Supplemental Table 1: Dose Escalation Schedule

Dose Level	Minimum Number of Subjects	Efatutazone Dose	Paclitaxel Dose
-1 ^a	3	0.10 mg every 12 hours	135 mg/m ² IV over 3 hours once every 3 weeks
1a ^b	3	0.15 mg every 12 hours	135 mg/m ² IV over 3 hours once every 3 weeks
1b ^b		0.15 mg every 12 hours	175 mg/m ² IV over 3 hours once every 3 weeks
2	3	0.30 mg every 12 hours	175 mg/m ² IV over 3 hours once every 3 weeks
3	3	0.50 mg every 12 hours	175 mg/m ² IV over 3 hours once every 3 weeks

Abbreviations: IV = intravenous; DLT = dose-limiting toxicity; BID = twice daily; RP2D = recommended Phase dose.

- a: Dose Level -1 is included in case unexpected DLTs occur during treatment on Dose Level 1 (starting dose level).
- b: Subjects completing 1 cycle of treatment at Dose Level 1a were treated at Dose Level 1b in the second treatment cycle. The only difference between Dose Levels 1a and 1b was the dose of paclitaxel. Three patients received only dose level 1a and four received dose 1b.

Supplemental Table 2: Instances of Edema and/or Swelling

Indication	Efatutazone (BID) Dose (mg)	CTCAE Grade
FACE EDEMA/SWELLING		
Subject 03	0.15	2
Subject 05	0.15	2
Subject 08	0.30	1
LOCALIZED EDEMA		
Subject 09	0.30	3
JOINT SWELLING		
Subject 08	0.30	1
PERIPHERAL EDEMA		
Subject 06	0.15	2
Subject 09*	0.30	1
Subject 09*	0.30	1
Subject 09*	0.30	2
Subject 05	0.15	1
Subject 13	0.30	3
Subject 15	0.30	1
Subject 16	0.30	1

^{*:} Subject 09 had 3 events of peripheral edema.

Abbreviations: CTCAE = Common Terminology Criteria for Adverse Events

Supplemental Table 3: All Treatment Emergent Adverse Events

<u>Efatutazone Dosage:</u>	0.15 mg BID (n=7)						0.30 n	ng BII) (n=6	j)	0.50 mg BID (n=2)					
Worst CTCAE Grade:	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	
	# Patients with AE Grade					# P	atients	with	AE G	rade	# Patients with AE Grade					
Subjects With Any TEAEs		3	1		2*		1	3	2				1	1		
Blood and Lymphatic System																
Disorders																
Anemia	1	2					2		1							
Leukopenia	1	1														
Lymphopenia		1														
INR/prothrombin time increased	1															
Neutrophil Count Decreased									1							
Platelet Count Decreased						1										
Gastrointestinal Disorders																
Abdominal Distension	1															
Abdominal Pain	1					1					1					
Constipation	2															
Diarrhea	1															
Dysphagia			1			1										
Nausea	1					3										
General/Administration Site																
Conditions																
Edema	3	1				1	1	2								
Fatigue	1	1				2	1	1			1	1				
Chills/Feeling Cold	1					1										
Pyrexia						1										
Infections																
Pneumonia		1						1								
Septic Shock				1												
Cellulitis							1									
Clostridial Infection							1									
Rhinitis						1										
Metabolism and Nutrition Disorders																
Weight Decreased	1					1										
Weight Increased		1				2	1									

Anorexia					1						
Hyperlipidemia	1										
Hypoalbuminemia		1				1					
Hyponatremia	1										
Hypophosphatemia	1				1						
Hypovolemia			1								
Blood creatinine increased						1					
Fluid retention					1						
Hypertriglyceridemia					1						
Hypocalcemia						1					
Musculoskeletal/Connective Tissue											
Disorders											
Arthralgia	1										
Back Pain	1	1				1					
Groin Pain	1										
Muscle Spasms/stiffness	1	1									
Joint stiffness					1						
Joint swelling					1						
Myalgia					1	1					
Neck pain					1				1		
Psychiatric Disorders											
Anxiety	1				1						
Confusional State	1										
Insomnia	1				2						
Depression					2						
Respiratory/Thoracic/Mediastinal											
Disorders											
Cough	1	1						1			
Dysphonia	1										
Throat Tightness	1										
Aspiration					1						
Dyspnea					3		1	1			
Hemoptysis					1						
Pleural Effusion					1						
Sinus Congestion					1						

Wheezing							1				
Skin and Subcutaneous Tissue											
Disorders											
Alopecia	2	1			2						
Erythema	1										
Pain Of Skin	1										
Pruritus	1										
Rash	1			1							
Swelling Face				1							
Vascular Disorders											
Hypotension					1						
Nervous System Disorders											
Dizziness				1				1			
Headache				1			1				
Hypoesthesia				1							
Neuropathy Peripheral				1	2						
Loss of consciousness									1		
Immune System Disorders											
Anaphylactic Reaction										1	