape the BCL-2 landscape" ([64] www.fiercepharma.com) that has been dominated by venetoclax.

The **promise** of sonrotoclax is that it provides a new option for patients and physicians grappling with relapsed MCL, potentially leading to longer remissions and better quality of life. Early signs – expert endorsements, patient advocacy support, and rapid regulatory green lights in the U.S. and China – all underscore the **significance** of this advance ([10] www.nasdaq.com) ([32] www.fiercepharma.com). As with any new therapy, caution and critical follow-up will be required: confirmatory trials must verify real-world benefit, long-term follow-up must confirm safety, and cost/access issues must be managed.

Nevertheless, in an area of need, Beqalzi appears poised to make a marked difference. In the words of one clinician, it "fundamentally changes how we think about sequencing therapy" in MCL ([9] www.nasdaq.com). Researchers, oncologists, and patients alike will watch closely as sonrotoclax moves from approval to practice, and as its story continues – perhaps all the way to challenging venetoclax's throne in the broad realm of B-cell cancers.

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